FINAL REPORT

EVIDENCE MAP OF SYSTEMATIC REVIEWS (SRS) TO INFORM THE PREVENTION, TREATMENT AND/OR HARM REDUCTION FOR ILLICIT DRUG USE

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EXECUTIVE SUMMARY

KEY FINDINGS

GUIDING QUESTION & PRIORITIZATION

- The guiding objective for this mapping exercise was to determine what systematic reviews (SRs) exist to inform the prevention, treatment and/or harm reduction for illicit drug use.
- The intent was to describe the main characteristics of these published SRs that were directly focused on relevant illicit drug interventions.

SEARCHING & STUDY SELECTION

- A total of 10,311 citations were identified from literature searching based on the primary question posed for this evidence map.
- Of these, 651 potentially relevant articles were reviewed in full text.
- A total of 124 citations describing 117 unique SRs met the inclusion criteria for the primary question.
- An additional 71 potentially relevant non-English and non French articles were also identified.

EVIDENCE MAPPING

GENERAL FINDINGS:

- Included SRs were published between 1970 and 2010 by authors from across 20 countries.
- Cochrane Reviews accounted for 40% of all included reviews.
- Several of the SRs reviewed more than one intervention (prevention, treatment and/or harms reduction).
- Overall, the majority of included SRs were assessed as moderate to high quality.

FOR PREVENTION-RELATED INTERVENTIONS (7 SRS IDENTIFIED)

- Few SRs published on prevention were identified.
- Most SRs investigated school-based drug education programs to target substance use (usually not otherwise defined).
- Two Cochrane Reviews were identified.
- Overall, prevention-related SRs were primarily assessed as moderate to high quality.

FOR TREATMENT-RELATED INTERVENTIONS (108 SRS IDENTIFIED)

- Several published SRs on treatment interventions were identified including 75 SRs that reviewed somatic interventions (pharmacological and/or other), and 61 SRs that reviewed psychosocial interventions.
- Over one quarter of SRs reported on a combination of pharmacological and psychosocial interventions.

- Agonist maintenance therapies, medications to decrease withdrawal symptoms, and pharmacological interventions to treat specific dependence were the most common somatic-pharmacological interventions.
- Acupuncture was the most frequently cited somatic-'non-pharmacological' intervention.
- General behavioural therapies, specific cognitive behavioural therapy, and motivational interviewing were the psychosocial interventions most reported.
- Several SRs did not specify the targeted illicit substance(s) under review only making general reference to illicit drug use. However, when reported, the class of opioids and morphine derivatives was most common followed by specific substance use of heroin and marijuana.
- A total of 46 Cochrane Reviews were identified.
- Overall, treatment-related SRs were primarily assessed as moderate to high quality.

For Harms Reduction-Related Interventions (20 SRs Identified)

- Of the identified SRs published on harms reduction, they primarily investigated HIV or Hepatitis C virus prevention measures, or substitution programs.
- Only one Cochrane Review was identified.
- Overall, harms reduction-related SRs were mainly assessed as moderate to high quality.

Evidence mapping is a good 'intelligence gathering exercise' for the identification of evidence pertaining to interventions for illicit drug use. The strengths of this mapping process lie in the transparent, reproducible and systematic methods used. The findings from this exercise can be used to inform priorities for research for the Institute of Neuroscience, Addiction & Mental Health's (INMHA) (and other funding agencies) by identifying areas of uncertainty and promoting the conduct of high quality relevant knowledge syntheses and/or primary studies.

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1. INTRODUCTION

According to the 2009 Canadian Alcohol and Drug Use Monitoring Survey (CADUMS),[1] an on-going general population survey of alcohol and illicit drug use among Canadians aged 15 years and older, 11.1% of Canadians used at least one of the following drugs: cannabis, cocaine or crack, speed, ecstasy, hallucinogens or heroin. The rate of past-year use of any drug was higher among men than women (15.1% versus 7.9%, respectively) and several times higher among youth 15 to 24 years of age when compared to adults 25 years and older (28.1% versus 8.1%, respectively). In addition, trend data examining illicit drug incidents and persons charged in Canada between 1977 and 2004 saw an overall increase from 1992 to 2004.[2]

According to a 2001 Canadian Auditor General report on illicit drug use, 11 federal departments and agencies spend approximately $500 million annually to address illicit drug use in Canada.[3] Moreover, the economic costs of illegal drug use relating to health care, lost productivity, property crime, and enforcement in Canada are estimated to exceed $5 billion annually.[3] Therefore, drug abuse and addiction continue to cause immeasurable costs to society.

An evidence map of systematic reviews (SRs) that address prevention, treatment and harm reduction approaches for illicit drug use was conducted for the CIHR Institute of Neuroscience, Mental Health and Addiction (INMHA). An evidence map is an overview of the available evidence underpinning a research area that describes the volume, nature, and characteristics of the available literature.[4;5] As a complement to traditional SRs, evidence maps may examine the extent, and nature of research activity; aid in determining the value of undertaking a full SR; provide a mechanism for summarizing and disseminating research findings; and serve to identify research gaps in the existing literature.[4]

OBJECTIVES

The purpose of this report was to complete a preliminary evidence map of the SRs related to the prevention, treatment and/or harm reduction approaches for illicit drug use. Given project resource constraints, the aim was to provide an initial assessment of a variety of issues related to illicit drug use from across a select group of sources in order to informing priorities for future research in this field including the conduct of SRs in this field.

The completed report provides an overview and categorization of the available literature for the following key question:

PRIMARY QUESTION: What evidence from systematic reviews (SRs) exists to inform decisions about the prevention, treatment and/or harm reduction for illicit drug use?

2. METHODS

STUDY IDENTIFICATION

SEARCH STRATEGY

An initial search for systematic reviews (SRs) related to prevention, treatment and/or harm reduction for illicit drug use was conducted. Conceptual analysis was undertaken by one information specialist, and translation of the concepts and the Boolean logic of their combinations were confirmed by a second information specialist. No limitations were placed on search terms to maximise sensitivity. Searches were initially run to March 2010. However, searches were rerun to October, 2010 in order to update the report. Searching was limited to the following databases: the Cochrane Database of Systematic Reviews (CDSR), the Database of Abstracts of Reviews of Effectiveness (DARE); Pub Med®; and The Campbell Library (database of the Campbell Collaboration). All electronic search strategies used were peer reviewed using the PEER process prior to implementation.[6] The search strategies were previously provided as a separate attachment entitled, *'Search Strategies – Phase 1: Deliverable 2'*. Adjustments were made to the search when run in other databases to account for differences in indexing. 'Grey literature' searches for potentially relevant SRs included searches of web sites of health technology assessment/evidence-based review organizations, and relevant organizations which for this project was limited to the Centre for Addiction and Mental Health (CAMH), Canadian Centre on Substance Abuse (CCSA), the Substance Abuse and Mental Health Services Administration (SAMHSA), National Institute for Drug Abuse (NIDA), Centre for Addictions Research BC (CARBC), and the American Psychiatric Association (APA).

A search for unpublished French language studies related to prevention, treatment and/or harm reduction was conducted. In order to access a listing of international agencies publishing guidelines in French, the *AGREE Collaboration* website was searched (www.agreecollaboration.org/partners). A link to the *Institute Universitaire de Medicine Sociale et Preventive* (http://www.iumsp.ch/) was scanned using the search terms "toxicomanie," "drogues," and "revue systematique." Next, we searched the website of *Health Technology Assessment International* (www.htai.org), which linked to *Switzerland's Federal Office of Public Health* (http://www.bag.admin.ch/index.html?lang=en). Additional references were found using the search terms "toxicomanie," "drogues," and "revue systematique." From HTAI, we linked to the *French National Authority for Health* (http://www.has sante.fr/portail/jcms/j_5/home).

The Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS, the Québec government agency responsible for health services and technology assessment) website (http://www.aetmis.gouv.qc.ca/site/en_agence.phtml) was searched which also linked to the *Association des centres de récidaptation en dependence du Quebec (ACRDQ)* (www.acrdq.qc.ca). Various organizations listed on ACRDQ's website were also searched, including: *Recherche et Intervention sur les Substances psychoactives (RISQ); Group de Recherche sur l'Inadaptation Psychosociale chez l'enfant* (Université de Montreal); *Programme de recherché sur la toxicomane* (Hopital Douglas); *Groupe de Recherche sur les Aspects Sociaux de la santé et de la prevention* (Université de Montreal); *Institut Suisse de prevention de l'alcolisme et autres toxicomanies (ISPA)*; *Association nationale des intervenants en toxicomanie*; *Observatoire Européen des Drogues et des toxicomanies (OEDT)*; *Observatoire*

français des drogues et des toxicomanies; and *Association Française pour la reduction des risques.*

Due to time and cost involved in translating material, only English and French language citations were included in searching and screening. Other languages were not excluded from searching but were excluded during the screening process. However, a list these non-English titles and abstracts have been provided as a separate appendix.(Appendix H)

All records were downloaded and imported into the Reference Manager software, and duplicate records were removed.

Operational Definitions Based on the Key Question

In order to ensure consistency in terminology, the following operational definitions were used for this exercise.(Table 1)

Table 1. Operational Definitions of Terms as Related to the Evidence Mapping Key Question(s)

Term	Defined
Systematic Review (SR)	For the purposes of this project, a systematic review was defined as a review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies. See also Cochrane Review.[7]
Illicit Drugs	To facilitate categorization of illicit drugs, the National Institute on Drug Abuse (NIDA) list of Commonly Abused Drugs was the drug reference selected. Please note, nicotine and alcohol were excluded. Also, 'Other Compounds' including anabolic steroids, Dextromethorphan (DXM) and inhalants were not included within the confines of this scoping exercise. (Appendix A) For a listing of the illicit drugs as per the NIDA Chart of Commonly Abused Drugs, please refer to the following:(http://www.drugabuse.gov/DrugPages/DrugsofAbuse.html).[8]
Prevention	Substance abuse prevention was defined as the promotion of constructive lifestyles and norms that discourage drug use, and may include the application of multiple strategies.[9] The term "prevention" was reserved for those interventions that occur before the initial onset of disorder, thus for 'non-users'.
Treatment	Treatment was referred to as the therapeutic process that may involve somatic and/or psychosocial interventions.[10] Such interventions may be delivered during any phase of treatment: detoxification, general treatment, & relapse-prevention. In addition, treatment may be provided across a variety of settings. Somatic interventions include pharmacological medications that offer assistance in suppressing withdrawal symptoms during detoxification, medications that help to re-establish normal brain function and to prevent relapse and diminish cravings. Somatic interventions may also include other physical interventions (e.g., acupuncture, physical activity etc.). Psychosocial interventions are those that can be delivered in many different settings using a variety of behavioural approaches.[10-12]
Harm Reduction	Harm reduction, or harm minimisation, referred to a range of pragmatic and evidence-based public health policies designed to reduce the harmful consequences associated with drug use and other high risk activities.[11;12] They include measures shown to reduce major health and social consequences.

	Examples of risk reduction measures include making clean syringes available, which has proved to reduce the risk for human immunodeficiency virus (HIV) infection and hepatitis B, or substitution treatment, which reduces crime levels in the streets.[13] Reduction of harm is a somewhat different approach from prevention, and although considered as part of treatment was considered separately for the purposes of this mapping exercise.

Eligibility Criteria

Published English & French language studies, examining relevant interventions in humans, were eligible for inclusion, as follows:

1. If citations were determined to be a SR (operationally defined as reviews that reported at least one eligibility criterion was provided, searched at least one database (with accompanying search dates), undertook quality assessment of included studies and qualitative or quantitative synthesis of the evidence).
2. If citations directly reported to investigate prevention, treatment and/or harms reduction of one or more of a commonly abused drug as charted by the National Institute on drug abuse (available at: http://www.drugabuse.gov/DrugPages/DrugsofAbuse.html, accessed Feb. 2010). Additionally, SRs that investigate reduction in harms associated with the route or mode of drug administration but not the abused drug per se (e.g. HCV and HIV infections in intravenous drug users) were also included.

Exclusion Criteria

1. Overview of reviews were excluded
2. SRs published only as books or chapters in books due to time constraints were also excluded.
3. SRs of nicotine, caffeine, anabolic steroids; inhalants/solvents; and Dextromethorphan (DXM) were not included within the confines of this mapping exercise.

The list of specific criteria used for title and abstract screening (Level 1 & 2) and full text screening (Level 3) is presented in Appendix B.

Study Selection Process

The results of the literature search were uploaded to the software program DistillerSR along with screening questions developed by the review team and any supplemental instructions. Prior to the formal screening process, a calibration exercise was undertaken to pilot and refine the screening process. The results of the literature search were assessed using a three-step process. First, bibliographic records (i.e., title, authors, key words, and abstract) were screened using a broad screening question, by one reviewer (Appendix B – Level 1). This was followed by the screening of title, authors, key words and abstract, by two reviewers (Appendix B – Level 2). All potentially relevant records and those records that did not contain enough information to determine eligibility (e.g., no available abstract) were retained.

Full text relevance screening was performed independently by two reviewers and discrepancies resolved by consensus or third party (Appendix B - Level 3). The reasons for exclusion were noted using a PRISMA format (Figure 1). The level of evidence reviewed was limited to SRs.

Data Abstraction

Following a calibration exercise, one reviewer independently abstracted relevant information from each included study using a data abstraction form developed a priori for this review. (Appendix C) Prior to performing the data abstraction, a calibration exercise was conducted on a sample of five of the included SRs to ensure consistency in extraction. Abstracted data included general characteristics of the SRs (journal; publication date; country of the corresponding author; sources of evidence; search dates reported by range; and if funding sources were reported). In addition, the number of included studies corresponding to the illicit drug use interventions of interest and the types of illicit drugs involved were identified.

Extraction also included more SR specific information related to the interventions including: classification according to either prevention; treatment and/or harm reduction. Treatment interventions were sub classified according to treatment phase, and treatment type (by somatic interventions including pharmacological and/or by psychosocial interventions). Further, patient population(s), the spectrum of use as reported in the SR and information about the setting was captured. As well, the type of analyses conducted was abstracted (i.e., whether a meta-analyses was included). Wherever possible, an attempt was made to operationally define all data extraction categories and their respective subset of responses. Several co-publications and companion studies were also identified as this stage of extraction and are reported on across the prevention, treatment and harms reduction sections.

In order to provide a cursory overview of outcomes reporting for this literature base, an additional data set on outcomes was extracted independently by one reviewer, and was verified by a second reviewer. First it was determined if outcomes were specifically identified a priori (i.e., prior to being presented in the results section); generally referred to in the report text (e.g., ‘drug use behaviour’); or not reported a priori. We only captured specific outcomes information for those SRs that explicitly stated pre-specified outcomes up to and including the first four reported outcomes as stated in the text by the author(s) and according to the order presented. For those pre-specified, it was noted if a definition and/or specific measurements accompanied each outcome; if SRs reported more than five pre-specified outcomes; whether all the pre-specified outcomes were reported in the results; and whether there were any outcomes reported for harms.

Data Assessment

Data Charting

The primary aim of this initial mapping exercise was to provide numerical analysis of the extent, nature and distribution of the SRs included. Data was charted in order to map overall findings from the indentified SRs. In order to contextualise the findings, specific data charting was also undertaken across several key variables by specific intervention types (prevention, treatment and harms reduction categories). In particular, the evidence was mapped by specific interventions, by population and underlying substances. Information on meta-analyses conducted and the number

of Cochrane Reviews identified for each category were also provided. Information for each category was summarized with accompanying tables and graphs.

Quality of the Included Systematic Reviews (SRs)

An independent reviewer assessed the risk of bias associated with each included SR using AMSTAR, an 11-item checklist instrument to assess the methodological quality of SRs.[14] The AMSTAR form is provided in Appendix D. Categories of quality were determined as follows: low (score 0 to 3); moderate (score 4 to 7); and high (score 8 to 11) as per recommendations by the Canadian Agency for Drugs and Technologies in Health. (http://www.cadth.ca/index.php/en/compus/optimal-ther-resources/interventions/methods).

3. EVIDENCE MAPPING

RESULTS OF THE LITERATURE SEARCH

The results of the literature search are presented in Figure 1. Literature searching identified a total of 10,311 potentially relevant bibliographic records. The reviewers nominated one additional potentially relevant study and 43 citations were identified by a grey literature search. In addition, a specific Internet search of relevant French-language agencies yielded an additional 743 citations. After 2,070 duplicate articles were removed, 9,028 unique records remained eligible for broad relevance assessment. These reports were evaluated against the eligibility criteria and after the initial screening for relevance at the title level, 7,406 records were excluded. The remaining 1,622 records were screened for relevance at the abstract level for which an additional 971 records were excluded. Records were then retrieved and subjected to a more detailed relevance assessment using the full text; 476 of the 651 reports failed to meet the inclusion criteria as determined by consensus. Additionally, one study[15] was unavailable for full text relevance assessment by our study cut off date (Dec. 1, 2010). The reasons for exclusion are listed in the PRISMA flow chart (Figure 1) with primary reasons for exclusion per full-text citation listed in Appendix E.

In total, 175 studies met our inclusion criteria. In this initial mapping exercise, two additional criteria were then applied to these 175 remaining studies. If the intent of the SRs was indirectly related to the prevention, treatment and/or harm reduction of illicit drug use (i.e., a secondary aim of the SR), it was not incorporated into the evidence map at this time. An example of this is the SR entitled, "*A systematic review of neurological and clinical features of mindfulness meditations"* in which the evidence related to substance abuse treatment comprised only 2% of the overall included evidence and therefore was clearly not the primary focus of the SR.(Appendix F) In addition, if SRs did not report formal risk of bias assessment they were not further addressed at this stage. (Appendix G) A brief summary of the SRs including study characteristics and interventions are presented with accompanying tables within the prevention, treatment and harms reduction sections.

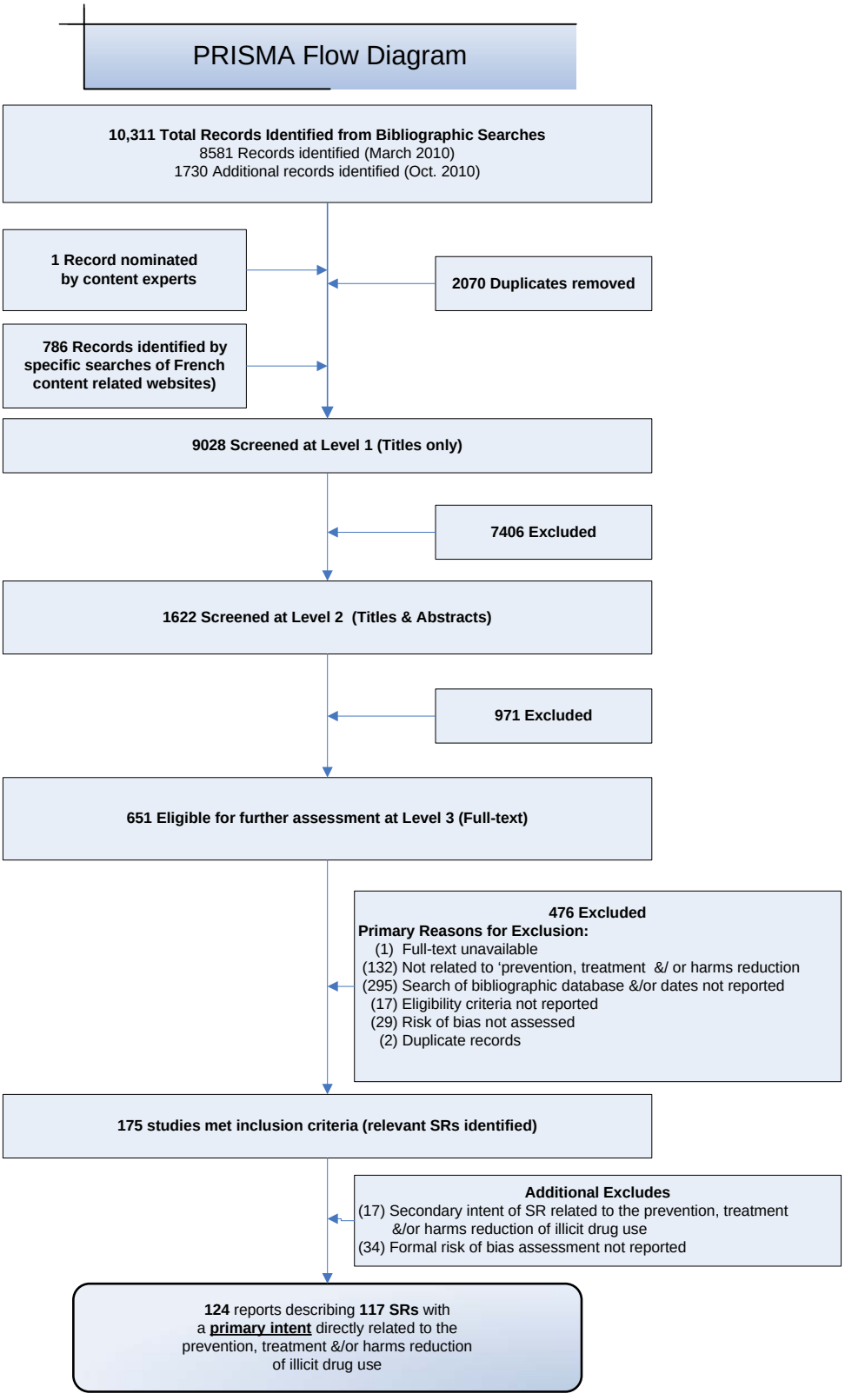

FIGURE 1. PRISMA FLOW DIAGRAM

OVERVIEW OF RELEVANT SYSTEMATIC REVIEWS (SRS)

In total, 124 reports describing 117 unique SRs with a primary aim related to the prevention, treatment and/or harms reduction of illicit drug use were identified and included in this evidence mapping.[16-139] Companion studies and co-publications are noted under the prevention, treatment and harms reduction sections, respectively.

GENERAL CHARACTERISTICS

The identified SRs were published across 53 various journals and/or health care research organizations between the years of 1979 and 2010. Cochrane Reviews accounted for 40% (49/124) of all included studies. Apart from SRs published in the Cochrane Library, the highest number of publications were found in the journal *Addiction* (n=11/124), which is published on behalf of the Society for the Study of Addiction (SSA). Funding sources were reported in 75% (93/124) of the SRs of which 98% (91/93) were funded by non-profit sources. Only one SR reported for-profit sponsorship and one study reported receiving a both non-profit and for-profit funding. The corresponding first authors of the SRs represented 20 countries with the majority of authors from the United Kingdom (29/124); Australia (23/124); United States (22/124); and Italy (16/224). Six of the corresponding authors were from Canada.[20;42;57;84;134;135]

Of the SRs included, the mean number of databases searched was 4.4 per SR and included the following: MEDLINE®/Pub Med (116/124); Cochrane Library (93/124); PsycINFO® (83/124); Embase (Excerpta Medica) (86/124); CINAHL® (Cumulative Index to Nursing and Allied Health Literature) (51/124); ERIC (Education Resources Information Centre) (11/124); and 'other sources' (106/124) including for example, Cork Database, Pasqual, Current Contents; LILACS (Latin American and Caribbean Health Sciences Literature); specialized Cochrane Trials Registries; Dissertation Abstracts; Scopus; Biological Abstracts; Sociological Abstracts, Psychological Abstracts, Toxibase; Science Citation Index etc. In addition, across the 124 SRs, websites (n=23); books (n=10); hand searches (n=21); and cross checking reference lists (n=84) were reported as 'other sources of information'. Further, several SRs reported contacting authors and experts as well as searching conference proceedings etc. In total, 67/124 (54%) of the included SRs reported a meta-analyses. Settings, populations, substances, level of substance abuse and outcomes described across the included SRs varied, and are discussed separately by category of interventions. Mapping the included SRs by categories of interventions identified the following: seven reports describing six SRs on prevention-related interventions; 108 reports described 102 SRs on treatment interventions; and 20 reports described 19 SRs related to harms interventions. When examining those SRs that reviewed more than one intervention category, the numbers were as follows: (Figure 2)

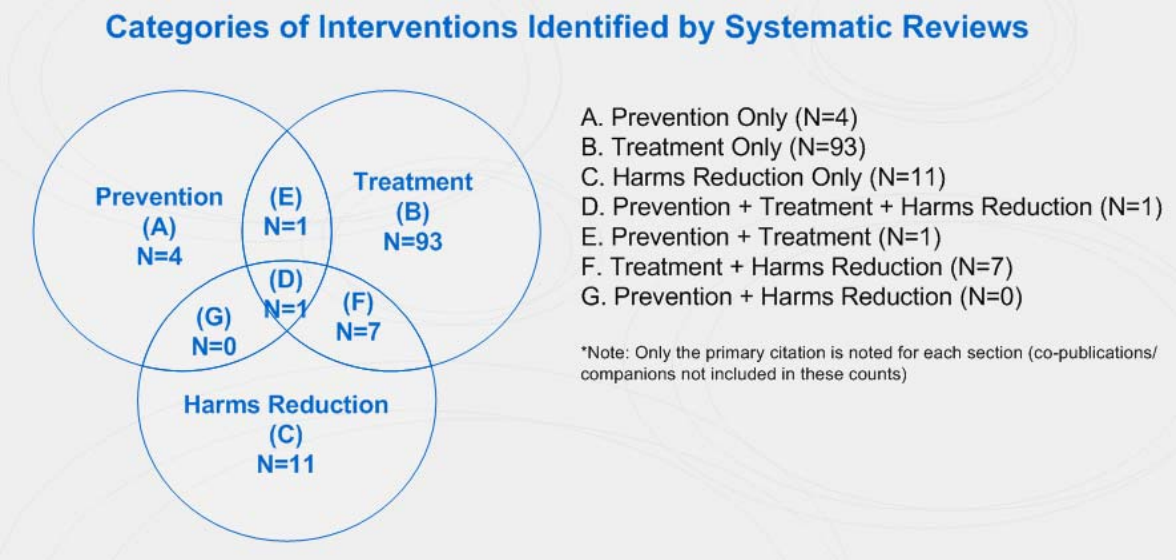

FIGURE 2. INTERVENTION CATEGORIES

QUALITY ASSESSMENT

The quality of the SRs was assessed using AMSTAR (A MeaSurement Tool to Assess Reviews). This tool provided an overall quality rating on a scale of 0 to 11, where 11 represents a review of the highest quality. Categories of quality were determined, as follows: low (score 0 to 3), moderate (score 4 to 7), and high (score 8 to 11). Three studies were rated out of a maximum score of 10 because some of the items were deemed not applicable to the SRs.[46;92;123] Please refer to Appendix J for detailed information on the quality for the individual SRs. It total, 64 SRs were assessed as high quality, 44 as moderate quality, and 9 as low quality. At the item-specific level, most SRs appropriately reported characteristics of the included studies (109/117), conducted study selection and data abstraction in duplicate (107/117), adequately assessed and documented the scientific quality of the included studies (107/117), and used the scientific quality of the included studies appropriately in formulating the conclusions (106/117). However, conflict of interest, which should be acknowledged in both the SR and noted for the included studies of the SR, was identified by few of the SRs (6/117). Further, the minority of SRs reported to have assessed for publication bias (36/117). Providing the research question and inclusion criteria with reference to a protocol, research ethics approval or pre-determined published research objectives (61/117), and providing or referencing a list of included and excluded studies (64/117) was also reported to a lesser extent. (Table 2)

TABLE 2. AMSTAR (A MEASUREMENT TOOL TO ASSESS REVIEWS) ITEMS ACROSS ALL INCLUDED SRS.

AMSTAR Items	SRs (%) (n=117) Indicating "yes"/Item
1. Was an 'a priori' design provided?	61 (52%)
2. Was there duplicate study selection and data extraction?	82 (70%)

3. Was a comprehensive literature search performed?	107 (91%)
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	82 (70%)
5. Was a list of studies (included and excluded) provided?	64 (55%)
6. Were the characteristics of the included studies provided?	109 (93%)
7. Was the scientific quality of the included studies assessed and documented?	106 (91%)
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	107 (91%)
9. Were the methods used to combine the findings of studies appropriate?	98 (84%)
10. Was the likelihood of publication bias assessed?	36 (31%)
11. Was the conflict of interest stated?	6 (5%)

MAPPING PREVENTION-RELATED SYSTEMATIC REVIEWS (SRS)

A total of seven reports describing six unique SRs related to prevention interventions were identified.[18;22;50;51;121;122;135] One publication was a co-publication paper[51;122], and we refer to the primary record with the most relevant data in the results.[122] Overall, there were four school-based drug education prevention programs; one community-based psycho-educational prevention program and one non-school based program with the setting unspecified. Substances were not specified in three of the SRs, while three SRs reviewed marijuana, cocaine and amphetamines. Three SRs described level of substance use by participants as 'substance abuse' versus misuse, abuse and/or dependence; one SR reported mixed level of use not otherwise specified; and two did not specify this as a characteristic of the included studies within their respective SRs. Children and adolescent populations were included in all six of the prevention reviews while two also included adults. Two SRs were identified as Cochrane Reviews and three SRs reported a meta-analysis.(Table 4)

OUTCOMES

Of the six unique SRs, four pre-specified the outcomes of interest prior to presentation of the SR results. One referenced a general class of outcomes (i.e., *'drug-related behaviour change)*. One SR did not report any outcomes a priori. Please refer to Appendix I – Table A for detailed information on the outcomes reported for the prevention-related interventions. A total of 13 outcomes were identified across four SRs.* Although seven of 13 outcomes reported the type of outcome measures (e.g., *self-reported, specific tests - not otherwise specified, or biologically validated*), only one outcome referenced a formal definition. Of the four SRs that pre-specified outcomes, three reported more than five outcomes ranging from six to 33. All SRs reported on all pre-specified outcomes in the results sections. None of the prevention-related SRs reported outcomes related to harms or adverse events.(Appendix I – Table A)

QUALITY ASSESSMENT

The quality of the SRs identified as prevention-related interventions ranged from 4 to 9 (with 11 being the maximum score). Please refer to Appendix J for detailed information on the quality items for the individual SRs. It total, three SRs were assessed as high quality (8-11) and three as moderate quality (4-7). At the item-specific level, all six SRs were assessed as having conducted comprehensive literature searches, and for appropriately having used the scientific quality of the included studies in formulating the conclusions of the SR. However, none of the identified SRs reported on conflict of interest. Publication bias was formally assessed in only two of the six SRs. Further, providing or referencing a list of included and excluded studies was also reported for only two of the six SRs.(Table 3)

* Note – only pre-specified outcomes were extracted to a maximum of four per SR. Therefore, the numbers presented do not refer to those SRs reporting >5 outcomes a priori; to those SRs that only referenced a general class of outcomes a priori; or to those that reported no outcomes prior to presenting results.

TABLE 3. AMSTAR (A MEASUREMENT TOOL TO ASSESS REVIEWS) ITEMS ACROSS PREVENTION SRS.

AMSTAR Items	SRs (%) (n=6) Indicating "yes"/Item
1. Was an 'a priori' design provided?	2 (33%)
2. Was there duplicate study selection and data extraction?	5 (83%)
3. Was a comprehensive literature search performed?	6 (100%)
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	5 (83%)
5. Was a list of studies (included and excluded) provided?	2 (33%)
6. Were the characteristics of the included studies provided?	5 (83%)
7. Was the scientific quality of the included studies assessed and documented?	5 (83%)
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	6 (100%)
9. Were the methods used to combine the findings of studies appropriate?	5 (83%)
10. Was the likelihood of publication bias assessed?	2 (33%)
11. Was the conflict of interest stated?	0

TABLE 4. INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO PREVENTION INTERVENTIONS

Author (Country of 1st Author)/ AMSTAR	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Intervention
Faggiano[122] (Italy) AMSTAR 9/11 - Faggiano[51] (co-publication) A	2005	Cochrane Database Syst.Rev	Yes (Non-profit)	32	Adolescents; Children	▪ Community-based [School-based]	Substance use	Cannabinoids – **marijuana;** Stimulants - **cocaine/crack**	Yes	School-based drug education prevention program to prevent illicit drug use
Fletcher[50] (UK) AMSTAR 7/11 E	2008	J Adolesc. Health	Yes (Non-profit)	4	Adolescents; Children	▪ Community-based [School-based]	Not specified/ unclear	Substance(s)/Drug(s) - NOS	No	School-level interventions
Gates[121] (UK) AMSTAR 8/11 A	2006	Cochrane Database Syst.Rev	Yes (Non-profit)	17	Adults (not defined); Adolescents; Children	▪ Not specified	Substance use	Substance(s)/Drug(s) - NOS	No	Interventions for prevention of drug use by young people delivered in non-school settings
McBride[22] (Australia) AMSTAR 4/11 A	2003	Health Educ Res	No	5	Adolescents; Children	▪ Community-based [School-based]	Not specified/ unclear	Substance(s)/Drug(s) - NOS	No	School drug education programs

*A – SR prevention only interventions; B – SR treatment only interventions; C – SR harms reduction only interventions; D – SR prevention + treatment + harms reduction interventions; E – SR prevention + treatment interventions; F – SR treatment + harms reduction interventions; G – SR prevention + harms reduction interventions; NOS – not otherwise specified

TABLE 4. CON'T - INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO PREVENTION INTERVENTIONS

Author (Country of 1st Author)	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Intervention
Porath-Waller[135] (Canada) AMSTAR 8/11 A	2010	Health Educ Behav	No	15	Adolescents	▪ Community-based [School-based]	Substance use	Cannabinoids – **marijuana;**	Yes	School-based prevention programming in reducing cannabis use among youth aged 12 to 19
White[18] (UK) AMSTAR 7/11 D	1998	Addiction	Yes (Non-profit)	71	Adults (mixed); Adolescents; Children	▪ Community-based [General]	Reported as mixed	Cannabinoids – **marijuana;** Stimulants – **amphetamine;** Stimulants - **cocaine/crack**	Yes	Psycho-educational prevention measures (preventing or delay onset of drug use, or leading to cessation of use or minimize the harm associated with substance abuse)

*A – SR prevention only interventions; B – SR treatment only interventions; C – SR harms reduction only interventions; D – SR prevention + treatment + harms reduction interventions; E – SR prevention + treatment interventions; F – SR treatment + harms reduction interventions; G – SR prevention + harms reduction interventions; NOS – not otherwise specified

MAPPING TREATMENT-RELATED SYSTEMATIC REVIEWS (SRS)

In total, 108 reports describing 102 unique SRs related to treatment interventions were identified.[16-21;23-33;35-50;52-55;59-62;64-66;68-92;94-107;109-111;113-115;117-120;123-128;130-134;138;139](Tables 8 & 9) Two co-publication papers were noted,[31;91 & 72;93] and we refer to the primary records with the most relevant data in the results.[72;91] In addition, one co-publication paper and an update was identified,[138;119;79] and we refer to the update as the record with the most relevant data in the results for this collection of studies.[138] As well, two companion papers were identified for two SRs,[95;115 & 58;140] and we refer to the primary records for the results provided. [95;140]

Treatment interventions reported were classified according to two broad treatment types: a) somatic (pharmacological and/or other); and/or b) psychosocial. Overall, 75 SRs reported on somatic interventions (pharmacological n=67; other=8) while 61 SRs reported on psychosocial interventions. It was not uncommon for SRs to report on a combination of treatment interventions with pharmacological/psychosocial being the most common (26%; 27/102); a reflection of current treatment practices. Figure 3 provides an overview of the broad intervention types by discrete categories.

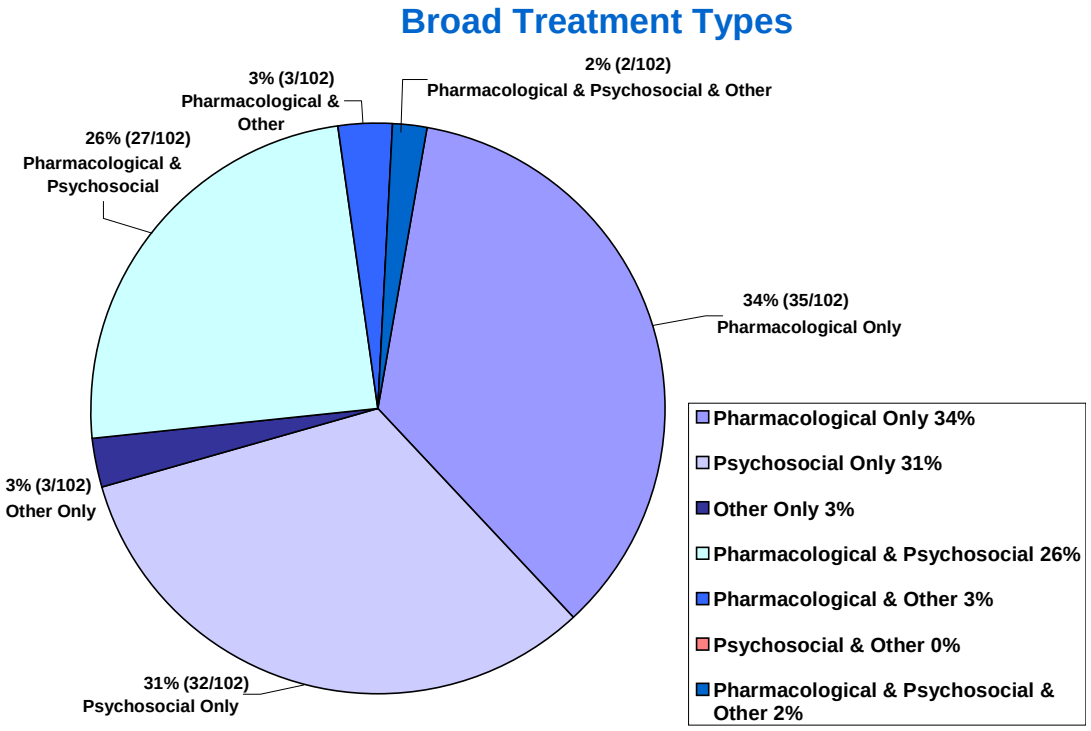

FIGURE 3. BROAD TREATMENT INTERVENTION TYPES

More specifically, in terms of somatic-pharmacological interventions the most commonly reviewed interventions involved opioids agonist maintenance therapy (AMT). This included either methadone, buprenorphine (alone) or in combination with naloxone, and LAAM.(Table 5) This was followed by medications to decrease withdrawal symptoms, which primarily

involved opioid withdrawal using methadone; buprenorphine; and clonidine. SRs also investigated pharmacological interventions to treat specific dependence (e.g., medication to treat cocaine dependence including antidepressants, dopamine agonists, carbamazepine, and other drugs like disulfiram; pharmacological agents to treat methaqualone dependence etc.). The most common somatic non-pharmacological intervention reported was acupuncture. There were several psychosocial interventions reported. The most widespread were behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy), specific cognitive behaviour therapies (e.g., relapse prevention, social skills training); group therapy; and motivational interviewing including motivational enhancement therapy.(Table 5) Specific information on the treatment interventions for each of the included SRs is provided in Tables 8 & 9.

TABLE 5. SPECIFIC TREATMENT INTERVENTIONS REPORTED

Specific Treatment Interventions Reported in the Included SRs	
SOMATIC-PHARMACOLOGICAL INTERVENTIONS	
Medications to treat intoxication states:	
Intoxication	
▪ Naloxone (agonist for acute opioid overdose)	3
▪ Flumazenil (acute benzodiazepine overdose)	-
▪ Other(s): [Lofexidine (1)]	1
Overdose	
▪ Anticholinergics	-
▪ Adrenergic pressor agents	-
▪ Anti-arrythmics	-
▪ Anticonvulsants	-
▪ Other(s):	-
Medications to decrease withdrawal symptoms:	
▪ Methadone (opioids withdrawal)	13
▪ Buprenorphine (opioids withdrawal)	10
▪ Clonidine (opioids withdrawal symptoms)	6
▪ Medications to treat non-specific withdrawal symptoms (e.g., upset stomach, headache) [benzodiazepines (1); benzodiazepine, barbiturate or neuroleptic agent (1)]	2
▪ Medications to decrease withdrawal symptoms - Other(s) [Barbiturates, diazepam, morphine (1); dopamine agonists for cocaine dependence (1); opiates, phenobarbitone, diazepam (1); opioids antagonists with heavy sedation (1); opioids antagonists with adrenergic agonists versus Alpha 2 adrenergic agonists (1); treatment for amphetamine withdrawal (amineptine, mirtazapine) (1); Alpha adrenergic agonists for opioids withdrawal (1); Alpha adrenergic agonists and opioids agonists for opioids withdrawal (1); dihydrocodeine (1)]	9
Agonist maintenance therapies	
Opioid agonist maintenance therapies:	

▪ Methadone	20
▪ Buprenorphine (alone)	11
▪ Buprenorphine (in combination with naloxone)	1
▪ LAAM (withdrawn)	7
▪ Other(s): [alpha2 adrenergic agonists such as lofexidine and clonidine (2); oral slow morphine (1); Codeine (1)]	4
Antagonist therapies	
▪ Naltrexone [for opioids (heroin)]	8
Medications to treat co-morbid psychiatric conditions	
▪ Mood stabilizers	2
▪ Antipsychotics	2
▪ Antidepressants	3
▪ Other(s) [Anticonvulsive (1); neuroleptics, benzodiazepines; anti-craving agents (1); d-amphetamine (1)]	3
****Medications to treat dependence - Others (not covered above):**	20
SOMATIC-OTHER:	
▪ Non-pharmacological [Acupuncture (5); boot camps (1); Chinese herbal medicine (1); Supportive treatments (e.g., swaddling, settling, massage, relaxation baths, pacifiers or waterbeds) (1)]	8
PSYCHOSOCIAL INTERVENTIONS	
▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training)	20
▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET))	13
▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy)	24
▪ Psychodynamic therapy/interpersonal therapy (ITP)	5
▪ Group therapy	17
▪ Family therapies (may include the nuclear family, couples/marital therapy, concurrent for patients, spouses or partners, and siblings; multi-family parties; social networks)	9
▪ Self-help groups & 12-step facilitation (TSF)	10
▪ Brief therapies	6
▪ Self-guided therapies (guided by written, programmed, or Internet-based instruction; self-help manuals; behavioural self-control)	5
▪ Case management	9
▪ Other(s) [Examples include therapeutic communities; mindfulness meditation; yoga; breathing exercises; parenting programs; psychotherapy; individual counseling NOS; Assertive	41

Community Treatment (ACT); Social Skills Training; child and parenting services NOS; employee assistance programs; general counseling; and psycho-education programs etc.],	
*NOS – not otherwise specified	

Substances covered across the treatment intervention SRs were not otherwise specified in 43 of the SRs included. Of those that did report by specific substances (class or agent), most were related to the class of opioid and morphine derivatives (n=34). This was followed by specific substance use of heroin (n=21) and marijuana (n=11).(Table 6) It should be noted that of the 102 SRs in the treatment intervention category, 29 reported to include poly-substances.

TABLE 6. SYSTEMATIC REVIEWS (SRS) - TREATMENT INTERVENTIONS – REPORTED SUBSTANCES

SR Treatment Interventions – Reported Substances:	
Substance(s) – not otherwise specified	43
Cannabinoids (Class Only – NOS)	2
▪ hashish	1
▪ marijuana	11
Depressants (Class Only – NOS)	-
▪ barbiturates	2
▪ benzodiazepines (other than flunitrazepam)	2
▪ flunitrazepam	-
▪ GHB	-
▪ methaqualone	1
Dissociative Anesthetics (Class Only – NOS)	
▪ ketamine	-
▪ PCP and analogs	1
Hallucinogens (Class Only – NOS)	1
▪ LSD	-
▪ mescaline	-
▪ psilocybin	-
Opioids and Morphine Derivatives (Class Only – NOS)	33
▪ codeine	1
▪ fentanyl and fentanyl analogs	-
▪ heroin	21
▪ morphine	1
▪ hydro morphine (Dilaudid)	-
▪ opium	-
▪ oxycodone HCL	-
▪ hydrocodone bitartrate, acetaminophen	-
Stimulants (Class Only – NOS)	-
▪ amphetamine	7
▪ cocaine/crack	26

▪ MDMA (methylenedioxy-methamphetamine)	-
▪ methamphetamine	3
▪ methylphenidate (safe and effective for treatment of ADHD)	-
Other(s) ▪ Narcotics (NOS) (2) ▪ Methadone (1)	3
*NOS – not otherwise specified	

Several of the included SRs did not report on a specific treatment setting (n=79/102). However, 24 of the treatment intervention SRs reported to have reviewed studies from one or more of the following specific settings: general community-based (n=4); school-based (n=1); hospital-based (n=5); community residential-based (n=3); outpatient intensive-based (n=4); and general outpatient settings including mental health clinics, private practices, primary care clinics etc. (n=8). 'Other' settings reported included therapeutic clinics (n=1); correctional facilities (n=3); home of patients (n=1); and a homeless shelter (n=1).(Table 8) Specific treatment phases were reported in several of the SRs as follows: detoxification only (n=14); therapeutic treatment only (n=77); relapse-prevention only (n=3); detoxification, treatment and relapse-prevention (n=2); detoxification and treatment (n=5); and treatment and relapse-prevention (n=1). The treatment phase was not specified in two SRs.(Table 9)

Forty-four of the SRs described the level of substance use by participants as 'substance dependence'; 20 SRs reported 'substance use'; 19 SRs reported 'substance abuse'; seven SRs reported 'substance misuse'; and seven SRs reported more than one specific level of use. An additional seven SRs reported 'mixed use' not otherwise specified, while 15 did not specify this as a characteristic of the included studies within their respective SRs. The SRs also reported to include one or more of the following populations: adults (undefined) (n=23); adults (mixed male/females) (n=16); adults (women only) (n=1); adolescents (n=15); children (n=5); infants exposed prenatally/neonates (n=6); pregnant women (n=6); and individuals with dual diagnosis (n=8). In addition, 'other' populations such as homeless drug users (n=1); post-partum women (n=1); and all-ages (n=1) were identified. The population was not specified in 38 SRs. Forty-six SRs were identified as Cochrane Reviews and 58 SRs reported a meta-analysis.(Tables 8 & 9)

OUTCOMES

Of the 102 unique SRs, 71 pre-specified outcomes of interest prior to presentation of SR results. Thirteen SRs referenced a general class of outcomes (e.g., *'evaluate the clinical significance of changes in substance use associated with each intervention'; 'program outcomes – not otherwise specified'; 'outcomes for the spectrum of mental illnesses and substance use disorder are included', etc.).* Eighteen SRs did not report any primary outcomes in advance of presenting the results. Please refer to Appendix I – Table B for detailed information on the outcomes reported for the treatment-related interventions. A total of 257

outcomes were identified across the 71 SRs,* of which 165 provided some additional accompanying information with regards to the outcomes in the form of a recognized definition; a listing of specific measurement tools to be used; to less specific detail indicating only the type of measurement to be used (e.g., '*assessed either qualitatively or through scales'; 'change in illicit drug use – not otherwise specified'; 'concordance with and retention in treatment', etc.*). Of the 71 SRs that pre-specified outcomes, 42 reported more than five outcomes with one study reporting more than 50 outcomes.[139] Sixty-eight of the 71 SRs provided results on the pre-specified outcomes in the results sections, and 50 SRs reported outcomes related to harms or adverse events.(Appendix I – Table B)

Quality Assessment

The quality of the SRs identified as treatment interventions ranged from 1 to 11 (with 11 being the maximum score). Please refer to Appendix J for detailed information on the quality for the individual SRs. In total, 59 SRs were assessed as high quality (8-11), 37 as moderate quality (4-7), and six as low quality (0-3). At the item-specific level, most treatment SRs adequately assessed and documented the scientific quality of the included studies (96/102), used the scientific quality of the included studies appropriately in formulating the conclusions (96/102), performed a comprehensive literature search (94/102), and appropriately reported characteristics of the included studies (94/102). However, conflict of interest was identified for few of the treatment SRs (5/102). Further, the minority of SRs reported to have assessed for publication bias (33/102).(Table 7)

Table 7. AMSTAR (A MeaSurement Tool to Assess Reviews) Items Across Treatment SRs.

AMSTAR Items	SRs (%) (n=102) Indicating "yes"/Item
1. Was an 'a priori' design provided?	58 (57%)
2. Was there duplicate study selection and data extraction?	73 (72%)
3. Was a comprehensive literature search performed?	94 (92%)
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	73 (72%)
5. Was a list of studies (included and excluded) provided?	59 (58%)
6. Were the characteristics of the included studies provided?	94 (92%)
7. Was the scientific quality of the included studies assessed and documented?	96 (94%)
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	96 (94%)
9. Were the methods used to combine the findings of studies appropriate?	86 (84%)
10. Was the likelihood of publication bias assessed?	33 (32%)
11. Was the conflict of interest stated?	5 (5%)

* Note – only pre-specified outcomes were extracted to a maximum of four per SR. Therefore, the numbers presented do not refer to those SRs reporting >5 outcomes a priori; to those SRs that only referenced a general class of outcomes a priori; or to those that reported no outcomes prior to presenting results.

TABLE 8. INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS

Author (Country of 1st Author)	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Type(s) of Treatment Intervention(s)
Adi[64] (UK) AMSTAR 8/11 B	2007	Health Technol Assess	Yes (Non-profit)	26	Not specified/unclear	▪ No	Substance use	Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological ▪ Psychosocial
Alvarez[85] (Spain) AMSTAR 7/11 B	2010	J Subst.Abuse Treat.	Yes (Non-profit)	15	Adults (mixed)	▪ No	Substance abuse	Stimulants - **cocaine/crack**	Yes	▪ Somatic-Pharmacological
Amato[38] (Italy) AMSTAR 10/11 B	2005	Cochrane Database Syst.Rev	Yes (Non-profit)	20	Not specified/unclear	▪ No	Substance abuse; Substance dependence	Opioids & Morphine (class only)	No	▪ Somatic-Pharmacological
Amato[59] (Italy) AMSTAR 10/11 B	2007	Cochrane Database Syst.Rev	Yes (Non-profit)	7	Adults (mixed)	▪ No	Substance dependence	Stimulants - **cocaine/crack**	Yes	▪ Somatic-Pharmacological
Amato[96] (Italy) AMSTAR 9/11 B	2008	Cochrane Database Syst.Rev	Yes (Non-profit)	9	Adults (not defined)	▪ No	Substance dependence	Opioids & Morphine Derivatives – **heroin;** Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological ▪ Psychosocial
Amato[97] (Italy) AMSTAR 10/11 B	2008	Cochrane Database Syst.Rev	Yes (Non-profit)	28	Adults (not defined)	▪ No	Substance dependence	Opioids & Morphine Derivatives – **heroin;** Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological ▪ Psychosocial

*A – SR prevention only interventions; B – SR treatment only interventions; C – SR harms reduction only interventions; D – SR prevention + treatment + harms reduction interventions; E – SR prevention + treatment interventions; F – SR treatment + harms reduction interventions; G – SR prevention + harms reduction interventions; NOS – not otherwise specified; NICE – National Institute for Health and Clinical Excellence (UK); NOS – not otherwise specified; HIV - Human immunodeficiency virus; HCV - hepatitis C virus

TABLE 8. CON'T - INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS

Author (Country of 1st Author)	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Type(s) of Treatment Intervention(s)
Austin[113] (USA) AMSTAR 4/11 B	2005	Research on Social Work Practice	No	5	Adolescents	▪ No	Substance use	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial
Bale[16] (USA) AMSTAR 1/11 B	1979	Int J Addict.	Yes (Non-profit)	25	Not specified/unclear	▪ No	Substance abuse	Substance(s)/Drug(s) - NOS; Depressants – **barbiturates;** Opioids & Morphine Derivatives – **heroin;** Other(s): narcotics	No	▪ Psychosocial
Bosch-Capblanch[127] (Switzerland) AMSTAR 9/11 B	2007		Yes (Non-profit)	10	Adults (not defined)	▪ No	Substance abuse	Substance(s)/Drug(s) - NOS	Yes	▪ Psychosocial
Castells[53] (Spain) AMSTAR 1/11 B	2007	Addiction	Yes (Mixed)	9	Not specified/unclear	▪ No	Substance dependence	Opioids & Morphine Derivatives - **codeine**	Yes	▪ Somatic-Pharmacological
Castells[130] (Spain) AMSTAR 10/11 B	2010	Cochrane Database Syst.Rev	No	16	Adults (not defined); Individuals with a dual-diagnosis	▪ No	Substance dependence	Opioids & Morphine Derivatives – **heroin;** Stimulants - **cocaine/crack**	Yes	▪ Somatic-Pharmacological ▪ Psychosocial

*A – SR prevention only interventions; B – SR treatment only interventions; C – SR harms reduction only interventions; D – SR prevention + treatment + harms reduction interventions; E – SR prevention + treatment interventions; F – SR treatment + harms reduction interventions; G – SR prevention + harms reduction interventions; NOS – not otherwise specified; NICE – National Institute for Health and Clinical Excellence (UK); NOS – not otherwise specified; HIV - Human immunodeficiency virus; HCV - hepatitis C virus

TABLE 8. CON'T - INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS

Author (Country of 1st Author)	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Type(s) of Treatment Intervention(s)
Clark[29] (Australia) AMSTAR 10/11 B	2002	Cochrane Database Syst.Rev	Yes (Non-profit)	18	Not specified/unclear	▪ No	Substance dependence	Opioids & Morphine Derivatives - **heroin**	Yes	▪ Somatic-Pharmacological
Cleary[95] (Australia) AMSTAR 6/11 - Cleary[115] (companion) B	2009	J Adv.Nurs	Yes (For profit)	54	Individuals with a dual-diagnosis	▪ Outpatient settings	Substance misuse	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial
Cleary[110] (Australia) AMSTAR 10/11 B	2008	Cochrane Database Syst.Rev	Yes (Non-profit)	25	Adults (mixed)	▪ No	Substance misuse	Substance(s)/Drug(s) - NOS; Cannabinoids - **hashish**	Yes	▪ Psychosocial
Colantonio[17] (USA) AMSTAR 5/11 B	1989	Yale J Biol.Med	Yes (Non-profit)	13	Adults (not defined)	▪ No	Substance abuse	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial

*A – SR prevention only interventions; B – SR treatment only interventions; C – SR harms reduction only interventions; D – SR prevention + treatment + harms reduction interventions; E – SR prevention + treatment interventions; F – SR treatment + harms reduction interventions; G – SR prevention + harms reduction interventions; NOS – not otherwise specified; NICE – National Institute for Health and Clinical Excellence (UK); NOS – not otherwise specified; HIV - Human immunodeficiency virus; HCV - hepatitis C virus

TABLE 8. CON'T - INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS

Author (Country of 1st Author)	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Type(s) of Treatment Intervention(s)
Connock[62] (UK) AMSTAR 9/11 B	2007	Health Technol Assess	Yes (Non-profit)	clinical effectiveness: 31 SRs & 28 RCTs; cost effectiveness: 11 RCTs	Adults (not defined)	▪ No	Substance dependence	Opioids & Morphine (class only)	No	▪ Somatic-Pharmacological ▪ Psychosocial
D'Alberto[45] (UK) AMSTAR 5/11 B	2004	J Altern Complement Med	No	6	Not specified/unclear	▪ No	Substance abuse; Substance dependence	Stimulants - **cocaine/crack**	Yes	▪ Somatic-Other
Day[120] (UK) AMSTAR 9/11 B	2005		Yes (Non-profit)		Adults (mixed)	▪ No	Substance dependence	Opioids & Morphine Derivatives - **heroin**	No	▪ Somatic-Pharmacological ▪ Psychosocial
de Lima[28] (Brazil) AMSTAR 8/11 B	2002	Addiction	No	45	Not specified/unclear	▪ No	Substance dependence	Stimulants - **cocaine/crack**	Yes	▪ Somatic-Pharmacological
Denis[70] (France) AMSTAR 9/11 B	2006	Cochrane Database Syst.Rev	No	6	Adults (mixed)	▪ Outpatient (intensive) treatment ▪ Outpatient settings	Substance abuse; Substance dependence	Cannabinoids (class only)	No	▪ Psychosocial
Denis[71] (France) AMSTAR 9/11 B	2006	Cochrane Database Syst.Rev	Yes (Non-profit)	8	Not specified/unclear	▪ Outpatient (intensive) treatment ▪ Outpatient settings	Substance dependence	Depressants - **benzodiazepines**	No	▪ Somatic-Pharmacological

*A – SR prevention only interventions; B – SR treatment only interventions; C – SR harms reduction only interventions; D – SR prevention + treatment + harms reduction interventions; E – SR prevention + treatment interventions; F – SR treatment + harms reduction interventions; G – SR prevention + harms reduction interventions; NOS – not otherwise specified; NICE – National Institute for Health and Clinical Excellence (UK); NOS – not otherwise specified; HIV - Human immunodeficiency virus; HCV - hepatitis C virus

TABLE 8. CON'T - INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS

Author (Country of 1st Author)	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Type(s) of Treatment Intervention(s)
Doggett[36] (Australia) AMSTAR 10/11 B	2005	Cochrane Database Syst.Rev	Yes (Non-profit)	6	Pregnant women Other(s): postpartum women	▪ Other(s): home of patients	Other(s): pregnant women with drug problems	Substance(s)/Drug(s) - NOS	Yes	▪ Psychosocial
Donald[46] (Australia) AMSTAR 2/10 B	2005	Soc Sci.Med	Yes (Non-profit)	10	Adults (not defined); Individuals with a dual-diagnosis	▪ No	Substance use	Substance(s)/Drug(s) - NOS	No	▪ Somatic-Pharmacological ▪ Psychosocial
Doran[102] (Australia) AMSTAR 5/11 B	2008	Pharmacoeconomics.	Yes (Non-profit)	259	Pregnant women; Not specified/unclear	▪ Hospitalization (regular and/or psychiatric hospitals) ▪ Community residential facilities (half-way or sober houses) ▪ Outpatient settings ▪ Other(s): Prison	Substance dependence	Opioids & Morphine (class only)	No	▪ Somatic-Pharmacological ▪ Psychosocial
Druss[118] (USA) AMSTAR 7/11 B	2006	General Hospital Psychiatry	Yes (Non-profit)	6	Not specified/unclear	▪ No	Not specified/unclear	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial
Elliott[41] (UK) AMSTAR 6/11 F	2005	Adolescence	Yes (Non-profit)	9	Adolescents; Children	▪ No	Substance abuse	Substance(s)/Drug(s) - NOS	No	▪ Somatic-Pharmacological ▪ Psychosocial

*A – SR prevention only interventions; B – SR treatment only interventions; C – SR harms reduction only interventions; D – SR prevention + treatment + harms reduction interventions; E – SR prevention + treatment interventions; F – SR treatment + harms reduction interventions; G – SR prevention + harms reduction interventions; NOS – not otherwise specified; NICE – National Institute for Health and Clinical Excellence (UK); NOS – not otherwise specified; HIV - Human immunodeficiency virus; HCV - hepatitis C virus

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Author (Country of 1st Author)	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Type(s) of Treatment Intervention(s)
Faggiano[23] (Italy) AMSTAR 10/11 B	2003	Cochrane Database Syst.Rev	Yes (Non-profit)	21	Not specified/unclear	▪ No	Substance dependence	Opioids & Morphine Derivatives – **heroin;** Stimulants - **cocaine/crack**	Yes	▪ Somatic-Pharmacological
Farre[32] (Spain) AMSTAR 6/11 B	2002	Drug Alcohol Depend.	Yes (Non-profit)	13	Not specified/unclear	▪ No	Substance abuse	Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological
Farre[32] (Spain) AMSTAR 7/11 B	2002	Drug Alcohol Depend.	Yes (Non-profit)	13	Not specified/unclear	▪ No	Substance abuse	Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological
Ferri[138] (Italy) AMSTAR 10/11 - Ferri[119] (original review); [79] (co-publication) B	2010	Cochrane Database Syst.Rev	Yes (Non-profit)	8	Adults (mixed)	▪ Outpatient (intensive) treatment	Substance dependence	Opioids & Morphine Derivatives - **heroin**	Yes	▪ Somatic-Pharmacological ▪ Psychosocial
Fletcher[50] (UK) AMSTAR 7/11 E	2008	J Adolesc.Health	Yes (Non-profit)	4	Adolescents; Children	▪ Community-based [School-based]	Not specified/unclear	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial

*A – SR prevention only interventions; B – SR treatment only interventions; C – SR harms reduction only interventions; D – SR prevention + treatment + harms reduction interventions; E – SR prevention + treatment interventions; F – SR treatment + harms reduction interventions; G – SR prevention + harms reduction interventions; NOS – not otherwise specified; NICE – National Institute for Health and Clinical Excellence (UK); NOS – not otherwise specified; HIV - Human immunodeficiency virus; HCV - hepatitis C virus

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Gates[77] (UK) AMSTAR 9/11 B	2006	Cochrane Database Syst.Rev	Yes (Non-profit)	7	Not specified/unclear	▪ No	Substance dependence	Stimulants - **cocaine/crack**	Yes	▪ Somatic-Other
Gowing[74] (Australia) AMSTAR 8/11 B	2006	Cochrane Database Syst.Rev	Yes (Non-profit)	9	Not specified/unclear	▪ No	Substance dependence	Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological
Gowing[83] (Australia) AMSTAR 8/11 B	2009	Cochrane Database Syst.Rev	Yes (Non-profit)	9	Not specified/unclear	▪ No	Substance dependence	Opioids & Morphine (class only)	No	▪ Somatic-Pharmacological
Gowing[91] (Australia) AMSTAR 9/11 - Gowing[31] (co-publication) B	2009	Cochrane Database Syst.Rev	Yes (Non-profit)	24	Not specified/unclear	▪ No	Substance dependence	Opioids & Morphine Derivatives – **heroin;** Other(s): Methadone	Yes	▪ Somatic-Pharmacological
Gowing[106]. (Australia) AMSTAR 9/11 B	2008	Cochrane Database Syst.Rev	Yes (Non-profit)	33	Not specified/unclear	▪ No	Substance use	Opioids & Morphine Derivatives – **heroin;** Stimulants - **cocaine/crack;** Opioids & Morphine (class only)	No	▪ Somatic-Pharmacological

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Gowing[125] (Australia) AMSTAR 8/11 B	2009	Cochrane Database Syst.Rev	Yes (Non-profit)	22	Not specified/unclear	▪ No	Substance dependence	Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological
Harvey[114] (Australia) AMSTAR 5/11 F	2007	Drug and Alcohol Review	Yes (Non-profit)	20	Adults (mixed)	▪ No	Not specified/unclear	Substance(s)/Drug(s) - NOS	No	▪ Somatic-Pharmacological ▪ Psychosocial
Hesse[54] (Denmark) AMSTAR 10/11 B	2007	Cochrane Database Syst.Rev	Yes (Non-profit)	15	Not specified/unclear	▪ No	Substance use	Substance(s)/Drug(s) – NOS; Cannabinoids – **marijuana;** Stimulants – **amphetamine;** Stimulants - **cocaine/crack;** Hallucinogens (class only); Opioids & Morphine (class only)	Yes	▪ Psychosocial
Hjorthoj[92] (Denmark) AMSTAR 4/10 B	2009	Addict.Behav.	Yes (Non-profit)	41	Not specified/unclear	▪ No	Reported as mixed	Substance(s)/Drug(s) - NOS; Cannabinoids - **marijuana**	No	▪ Somatic-Pharmacological ▪ Psychosocial

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Hyde[100] (UK) AMSTAR 7/11 B	2008	J Health Psychol.	Yes (Non-profit)	10	Not specified/unclear	▪ No	Substance use	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial
Johansson[75] (Sweden) AMSTAR 8/11 B	2006	Addiction	Yes (Non-profit)	15	Adults (not defined)	▪ Outpatient settings	Substance abuse	Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological ▪ Psychosocial
Kirchmayer[27] (Italy) AMSTAR 8/11 B	2002	Addiction	No	14	Not specified/unclear	▪ No	Substance abuse	Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological
Knapp[60] (Brazil) AMSTAR 9/11 B	2007	Cochrane Database Syst.Rev	Yes (Non-profit)	27	Not specified/unclear	▪ No	Substance abuse; Substance dependence	Stimulants – **amphetamine;** Stimulants - **cocaine/crack**	No	▪ Psychosocial
Laker[52] (UK) AMSTAR 2/11 F	2007	J Psychiatr.Ment.Health Nurs	No	13	Individuals with a dual-diagnosis	▪ No	Substance misuse	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial
Larney[80] (Australia) AMSTAR 6/11 B	2010	Addiction	Yes (Non-profit)	5	Adults (not defined)	▪ Other(s): Prison	Substance use	Opioids & Morphine (class only)	No	▪ Somatic-Pharmacological

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Lima[26] (Brazil) AMSTAR 10/11 B	2003	Cochrane Database Syst.Rev	Yes (Non-profit)	20	Adults (mixed)	▪ No	Substance dependence	Substance(s)/Drug(s) - NOS; Dissociative Anesthetics - **PCP & analogs;** Opioids & Morphine Derivatives – **heroin;** Stimulants - **cocaine/crack**	Yes	▪ Somatic-Pharmacological
Liu[94] (China) AMSTAR 8/11 B	2009	Cell Mol.Neurobiol.	Yes (Non-profit)	21	Adults (not defined)	▪ No	Substance dependence	Opioids & Morphine Derivatives - **heroin**	Yes	▪ Somatic-Pharmacological ▪ Somatic-Other
Liu[99] (China) AMSTAR 7/11 B	2009	Cell Mol.Neurobiol.	Yes (Non-profit)	21	Adults (not defined)	▪ No	Substance dependence	Opioids & Morphine Derivatives - **heroin**	Yes	▪ Somatic-Pharmacological ▪ Somatic-Other
Lobmaier[105] (Norway) AMSTAR 9/11 B	2008	Cochrane Database Syst.Rev	Yes (Non-profit)	17	Adults (not defined); Adolescents	▪ No	Substance dependence	Opioids & Morphine Derivatives – **heroin;** Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological
Lussier[76] (USA) AMSTAR 7/11 B	2006	Addiction	Yes (Non-profit)	30	Not specified/unclear	▪ No	Substance use	Substance(s)/Drug(s) - NOS	Yes	▪ Psychosocial

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Mattick[86] (Australia) AMSTAR 9/11 - Johansson (2007)[58] (Sweden) (companion) B	2009	Cochrane Database Syst.Rev	Yes (Non-profit)	11	Not specified/unclear	▪ No	Substance dependence	Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological
Mattick[107] (Australia) AMSTAR 9/11 B	2008	Cochrane Database Syst.Rev	Yes (Non-profit)	24	Not specified/unclear	▪ No	Substance dependence	Depressants – **benzodiazepines;** Opioids & Morphine Derivatives – **morphine;** Stimulants - **cocaine/crack**	Yes	
Mayet[43] (UK) AMSTAR 9/11 B	2004	Cochrane Database Syst.Rev	Yes (Non-profit)	5	Not specified/unclear	▪ No	Substance dependence	Opioids & Morphine (class only)	No	▪ Psychosocial
McCarthy[124] (South Africa) AMSTAR 4/11 B	2005	Cochrane Database Syst.Rev	Yes (Non-profit)	0	Adults (not defined)	▪ No	Substance dependence;	Depressants – **methaqualone**	No	▪ Somatic-Pharmacological ▪ Psychosocial
McGuire[24] (UK) AMSTAR 7/11 B	2003	Arch Dis.Child Fetal Neonatal Ed	No	9	Infants (exposed prenatally but given post natal intervention)	▪ Hospitalization (regular and/or psychiatric hospitals)	Other(s): transplacental exposed infants	Opioids & Morphine (class only); Other(s): Narcotics	Yes	▪ Somatic-Pharmacological

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McGuire[128] (Australia) AMSTAR 8/11 B	2002	Cochrane Database Syst.Rev	Yes (Non-profit)	9	Infants (exposed prenatally but given post natal intervention)	▪ No	Other(s): exposed infants	Substance(s)/Drug(s) - NOS	Yes	▪ Somatic-Pharmacological
Meader[81] (UK) AMSTAR 6/11 B	2010	Drug Alcohol Depend.	No	23	Adults (mixed)	▪ No	Substance misuse	Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological
Milligan[134] (Canada) AMSTAR 11/11 B	2010	Subst Abuse Treat Prev Policy	Yes (Non-profit)	21	Adults (women only); Pregnant women; Children;	▪ No	Substance use	Cannabinoids – **marijuana;** Depressants – **barbiturates;** Stimulants - **cocaine/crack;**	Yes	▪ Somatic-Pharmacological ▪ Psychosocial
Mills[42] (Canada) AMSTAR 7/11 B	2005	Harm.Reduct.J	No	9	Not specified/unclear	▪ No	Substance dependence	Stimulants - **cocaine/crack**	Yes	▪ Somatic-Other
Minozzi[78] (Italy) AMSTAR 7/11 B	2006	Cochrane Database Syst.Rev	Yes (Non-profit)	10	Not specified/unclear	▪ No	Substance dependence	Opioids & Morphine Derivatives - **heroin**	Yes	▪ Somatic-Pharmacological ▪ Psychosocial
Minozzi[88] (Italy) AMSTAR 10/11 B	2009	Cochrane Database Syst.Rev	Yes (Non-profit)	2	Adolescents	▪ Outpatient (intensive) treatment	Substance dependence	Opioids & Morphine Derivatives - **heroin**	No	▪ Somatic-Pharmacological ▪ Psychosocial

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Minozzi[89] (Italy) AMSTAR 10/11 B	2009	Cochrane Database Syst.Rev	Yes (Non-profit)	2	Adolescents	▪ Outpatient (intensive) treatment	Substance dependence	Opioids & Morphine (class only)	No	▪ Somatic-Pharmacological ▪ Psychosocial
Minozzi[103] (Italy) AMSTAR 10/11 B	2008	Cochrane Database Syst.Rev	Yes (Non-profit)	15	Adults (mixed)	▪ No	Substance dependence	Stimulants - **cocaine/crack**	Yes	▪ Somatic-Pharmacological
Minozzi[104] (Italy) AMSTAR 10/11 B	2008	Cochrane Database Syst.Rev	Yes (Non-profit)	3	Infants (exposed prenatally but given post natal intervention); Pregnant women	▪ No	Substance dependence	Substance(s)/Drug(s) - NOS; Cannabinoids – **marijuana;** Depressants – **benzodiazepines;** Stimulants – **amphetamine;** Stimulants - **cocaine/crack;** Stimulants – **methamphetamine;** Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological
Mitchell[87] (UK) AMSTAR 7/11 B	2009	Br J Psychiatry	No	10	Not specified/unclear	▪ No	Not specified/unclear	Substance(s)/Drug(s) - NOS	No	▪ Somatic-Pharmacological ▪ Psychosocial

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Mitchell[131] (USA) AMSTAR 10/11 F	2006	Campbell Collaboration	Yes (Non-profit)	66	Adults (mixed)	▪ Other(s): correctional facilities	Substance use	Substance(s)/Drug(s) - NOS	Yes	▪ Somatic-Pharmacological ▪ Somatic-Other ▪ Psychosocial
NICE[132] (UK) AMSTAR 8/11 F	2007	NICE	Yes (Non-profit)	36	Adults (not defined); Adolescents	▪ Hospitalization (regular and/or psychiatric hospitals) ▪ Community residential facilities (half-way or sober houses) ▪ Other(s): prison	Substance misuse	Substance(s)/Drug(s) - NOS; Cannabinoids – **marijuana;** Opioids & Morphine Derivatives – **heroin;** Stimulants - **cocaine/crack;** Stimulants - **methamphetamine**	Yes	▪ Psychosocial
NICE[133] (UK) AMSTAR 10/11 B	2007	NICE	Yes (Non-profit)	35	Adults (not defined) Adolescents; Pregnant women	▪ Hospitalization (regular and/or psychiatric hospitals) ▪ Community residential facilities (half-way or sober houses) ▪ Community-based [General] Other(s): Prison	Substance misuse	Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological ▪ Somatic-Other Psychosocial

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Nolte[139] (Canada) AMSTAR 10/11 B	2004	Cochrane Database Syst.Rev	Yes (Non-profit)	4	Adults (mixed); Individuals with a dual-diagnosis	▪ Hospitalization (regular and/or psychiatric hospitals)	Not specified/unclear	Stimulants - **amphetamine**	No	▪ Somatic-Pharmacological
Nunes[48] (USA) AMSTAR 9/11 B	2004	JAMA	Yes	14	Adults (mixed)	▪ No	Reported as mixed	Substance(s)/Drug(s) - NOS	Yes	▪ Somatic-Pharmacological ▪ Psychosocial
O'Campo[84] (Canada) AMSTAR 6/11 B	2009	J Urban Health	Yes (Non-profit)	17	Adults (not defined); Individuals with a dual-diagnosis	▪ Community-based [General]	Substance use	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial
O'Connor[19] (USA) AMSTAR 5/11 B	1998	JAMA	No	21	Not specified/unclear	▪ No	Not specified/unclear	Opioids & Morphine (class only)	No	▪ Somatic-Pharmacological
Osborn[39] (Australia) AMSTAR 9/11 B	2005	Cochrane Database Syst.Rev	Yes (Non-profit)	7	Infants (exposed prenatally but given post natal intervention)	▪ No	Substance dependence	Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological ▪ Somatic-Other
Osborn[40] (Australia) AMSTAR 7/11 B	2005	Cochrane Database Syst.Rev	Yes (Non-profit)	6	Infants (exposed prenatally but given post natal intervention)	▪ No	Other(s): neonates born to mothers with an opiate dependence	Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological
O'Shea[65] (NR) AMSTAR 4/11 B	2007	Clin Evid (Online)	No	23	Not specified/unclear	▪ No	Substance dependence	Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological

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Pani[126] (Italy) AMSTAR 10/11 B	2010	Cochrane Database Syst.Rev	Yes (Non-profit)	7	Adults (mixed); Individuals with a dual-diagnosis	▪ Outpatient settings	Substance dependence	Stimulants - **cocaine/crack**	Yes	▪ Somatic-Pharmacological
Parr[117] (Australia) AMSTAR 6/11 B	2009	Addiction	No	32	Adults (not defined)	▪ Outpatient settings	Not specified/unclear	Depressants – **benzodiazepines**	Yes	▪ Somatic-Pharmacological ▪ Psychosocial
Perry[72] (UK) AMSTAR 11/11 - Perry [93] (co-publication) F	2006	Cochrane Database Syst.Rev	Yes (Non-profit)	24	Not specified/unclear	▪ Community-based [General] ▪ Other(s): courts and secure establishments	Substance use	Substance(s)/Drug(s) - NOS	Yes	▪ Somatic-Pharmacological ▪ Psychosocial
Petrie[69] (UK) AMSTAR 7/11 B	2007	Health Educ Res	Yes (Non-profit)	20	Adolescents; Children	▪ No	Substance misuse	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial
Prendergast[30] (USA) AMSTAR 9/11 F	2002	Drug Alcohol Depend.	Yes (Non-profit)	78	Adults (mixed)	▪ No	Substance abuse	Substance(s)/Drug(s) - NOS; Opioids & Morphine Derivatives – **heroin;** Stimulants - **cocaine/crack**	Yes	▪ Somatic-Pharmacological ▪ Psychosocial

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Prendergast[66] (USA) AMSTAR 8/11 B	2006	Addiction	Yes (Non-profit)	33	Adults (mixed); Adolescents	▪ No	Substance use	Substance(s)/Drug(s) - NOS; Stimulants - **cocaine/crack;** Opioids & Morphine (class only)	Yes	▪ Psychosocial
Rathbone[98] (UK) AMSTAR 9/11 B	2008	Cochrane Database Syst.Rev	Yes (Non-profit)	1	Individuals with a dual-diagnosis	▪ No	Substance use	Cannabinoids - **marijuana**	No	▪ Psychosocial
Roozen[35] (The Netherlands) AMSTAR 7/11 B	2006	Eur Neuropsychopharmacol.	No	7	Adults (not defined)	▪ Outpatient settings	Substance dependence	Opioids & Morphine (class only)	No	▪ Somatic-Pharmacological ▪ Psychosocial
Roozen[49] (The Netherlands) AMSTAR 8/11 B	2004	Drug Alcohol Depend.	Yes (Non-profit)	11	Adults (not defined)	▪ No	Reported as mixed	Stimulants - **cocaine/crack;** Opioids & Morphine (class only)	Yes	▪ Psychosocial
Shoptaw[90] (USA) AMSTAR 9/11 B	2009	Cochrane Database Syst.Rev	Yes (Non-profit)	4	Not specified/unclear	▪ No	Substance dependence	Stimulants - **amphetamine**	Yes	▪ Somatic-Pharmacological ▪ Psychosocial
Simoens[44] (Belgium) AMSTAR 7/11 B	2005	Br J Gen Pract	Yes (Non-profit)	45	Adults (not defined)	▪ Community-based [General]	Substance dependence	Opioids & Morphine (class only)	No	▪ Somatic-Pharmacological

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Smith[123] (UK) AMSTAR 7/10 B	2006	Cochrane Database Syst.Rev	Yes (Non-profit)	7	Not specified/unclear	▪ Therapeutic Communities (TCs)	Reported as mixed	Substance(s)/Drug(s) - NOS; Cannabinoids – **marijuana;** Stimulants - **cocaine/crack;** Opioids & Morphine (class only)	No	▪ Psychosocial
Soares[25] (Brazil) AMSTAR 10/11 B	2003	Cochrane Database Syst.Rev	Yes (Non-profit)	17	Other(s): Irrespective of age	▪ No	Substance dependence	Opioids & Morphine Derivatives – **heroin;** Stimulants - **cocaine/crack**	Yes	▪ Somatic-Pharmacological
Srisurapanont[3][3] (Thailand) AMSTAR 9/11 B	2001	Cochrane Database Syst.Rev	Yes (Non-profit)	4	Not specified/unclear	▪ No	Substance abuse Substance dependence	Stimulants - **amphetamine**	Yes	▪ Somatic-Pharmacological ▪ Psychosocial
Stoffel[47] (USA) AMSTAR 3/11 B	2004	Am J Occup.Ther	Yes (Non-profit)	4	Adults (not defined); Adolescents	▪ No	Substance use	Substance(s)/Drug(s) - NOS; Depressants - **benzodiazepines**	No	▪ Psychosocial
Tait[21] (Australia) AMSTAR 6/11 B	2003	Drug Alcohol Rev	Yes (Non-profit)	2	Adolescents	▪ No	Substance use	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial

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Terplan[55] (UK) AMSTAR 10/11 B	2007	Cochrane Database Syst.Rev	No	9	Pregnant women	▪ No	Reported as mixed	Substance(s)/Drug(s) - NOS; Cannabinoids – **marijuana;** Stimulants - **cocaine/crack;** Stimulants – **methamphetamine;** Cannabinoids (class only); Opioids & Morphine (class only)	Yes	▪ Somatic-Pharmacological ▪ Psychosocial
Theis[20] (Canada) AMSTAR 4/11 B	1997	Biol.Neonate	No	14	Infants (exposed prenatally but given post natal intervention)	▪ No	Other(s): Neonatal Abstinence Syndrome	Substance(s)/Drug(s) - NOS	No	▪ Somatic-Pharmacological
Vanderplasschen[61] (Belgium) AMSTAR 4/11 B	2007	J Psychoactive Drugs	No	36	Not specified/unclear	▪ No	Substance abuse	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial
Vaughn[111] (USA) AMSTAR 5/11 B	2004	Research on Social Work Practice	No	18	Adolescents; Other(s): included adults if mixed with adolescents	▪ No	Substance abuse	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial

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Author (Country of 1st Author)	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Type(s) of Treatment Intervention(s)
Voshaar[68] (NR) AMSTAR 8/11 B	2006	Br J Psychiatry	No	29	Not specified/unclear	▪ No	Substance use	Depressants – **benzodiazepines;**	Yes	▪ Somatic-Pharmacological ▪ Psychosocial
Waldron[101] (USA) AMSTAR 6/11 B	2008	J Clin Child Adolesc.Psychol.	Yes (Non-profit)	17	Adolescents	▪ No	Reported as mixed	Substance(s)/Drug(s) - NOS; Cannabinoids - **marijuana**	Yes	▪ Psychosocial
Watkins[37] (USA) AMSTAR 1/11 B	2005	Psychiatr.Serv.	No	127	Individuals with a dual-diagnosis	▪ No	Substance abuse	Substance(s)/Drug(s) - NOS; Opioids & Morphine Derivatives - **heroin**	No	▪ Somatic-Pharmacological ▪ Psychosocial
White[18] (UK) AMSTAR 7/11 D	1998	Addiction	Yes (Non-profit)	71	Adults (mixed); Adolescents; Children;	▪ Community-based [General]	Reported as mixed	Substance(s)/Drug(s) - NOS; Cannabinoids – **marijuana;** Stimulants – **amphetamine;** Stimulants - **cocaine/crack**	Yes	▪ Psychosocial

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TABLE 8. CON'T - INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS

Author (Country of 1st Author)	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Type(s) of Treatment Intervention(s)
Wobrock[109] (Germany) AMSTAR 4/11 B	2008	Prog.Neuropsychopharmacol.Biol.Psychiatry	Yes (Non-profit)	61	Individuals with a dual-diagnosis	▪ No	Substance use Substance abuse	Substance(s)/Drug(s) - NOS; Cannabinoids – **marijuana;** Opioids & Morphine Derivatives – **heroin;** Stimulants - **cocaine/crack**	No	▪ Somatic-Pharmacological
Wright[73] (UK) AMSTAR 8/11 B	2006	AIDS Care	No	6	Other(s): homeless drug users	▪ Other(s): homeless shelters	Substance use	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial
Zgierska[82] (USA) AMSTAR 8/11 B	2009	Subst.Abus.	Yes (Non-profit)	25	Not specified/unclear	▪ No	Substance use; Substance abuse; Substance dependence	Substance(s)/Drug(s) - NOS	No	▪ Psychosocial

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TABLE 9. TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Adi[64] (UK) B	2007	▪ Relapse-prevention	**Somatic-Pharmacological** **Psychosocial**	▪ Antagonist therapies - naltrexone (for opioids/heroin) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy)
Alvarez[85] (Spain) B	2010	▪ Treatment	**Somatic-Pharmacological**	▪ Medications to treat co-morbid psychiatric conditions - mood stabilizers ▪ Medications to treat co-morbid psychiatric conditions - Other(s): anticonvulsive
Amato[38] (Italy) B	2005	▪ Treatment	**Somatic-Pharmacological**	▪ Medications to decrease withdrawal symptoms - methadone (opioids withdrawal) ▪ AMT - Opioids AMT - methadone
Amato[59] (Italy) B	2007	▪ Treatment	**Somatic-Pharmacological**	▪ Medications to treat co-morbid psychiatric conditions - antipsychotics
Amato[96] (Italy) B	2008	▪ Detoxification	**Somatic-Pharmacological** **Psychosocial**	▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT - Buprenorphine (alone) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy)
Amato[97] (Italy) B	2008	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT - Buprenorphine (alone) ▪ AMT - Opioids AMT - LAAM (withdrawn) ▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Self-help groups & 12-step facilitation (TSF) ▪ Other(s): Counselling
Austin[113] (USA) B	2005	▪ Treatment	**Psychosocial**	▪ Family therapies (may include the nuclear family, couples/marital therapy, concurrent for patients, spouses or partners, and siblings; multi-family parties; social networks)

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Bale[16] (USA) B	1979	▪ Treatment	**Psychosocial**	▪ Other(s): therapeutic communities as a broad category
Bosch-Capblanch[127] (Switzerland) B	2007	▪ Treatment	**Psychosocial**	▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy)
Castells[53] (Spain) B	2007	▪ Treatment	**Somatic-Pharmacological**	▪ Medications to Treat dependence - Other (not covered above) [e.g., antidepressants to treat cocaine dependence]: CNS stimulants to treat cocaine dependence
Castells[130] (Spain) B	2010	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to Treat dependence - Other (not covered above) [e.g., antidepressants to treat cocaine dependence]: bupropion, dexamphetamine, methylphenidate, modafinil, mazindol, methamphetamine and selegilin ▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Group therapy ▪ Case management ▪ Other(s): general counselling
Clark[29] (Australia) B	2002	▪ Treatment	**Somatic-Pharmacological**	▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT - LAAM (withdrawn)

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Cleary[95] (Australia)/ - Clearly[115] (companion) B	2009	▪ Treatment	**Psychosocial**	▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Self-guided therapies (guided by written, programmed, or Internet-based instruction; self help manuals; behavioural self-control)
Cleary[115] (Australia) / - Cleary[95] (companion) B	2008	▪ Treatment	**Psychosocial**	▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET) ▪ Group therapy ▪ Brief therapies ▪ Case management ▪ Other(s): Assertive Community Treatment (ACT); Social Skills Training
Cleary[110] (Australia) B	2008	▪ Treatment	**Psychosocial**	▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET) ▪ Group therapy
Colantonio[17] (USA) B	1989	▪ Treatment	**Psychosocial**	▪ Other(s): Employee assistance programs (counselling, psychotherapy, relaxation training etc.)
Connock[62] (UK) B	2007	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ AMT - Opioids AMT – methadone AMT - Opioids AMT - Buprenorphine (alone) ▪ Case management
D'Alberto[45] (UK) B	2004	▪ Treatment	**Somatic-Other**	▪ Acupuncture for cocaine/crack addiction

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Day[120] (UK) B	2005	▪ Detoxification	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to decrease withdrawal symptoms - methadone (opioids withdrawal) ▪ Other(s): Individual counselling
de Lima[28] (Brazil) B	2002	▪ Treatment	**Somatic-Pharmacological**	▪ AMT - Opioids ▪ AMT - Other(s) ▪ Medications to treat co-morbid psychiatric conditions - Other(s) ▪ Medications to treat dependence – Other (not covered above): medication to treat cocaine dependence including antidepressants; dopamine agonists; carbamazepine, and other drugs
Denis[70] (France) B	2006	▪ Treatment	**Psychosocial**	▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Psychodynamic therapy/interpersonal therapy (ITP) ▪ Group therapy ▪ Family therapies (may include the nuclear family, couples/marital therapy, concurrent for patients, spouses or partners, and siblings; multi-family parties; social networks) ▪ Self-help groups & 12-step facilitation (TSF) ▪ Brief therapies ▪ Self-guided therapies (guided by written, programmed, or Internet-based instruction; self help manuals; behavioural self-control) ▪ Case management ▪ Other(s): all psychosocial interventions
Denis[71] (France) B	2006	▪ Treatment	**Somatic-Pharmacological**	▪ Medications to treat co-morbid psychiatric conditions – antidepressants ▪ Medications to treat dependence - Other (not covered above): all treat targeted for benzodiazepine dependency including half-life benzodiazepine, benzodiazepine taper; non-benzodiazepine anxiolytics; adjunctive medication antidepressants, serotoninergic anxiolytics, anticovulsants, beta-blockers, benzodiazepine antagonists
Doggett[36] (Australia) B	2005	▪ Treatment	**Psychosocial**	▪ Other(s): home visit

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Donald[46] (Australia) B	2005	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to treat dependence - Other (not covered above): ▪ Pharmacological agents for substance dependence integrated with treatment of psychiatric disorder ▪ Other(s): Psychosocial treatment of substance dependence integrated with treatment of psychiatric condition
Doran[102] (Australia) B	2008	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to decrease withdrawal symptoms - methadone (opioids withdrawal) ▪ Medications to decrease withdrawal symptoms - buprenorphine (opioids withdrawal) ▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT - Buprenorphine (alone) ▪ AMT - Opioids AMT - LAAM (withdrawn) ▪ Antagonist therapies - naltrexone (for opioids/heroin) ▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Group therapy
Druss[118] (USA) B	2006	▪ Treatment	**Psychosocial**	▪ Other(s): interventions to improve medical care, on-site medical consultation, through team-based approaches, to models involving facilitated referrals to primary care
Elliott[41] (UK) F	2005	▪ Detoxification ▪ Treatment ▪ Relapse-prevention	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to treat dependence - Other: any drug therapy as secondary prevention ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Self-help groups & 12-step facilitation (TSF) ▪ Other(s): residential therapy
Faggiano[23] (Italy) B	2003	▪ Treatment	**Somatic-Pharmacological**	▪ AMT - Opioids AMT - methadone
Farre[32] (Spain) B	2002	▪ Treatment	**Somatic-Pharmacological**	▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT - Buprenorphine (alone) ▪ AMT - Opioids AMT - LAAM (withdrawn)

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Ferri[138] (Italy) - Ferri (original review)[119]; (co-publication)[79] B	2010	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT – prescription heroin ▪ Case management ▪ Others: psychiatric appointments; psychological counselling; HIV prevention counselling; social and legal support services
Fletcher[50] (UK) E	2008	▪ Treatment	**Psychosocial**	▪ Group therapy ▪ Other(s): school level interventions
Gates[77] (UK) B	2006	▪ Treatment	**Somatic-Other**	▪ Acupuncture
Gowing[74] (Australia) B	2006	▪ Detoxification	**Somatic-Pharmacological**	▪ Medications to decrease withdrawal symptoms - methadone (opioids withdrawal) ▪ Medications to decrease withdrawal symptoms - buprenorphine (opioids withdrawal) ▪ Medications to decrease withdrawal symptoms - clonidine (opioids withdrawal symptoms) ▪ Medications to decrease withdrawal symptoms - Other(s): Opioids antagonists with heavy sedation
Gowing[83] (Australia) B	2009	▪ Detoxification	**Somatic-Pharmacological**	▪ Medications to decrease withdrawal symptoms - clonidine (opioids withdrawal symptoms) ▪ Medications to decrease withdrawal symptoms - Other(s): opioids antagonists with adrenergic agonists versus Alpha 2 adrenergic agonists

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Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Gowing[91] (Australia) - Gowing[31] (co-publication) B	2009	▪ Detoxification	**Somatic-Pharmacological**	▪ Medications to decrease withdrawal symptoms - methadone (opioids withdrawal) ▪ Medications to decrease withdrawal symptoms - Other(s): Alpha adrenergic agonists for opioids withdrawal
Gowing[106] (Australia) B	2008	▪ Treatment	**Somatic-Pharmacological**	▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT - Buprenorphine (alone) ▪ AMT - Opioids AMT - LAAM (withdrawn) ▪ AMT - Opioids AMT - Other(s): Codeine
Gowing[125] (Australia) B	2009	▪ Detoxification	**Somatic-Pharmacological**	▪ Medications to decrease withdrawal symptoms - buprenorphine (opioids withdrawal)
Harvey[114] (Australia) F	2007	▪ Not specified	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to decrease withdrawal symptoms - methadone (opioids withdrawal) ▪ Other(s): study examined diversion and aftercare programs, which encompass several types of interventions, both pharmacological and psychosocial.
Hesse[54] (Denmark) B	2007	▪ Treatment	**Psychosocial**	▪ Case management
Hjorthoj[92] (Denmark) B	2009	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to treat dependence - Other (not covered above): clozapine, quetiapine ▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET) ▪ Group therapy ▪ Case management ▪ Other(s): Community residence, psycho-education, skills training

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Hyde[100] (UK) B	2008	▪ Treatment	**Psychosocial**	▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training)
Johansson[75] (Sweden) B	2006	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Antagonist therapies - naltrexone (for opioids/heroin) ▪ Medications to treat dependence - Other (not covered above): Fluoxetine; naltrexone retention program ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Family therapies (may include the nuclear family, couples/marital therapy, concurrent for patients, spouses or partners, and siblings; multi-family parties; social networks)
Kirchmayer[27] (Italy) B	2002	▪ Treatment	**Somatic-Pharmacological**	▪ AMT - Opioids AMT - methadone
Knapp[60] (Brazil) B	2007	▪ Treatment	**Psychosocial**	▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Psychodynamic therapy/interpersonal therapy (ITP) ▪ Group therapy ▪ Family therapies (may include the nuclear family, couples/marital therapy, concurrent for patients, spouses or partners, and siblings; multi-family parties; social networks); ▪ Self-help groups & 12-step facilitation (TSF) ▪ Brief therapies ▪ Self-guided therapies (guided by written, programmed, or Internet-based instruction; self help manuals; behavioural self-control) ▪ Case management ▪ Other(s): all types of psychological interventions were included

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Laker[52] (UK)	2007	▪ Treatment	**Psychosocial**	▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET)
F				
Larney[80] (Australia)	2010	▪ Treatment	**Somatic-Pharmacological**	▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT - Buprenorphine (alone) ▪ Medications to Treat dependence - Other (not covered above): Opioids
B				
Lima[26] (Brazil)	2003	▪ Treatment	**Somatic-Pharmacological**	▪ Medications to treat dependence - Other (not covered above): Antidepressants to treat cocaine or cocaine/opioids dependence
B				
Liu[94] (China)	2009	▪ Detoxification	**Somatic-Pharmacological** **Somatic-Other**	▪ Medications to decrease withdrawal symptoms - methadone (opioids withdrawal) ▪ Medications to decrease withdrawal symptoms - buprenorphine (opioids withdrawal) ▪ Acupuncture
B				
Liu[99] (China)	2009	▪ Detoxification	**Somatic-Pharmacological** **Somatic-Other**	▪ Medications to decrease withdrawal symptoms - Other(s): Alpha adrenergic agonists and opioids agonists for opioids withdrawal ▪ Chinese herbal medicine
B				
Lobmaier[105] (Norway)	2008	▪ Treatment	**Somatic-Pharmacological**	▪ Antagonist therapies - naltrexone (for opioids/heroin)
B				
Lussier[76] (USA)	2006	▪ Treatment	**Psychosocial**	▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy)
B				

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Mattick[86] (Australia) - Johansson (2007)[58] (Sweden) (companion) B	2009	▪ Treatment	**Somatic-Pharmacological**	▪ AMT - Opioids AMT - methadone
Mattick[107] (Australia) B	2008	▪ Treatment	**Somatic-Pharmacological**	▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT - Buprenorphine (alone)
Mayet[43] (UK) B	2005	▪ Treatment	**Psychosocial**	▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Psychodynamic therapy/interpersonal therapy (ITP) ▪ Group therapy ▪ Family therapies (may include the nuclear family, couples/marital therapy, concurrent for patients, spouses or partners, and siblings; multi-family parties; social networks) ▪ Self-help groups & 12-step facilitation (TSF) ▪ Brief therapies ▪ Self-guided therapies (guided by written, programmed, or Internet-based instruction; self help manuals; behavioural self-control) ▪ Case management ▪ Other(s): all psychosocial intervention were included

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Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
McCarthy[124] (South Africa) B	2005	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to treat dependence - Other (not covered above): Pharmacological agents to treat methaqualone dependence ▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Group therapy ▪ Self-help groups & 12-step facilitation (TSF)
McGuire[24] (UK) B	2003	▪ Treatment	**Somatic-Pharmacological**	▪ Antagonist therapies - naltrexone (for opioids/heroin)
McGuire[128] (Australia) B	2002	▪ Treatment	**Somatic-Pharmacological**	▪ Medications to treat intoxication states - naloxone
Meader[81] (UK) B	2010	▪ Detoxification	**Somatic-Pharmacological**	▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT - Buprenorphine (alone) ▪ AMT - Opioids AMT - Other(s): alpha2 adrenergic agonists such as lofexidine and clonidine
Milligan[134] (Canada) B	2010	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to decrease withdrawal symptoms - methadone (opioids withdrawal) ▪ Other(s): psychotherapy, child and parenting services, not specified
Mills[42] (Canada) B	2005	▪ Treatment	**Somatic-Other**	▪ Acupuncture

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Minozzi[78] (Italy) B	2006	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Antagonist therapies - naltrexone (for opioids/heroin) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Psychodynamic therapy/interpersonal therapy (ITP) ▪ Other(s): psychosocial therapy; counselling
Minozzi[88] (Italy) B	2009	▪ Detoxification ▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to decrease withdrawal symptoms - buprenorphine (opioids withdrawal) ▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT - Buprenorphine (in combination with naloxone) ▪ AMT - Opioids AMT - LAAM (withdrawn) ▪ Group therapy ▪ Other(s): individual counselling
Minozzi[89] (Italy) B	2009	▪ Detoxification ▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to Treat intoxication states – naloxone ▪ Medications to decrease withdrawal symptoms - buprenorphine (opioids withdrawal) ▪ Medications to decrease withdrawal symptoms - clonidine (opioids withdrawal symptoms) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Group therapy
Minozzi[103] (Italy) B	2008	▪ Treatment	**Somatic-Pharmacological**	▪ Medications to treat dependence - Other (not covered above): anticonvulsants
Minozzi[104] (Italy) B	2008	▪ Treatment	**Somatic-Pharmacological**	▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT - Buprenorphine (alone) ▪ AMT - Opioids AMT - Other(s): oral slow morphine
Mitchell[87] (UK) B	2009	▪ not specified	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to treat dependence - Other (not covered above): not specified. ▪ Other(s): not specified

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES ES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Mitchell[131] (USA) F	2006	▪ Treatment	**Somatic-Pharmacological**	▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT - LAAM (withdrawn)
			Somatic-Other	▪ Boot camp programs
			Psychosocial	▪ Group therapy ▪ Other(s): Therapeutic communities
NICE[132] (UK) F	2007	▪ Treatment	**Psychosocial**	▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Family therapies (may include the nuclear family, couples/marital therapy, concurrent for patients, spouses or partners, and siblings; multi-family parties; social networks) ▪ Self-help groups & 12-step facilitation (TSF) ▪ Brief therapies
NICE[133] (UK) B	2007	▪ Detoxification	**Somatic-Pharmacological**	▪ Medications to treat intoxication states – naloxone ▪ Medications to treat intoxication states - Other(s): Lofexidine ▪ Medications to decrease withdrawal symptoms - methadone (opioids withdrawal) ▪ Medications to decrease withdrawal symptoms - buprenorphine (opioids withdrawal) ▪ Medications to decrease withdrawal symptoms - clonidine (opioids withdrawal symptoms) ▪ Medications to treat non-specific withdrawal symptoms (e.g., upset stomach, headache, fever): benzodiazepines ▪ Medications to decrease withdrawal symptoms - Other(s): dihydrocodeine ▪ Antagonist therapies - naltrexone (for opioids/heroin)
			Somatic-Other	▪ Acupuncture
			Psychosocial	▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Family therapies (may include the nuclear family, couples/marital therapy, concurrent for patients, spouses or partners, and siblings; multi-family parties; social networks)

*A – SR prevention only interventions; B – SR treatment only interventions; C – SR harms reduction only interventions; D – SR prevention + treatment + harms reduction interventions; E – SR prevention + treatment interventions; F – SR treatment + harms reduction interventions; G – SR prevention + harms reduction interventions; NOS – not otherwise specified; AMT – agonist maintenance therapy

TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Nolte[139] (UK) B	2004	▪ Treatment	**Somatic-Pharmacological**	▪ Medications to treat co-morbid psychiatric conditions – d-amphetamine
Nunes[48] (USA) B	2004	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to treat co-morbid psychiatric conditions – antidepressants ▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Psychodynamic therapy/interpersonal therapy (ITP) ▪ Group therapy ▪ Self-help groups & 12-step facilitation (TSF) ▪ Self-guided therapies (guided by written, programmed, or Internet-based instruction; self help manuals; behavioural self-control) ▪ Other(s): skills building
O'Campo[84] (Canada) B	2009	▪ Treatment	**Psychosocial**	▪ Other(s): Community-based treatment approaches (NOS)
O'Connor[19] (USA) B	1998	▪ Detoxification ▪ Treatment	**Somatic-Pharmacological**	▪ Medications to treat intoxication states - Other(s): not specified; all meds for detoxification in opioids users
Osborn[39] (Australia) B	2005	▪ Detoxification	**Somatic-Pharmacological** **Somatic-Other**	▪ Medications to decrease withdrawal symptoms - Other(s): Opiates, phenobarbitone, diazepam ▪ Supportive Treatments (swaddling, settling, massage, relaxation baths, pacifiers, or waterbeds)
Osborn[40] (Australia) B	2005	▪ Treatment	**Somatic-Pharmacological**	▪ Medications to decrease withdrawal symptoms - buprenorphine (opioids withdrawal) ▪ Medications to decrease withdrawal symptoms - clonidine (opioids withdrawal symptoms) ▪ Medications to treat non-specific withdrawal symptoms (e.g., upset stomach, headache, fever): benzodiazepine, barbiturate or neuroleptic agent

*A – SR prevention only interventions; B – SR treatment only interventions; C – SR harms reduction only interventions; D – SR prevention + treatment + harms reduction interventions; E – SR prevention + treatment interventions; F – SR treatment + harms reduction interventions; G – SR prevention + harms reduction interventions; NOS – not otherwise specified; AMT – agonist maintenance therapy

TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
O'Shea[65] (NR) B	2007	▪ Detoxification ▪ Treatment ▪ Relapse-prevention	**Somatic-Pharmacological**	▪ Medications to treat intoxication states – naloxone ▪ Medications to decrease withdrawal symptoms - methadone (opioids withdrawal) ▪ Medications to decrease withdrawal symptoms - buprenorphine (opioids withdrawal) ▪ Medications to decrease withdrawal symptoms - clonidine (opioids withdrawal symptoms) ▪ AMT - Opioids AMT – methadone ▪ AMT - Opioids AMT - Buprenorphine (alone)
Pani[126] (Italy) B	2010	▪ Treatment	**Somatic-Pharmacological**	▪ Medications to treat dependence - Other (not covered above): Disulfiram to treat cocaine dependence
Parr[117] (Australia) B	2009	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to treat dependence - Other (not covered above): Benzodiazepine substitutive pharmacotherapy (e.g. buspirone, melatonin, paroxetine, carbamazepine, etc) ▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Brief therapies ▪ Other(s): psycho education
Perry[72] (UK) - Perry [93] (co-publication) F	2006	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to treat dependence - Other (not covered above): Pharmacological Treatment for substance use by offenders ▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Self-help groups & 12-step facilitation (TSF) ▪ Case management ▪ Other(s): Punitive, substance abuse education, shock incarceration/boot camp, monitoring/surveillance; sentencing options (e.g., drug court, mental health court, diversion)

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Petrie[69] (UK) B	2007	▪ Treatment	**Psychosocial**	▪ Family therapies (may include the nuclear family, couples/marital therapy, concurrent for patients, spouses or partners, and siblings; multi-family parties; social networks) ▪ Other(s): Parenting programs
Prendergast[30] (USA) F	2002	▪ Detoxification ▪ Treatment ▪ not specified	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to decrease withdrawal symptoms - methadone (opioids withdrawal) ▪ Other(s): therapeutic communities and outpatient drug free programs
Prendergast[66] (USA) B	2006	▪ Treatment	**Psychosocial**	▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy)
Rathbone[98] (UK) B	2008	▪ Treatment	**Psychosocial**	▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy)
Roozen[35] (The Netherlands) B	2006	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Antagonist therapies - naltrexone (for opioids/heroin) ▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Group therapy ▪ Other(s): Counselling
Roozen[49] (The Netherlands) B	2004	▪ Treatment	**Psychosocial**	▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy)
Shoptaw[90] (USA) B	2009	▪ Detoxification	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to decrease withdrawal symptoms - Other(s): Treatment for amphetamine withdrawal (amineptine, mirtazapine) ▪ Other(s): any psychosocial (thought no study was found)

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Simoens[44] (Belgium) B	2005	▪ Treatment	**Somatic-Pharmacological**	▪ Medications to decrease withdrawal symptoms - methadone (opioids withdrawal) ▪ Medications to decrease withdrawal symptoms - buprenorphine (opioids withdrawal)
Smith[123] (UK) B	2006	▪ Treatment	**Psychosocial**	▪ Other(s): Therapeutic communities (TC)
Soares[25] (Brazil) B	2003	▪ Detoxification ▪ Treatment	**Somatic-Pharmacological**	▪ Medications to decrease withdrawal symptoms - Other(s): dopamine agonists for cocaine dependence ▪ Medications to treat dependence - Other (not covered above): dopamine agonists for cocaine dependence
Srisurapanont[3] [3] (Thailand) B	2001	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to treat dependence - Other (not covered above): Fluoxetine, amlodipine, imipramine and desipramine for amphetamine dependence and abuse ▪ Other(s): not specified (all were included)
Stoffel[47] (USA) B	2004	▪ Treatment	**Psychosocial**	▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET) ▪ Self-help groups & 12-step facilitation (TSF) ▪ Other(s): brief interventions
Tait[21] (Australia) B	2003	▪ Treatment	**Psychosocial**	▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET) ▪ Other(s): all brief interventions and motivational interviewing
Terplan[55] (UK) B	2007	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ AMT - Opioids AMT - methadone ▪ Motivational interviewing (MI) (including Motivational enhancement therapy (MET) ▪ Other(s): Contingency management

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
Theis[20] (Canada) B	1997	▪ Detoxification	**Somatic-Pharmacological**	▪ Medications to decrease withdrawal symptoms - methadone (opioids withdrawal) ▪ Medications to decrease withdrawal symptoms - Other(s): Barbiturates, diazepam, morphine
Vanderplasschen[61] (Belgium) B	2007	▪ Treatment	**Psychosocial**	▪ Case management
Vaughn[111] (USA) B	2004	▪ Treatment	**Psychosocial**	▪ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy) ▪ Other(s): all types of non-pharmacological interventions were included; pharmacological interventions were included only if combined with this category; no specific treat were identified
Voshaar[68] (NR) B	2006	▪ Detoxification	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to treat dependence - Other (not covered above): Pharmacological augmentation strategies with propranolol, buspirone, carbamazepine, trazodone and imipramine in treatment of benzodiazepine use ▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Other(s): minimal intervention in form of advice, letter etc.
Waldron[101] (USA) B	2008	▪ Treatment	**Psychosocial**	▪ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training) ▪ Group therapy ▪ Family therapies (may include the nuclear family, couples/marital therapy, concurrent for patients, spouses or partners, and siblings; multi-family parties; social networks) ▪ Other(s): minimal control treatment conditions
Watkins[37] (USA) B	2005	▪ Treatment	**Somatic-Pharmacological** **Psychosocial**	▪ Medications to treat dependence - Other (not covered above): not specified; all types of medication including those to treat psychiatric conditions were included ▪ Other(s): not specified

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TABLE 9. CON'T - TREATMENT INTERVENTIONS – SPECIFIC TREATMENT PHASES & TYPES

Author	Year	Treatment Phase	Somatic (Pharmacological/ Other) or Psychosocial Interventions	Specific Interventions Identified
White[18] (UK) D	1998	▪ Treatment	**Psychosocial**	▪ Group therapy ▪ Other(s): school/college based programs directed towards adolescents and young adults
Wobrock[109] (Germany) B	2008	▪ Treatment	**Somatic-Pharmacological**	▪ Medications to treat co-morbid psychiatric conditions - mood stabilizers ▪ Medications to treat co-morbid psychiatric conditions – antipsychotics ▪ Medications to treat co-morbid psychiatric conditions – antidepressants ▪ Medications to treat co-morbid psychiatric conditions - Other(s): neuroleptics, benzodiazepines; anti-craving agents
Wright[73] (UK) B	2006	▪ Treatment	**Psychosocial**	▪ Other(s): sexual health promotion intervention
Zgierska[82] (USA) B	2009	▪ Treatment ▪ Relapse-prevention	**Psychosocial**	▪ Other(s): mindfulness meditation (yoga, relaxation, breath practices, or other techniques compatible with mindfulness meditation)

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MAPPING HARMS REDUCTION-RELATED SYSTEMATIC REVIEWS (SRS)

In total, twenty reports of 19 unique SRs related to harms reduction interventions were identified.[18;30;34;41;52;56;57;63;67;93;108;112;114;116;129;131;132;136;137] One publication was a co-published paper,[72;93] and we refer to the record with the most relevant data in the results.[72] SRs included the following harms reduction interventions: substitution programs (n=4); HIV/HCV treatment or prevention measures (n=5); specific needle exchange program (n=2); and self-harm reduction (n=1).(Table 11) Several other harms reduction interventions were also included across the 19 SRs including general drug treatment as secondary prevention; street outreach; diversion and aftercare programs; therapeutic communities; drug courts; post-release supervision for drug users; incarceration-based treatment to reduce recidivism rates; outpatient drug-free programs; psychosocial interventions for reducing injection and sexual risk behaviour for preventing HIV in drug users; community pre-trial release with drug testing and sanctions; intense supervision; drug testing; and antibiotic treatment of endocarditis in intravenous drug users. The SRs examined one or more of the following substances: marijuana (n=2); crack/cocaine (n=4); heroin (n=2); methamphetamine (n=1); and amphetamine (n=1). In addition, four specified substance by drug class only (morphine/opioids) while 11 SRs did not specify the substances covered. Most settings were not specified across SRs (14/19). However, one SR indicated it was focused on community-based settings; one on correctional facilities; one on outpatient (intensive) treatment; one on hospital-based settings and one on both hospital-based and community residential facilities. Six SRs described the level of substance use by participants as 'substance use'; five reported as 'substance misuse'; three reported as 'substance abuse'; two reported 'mix level of use'; and two SRs did not specify this as a characteristic of the included studies within their respective SRs. The SRs also involved various populations including injection drug users (n=3); individuals with dual diagnosis (n=2); adults (mixed males/females or undefined) (n=8); adolescents (n=3); children (n=3). The population was not specified in six SRs. Only one SR was identified as Cochrane Review and seven SRs reported a meta-analysis. (Table 11)

OUTCOMES

Seven of the 19 SRs pre-specified the outcomes of interest prior to presentation of SR results. Five SRs referenced a general class of outcomes (e.g., *'impact on drug use', psychological or social problems associated with drug use', 'measure of criminal behaviour – not otherwise specified', 'reduction in the use of harmful substances', 'post-release criminal behaviour – not otherwise specified plus drug use', 'dependent variables such as injection practices and sexual behaviour').* Seven SRs did not report any primary outcomes in advance of the presenting the results section. Please refer to Appendix I – Table C for detailed information on the outcomes reported for the harms reduction-related interventions. A total of 15 outcomes were identified across the SRs* of which nine referenced a formal definition of the outcome, or specified the measurement tool used. Of the seven SRs that pre-specified outcomes, one reported on more than five outcomes (i.e., 15 unique outcomes across three report sections), and all provided

* Note – only pre-specified outcomes were extracted to a maximum of four per SR. Therefore, the numbers presented do not refer to those SRs reporting >5 outcomes a priori; to those SRs that only referenced a general class of outcomes a priori; or to those that reported no outcomes prior to presenting results.

results on these outcomes in the results sections. Three of the harms reduction-related SRs reported outcomes related to harms or adverse events.(Appendix I – Table C)

Quality Assessment

The quality of the SRs identified as harms reduction ranged from 2 to 10 (with 11 being the maximum score). Please refer to Appendix J for detailed information on the quality for the individual SRs. It total, sevens SRs were assessed as high quality (8-11), eight as moderate quality (4-7), and four as low quality (0-3). At the item-specific level, several of the SRs adequately reported the characteristics of the included studies (17/19), conducted comprehensive literature searches (16/19), and used appropriate methods to combine the findings of the studies (16/19). However, few of the identified SRs stated conflict of interest (2/19), or provided the research question and inclusion criteria with reference to a protocol, research ethics approval or pre-determined published research objectives (4/19). In addition, publication bias was formally assessed in only six of the SRs, while reporting or referencing a list of included and excluded studies was also noted for six of the SRs.(Table 10)

Table 10.AMSTAR (A Measurement Tool to Assess Reviews) Items Across Harms Reduction SRs.

AMSTAR Items	SRs (%) (n=19) Indicating "yes"/Item
1. Was an 'a priori' design provided?	4 (21%)
2. Was there duplicate study selection and data extraction?	9 (47%)
3. Was a comprehensive literature search performed?	16 (84%)
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	11 (58%)
5. Was a list of studies (included and excluded) provided?	6 (32%)
6. Were the characteristics of the included studies provided?	17 (89%)
7. Was the scientific quality of the included studies assessed and documented?	15 (79%)
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	15 (79%)
9. Were the methods used to combine the findings of studies appropriate?	16 (84%)
10. Was the likelihood of publication bias assessed?	6 (32%)
11. Was the conflict of interest stated?	2 (11%)

TABLE 11. INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO HARMS REDUCTION

Author (Country of 1st Author)/ AMSTAR	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Intervention
Baral[56] (USA) AMSTAR 3/11 C	2007	Lancet Infect.Dis.	Yes (Non-profit)	22	Injection drug users	▪ Not specified	Reported as mixed	Substance(s)/ Drug(s) - NOS	No	HIV/HCV treatment or prevention (e.g., vaccines for hepatitis etc)
Elliott41 (UK) AMSTAR 6/11 F	2005	Adolescence	Yes (Non-profit)	9	Adolescents; Children	Not specified	Substance abuse	Substance(s)/ Drug(s) - NOS	No	Other(s): general drug treatment as secondary prevention
Gibson[116] (USA) AMSTAR 3/11 C	1998	AIDS	Yes (Non-profit)	19	Not specified/ unclear	▪ Not specified	Substance use	Substance(s)/ Drug(s) - NOS	No	Other(s): group interventions; HIV testing and counselling; street outreach; social interventions
Harvey[114] (Australia) AMSTAR 5/11 F	2007	Drug and Alcohol Review	Yes (Non-profit)	20	Adults (mixed); Individuals with dual-diagnosis	▪ Not specified	Not specified/unclear	Substance(s)/ Drug(s) - NOS	No	Other(s): diversion and aftercare programs (several types of interventions, both pharmacological & psychosocial)

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TABLE 11. CON'T - INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO HARMS REDUCTION

Author (Country of 1st Author)/ AMSTAR	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Intervention
Holloway[63] (UK) AMSTAR 5/11 C	2006	Psicothema.	Yes (Non-profit)	28	Adults (mixed)	▪ Not specified	Substance misuse	Substance(s)/ Drug(s) - NOS	Yes	Substitution programs Other(s): therapeutic communities & drug courts; post-release supervision for drug-misusing offenders
Jones[137] (UK) AMSTAR 6/11 C	2010	Int J Drug Policy	Yes (Non-profit)	16	Injection drug users	▪ Not specified	Not specified/unclear	Opioids and Morphine (class only – not specified) Stimulants (class only – not specified)	No	Needle & syringe exchange program(s)
Laker52 (UK) AMSTAR 2/11 F	2007	J Psychiatr. Ment.Health Nurs	No	13	Individuals with dual-diagnosis	Not specified	Substance misuse	Substance(s)/ Drug(s) - NOS	No	Other(s): non-specific
Meader[129] (UK) AMSTAR 5/11 C	2010	Cochrane Database Syst.Rev	Yes (Non-profit)	34	Not specified/ unclear	▪ Not specified	Substance misuse	Stimulants - **cocaine/crack;** Opioids and Morphine (class only – not specified)	Yes	HIV/HCV treatment or prevention (e.g., vaccines for hepatitis etc) Others(s): Psychosocial interventions for reducing injection and sexual risk behaviour for preventing HIV in drug users

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TABLE 11. CON'T - INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO HARMS REDUCTION

Author (Country of 1st Author)/ AMSTAR	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Intervention
Mitchell[131] (USA) AMSTAR 10/11 F	2006	Campbell Collaboration	Yes (Non-profit)	66	Adults (mixed)	▪ Other(s): correctional facilities	Substance use	Substance(s)/ Drug(s) - NOS	Yes	Other(s): incarceration-based treatment to reduce both drug use & recidivism rates
NICE[132] (UK) AMSTAR 8/11 F	2007	NICE	Yes (Non-profit)	36	Adults (not defined); Adolescents	▪ Hospitalization (regular and/or psychiatric hospitals); ▪ Community residential facilities (half-way or sober houses); Other(s): prison	Substance misuse	Cannabinoids – **marijuana**; Opioids and Morphine Derivatives – **heroin**; Stimulants - **cocaine/crack**; Stimulants - **methamphetamine**	Yes	Needle & syringe exchange program(s)
Novick[108] (USA) AMSTAR 3/11 C	2008	Addiction	No	6	Not specified/ unclear	▪ Not specified	Substance dependence	Opioids and Morphine (class only – not specified)	No	HIV/HCV treatment or prevention (e.g., vaccines for hepatitis etc)

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TABLE 11. CON'T - INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO HARMS REDUCTION

Author (Country of 1st Author)/ AMSTAR	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Intervention
Perry[72] (UK) AMSTAR 11/11 - Perry[93] (co-publication) F	2006	Cochrane Database Syst.Rev	Yes (Non-profit)	24	Not specified/ unclear	▪ Community-based [General] ▪ Other(s): courts and secure establishments	Substance use	Substance(s)/ Drug(s) - NOS	Yes	Substitution programs Other(s): therapeutic communities; community pre-trial release with drug testing & sanctions; drug court; mental health drug court program; intensive supervision; drugs testing
Prendergast[30] (USA) AMSTAR 9/11 F	2002	Drug Alcohol Depend.	Yes (Non-profit)	78	Adults (mixed)	▪ Not specified	Substance abuse	Substance(s)/ Drug(s) - NOS Opioids and Morphine Derivatives – **heroin** Stimulants - **cocaine/crack**	Yes	Substitution programs; Other(s): therapeutic communities and outpatient drug free programs
Prendergast[34] (USA) AMSTAR 9/11 C	2001	J Consult Clin Psychol.	Yes (Non-profit)	18	Not specified/ unclear	▪ Not specified	Substance use; Substance dependence;	Substance(s)/ Drug(s) - NOS	No	HIV/HCV treatment or prevention (e.g., vaccines for hepatitis etc)

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TABLE 11. CON'T - INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO HARMS REDUCTION

Author (Country of 1st Author)/ AMSTAR	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Intervention
Sorensen[112] (USA) AMSTAR 4/11 C	2000	Drug and Alcohol Dependence.	Yes (Non-profit)	32	Not specified/ unclear	▪ Not specified	Substance abuse	Substance(s)/ Drug(s) - NOS	No	Substitution programs
Starrels[136] (USA) AMSTAR 7/11 C	2010	Ann Intern Med	Yes (Non-profit)	11	Adults (not defined)	▪ Outpatient (intensive) treatment	Substance misuse	Opioids and Morphine (class only – not specified)	No	Other(s): interventions to prevent prescription opioid misuse in chronic pain patients (including those with history of substance abuse)
White[18] (USA) AMSTAR 7/11 D	1998	Addiction	Yes (Non-profit)	71	Adults (mixed); Adolescents; Children;	▪ Community-based [General]	Reported as mixed	Substance(s)/ Drug(s) - NOS Cannabinoids - **marijuana** Stimulants - **amphetamine** Stimulants - **cocaine/crack**	Yes	Self-harm
Wright[67] (UK) AMSTAR 8/11 C	2006	Harm.Reduct.J	No	18	Injection drug users	▪ Not specified	Substance use	Substance(s)/ Drug(s) - NOS Opioids and Morphine (class only – not specified)	No	HIV/HCV treatment or prevention (e.g., vaccines for hepatitis etc)

*A – SR prevention only interventions; B – SR treatment only interventions; C – SR harms reduction only interventions; D – SR prevention + treatment + harms reduction interventions; E – SR prevention + treatment interventions; F – SR treatment + harms reduction interventions; G – SR prevention + harms reduction interventions; NICE – National Institute for Health and Clinical Excellence (UK); NOS – not otherwise specified; HIV - Human immunodeficiency virus; HCV - hepatitis C virus

TABLE 11. CON'T - INCLUDED SYSTEMATIC REVIEWS (SRS) RELATED TO HARMS REDUCTION

Author (Country of 1st Author)/ AMSTAR	Year	Journal Name	Funding Source (Type)	Number of relevant studies	Population(s)	Focused on a Specific Setting	Level of Substance Abuse	Substance(s)	Meta-analysis Reported	Intervention
Yung[57] (Canada) AMSTAR 9/11 C	2007	J Antimicrob. Chemother.	No	7	Adults (not defined)	▪ Hospitalization (regular and/or psychiatric hospitals)	Substance use	Substance(s)/ Drug(s) - NOS	No	Other(s): antibiotic treatment of right sided endocarditis in intravenous drug users

*A – SR prevention only interventions; B – SR treatment only interventions; C – SR harms reduction only interventions; D – SR prevention + treatment + harms reduction interventions; E – SR prevention + treatment interventions; F – SR treatment + harms reduction interventions; G – SR prevention + harms reduction interventions; NICE – National Institute for Health and Clinical Excellence (UK); NOS – not otherwise specified; HIV - Human immunodeficiency virus; HCV - hepatitis C virus

4. CONCLUSIONS & FUTURE DEVELOPMENTS

Evidence mapping has been described as a process emerging as a less comprehensive yet systematic and reproducible knowledge synthesis methodology that allows an understanding of the size and distribution of an evidence base.[141] Although this methodology is early on in its development and can vary in depth, when applied it serves to highlight what is known and where gaps may exist across a body of evidence. Given the wide-ranging scope of this project and the limited resources, it was an appropriate knowledge synthesis tool to draw upon as it provided a mechanism to determine the main characteristics of the published SRs across the field of illicit drug interventions. Further, it served to identify certain methodological issues researchers may encounter when synthesizing evidence in this field, and highlighted gaps in the evidence base. For example, at the outset when trying to determine what constituted illicit drugs, identified sources were inconsistent and were not comprehensive or specific to the Canadian context. For the prevention-related interventions, there were few SRs identified. This precluded applying our a priori definition of prevention as 'universal', 'selective' or 'indicative' as per the U.S. Institute of Medicine.[142] As well, the prevention SRs lacked populations other than children and/or adolescents; only covered a narrow range of interventions, substances and setting covered; and provided limited information on the level of substance abuse of the included participants. Regarding the treatment-related SRs, few pertained to the relapse-prevention phase of treatment. In addition, several SRs did not specify underlying substances under review; treatment settings; or populations reviewed. Most harm reduction-related SRs also did not specify substances covered or settings with limited reporting of populations involved.

Although we were only able to take a cursory look at the reported outcomes, it is evident that the reporting of primary outcomes that are clearly defined is varied. It is important to state outcomes of interest upfront in order to mitigate the potential for outcome reporting bias (i.e., when reviewers are more likely to have reported outcomes when they were statistically significant and not to have reported outcomes when they were not significant). In addition, having evaluated the methodological quality of the SRs, although over half were of high quality, improving the reporting of conflict of interest, conducting an assessment for publication bias (i.e., bias that occurs when the publication of research results depends on their nature and direction),[143] and providing information related to the advanced planning of the SR design and conduct (e.g., referencing a protocol etc.) will most notably serve in future to limit the potential for biasing the conduct of SRs in this field.

In terms of future developments, one could expand this exercise to include additional analysis of the SR findings; to examine study types beyond that of SRs; to conduct a formal process of identifying the gaps bringing together Canadian experts to assist in this process; conduct subsequent SRs based on the identified gaps in the literature; to develop of a database of illicit drug related SRs that could be linked to a webpage for public access similar to the Cochrane Corner webpage that has been established for the CIHR Institute of Infection and Immunity (III) [see: http://www.cihr-irsc.gc.ca/e/40754.html]; and to work to translate and further disseminate the results from this mapping in a way that will facilitate the uptake of these findings by those within the community of illicit drug research and practice.

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(140) Navarro-Mateu F, Garriga-Puerto A, Sanchez-Sanchez JA. [Tree decision analysis of the therapeutic alternatives for Panic Disorders in Primary Care.]. Aten Primaria 2009.

(141) Hetrick SE, Parker AG, Callahan P, Purcell R. Evidence mapping: illustrating an emerging methodology to improve evidence-based practice in youth mental health. J Eval Clin Pract 2010; 16(6):1025-1030.

(142) Mrazek PB, Haggerty RJ. Reducing risks for mental disorders: Frontiers for preventive intervention research. Washington D.C.: Natl Academy Pr; 1994.

(143) Dickersin K. The existence of publication bias and risk factors for its occurrence. JAMA 1990; 263(10):1385-1389.

APPENDIX A. EXCERPT OF THE COMMONLY ABUSED DRUGS LISTING BY THE U.S. NATIONAL INSTITUTE OF DRUG ABUSE (NIDA)

Substances: Category and Name (http://www.drugabuse.gov/DrugPages/DrugsofAbuse.html).[8]
Cannabinoids
▪ hashish
▪ marijuana
Depressants
▪ barbiturates
▪ benzodiazepines (other than flunitrazepam)
▪ flunitrazepam
▪ GHB
▪ methaqualone
Dissociative Anesthetics
▪ ketamine
▪ PCP and analogs
Hallucinogens
▪ LSD
▪ mescaline
▪ psilocybin
Opioids and Morphine Derivatives
▪ codeine
▪ fentanyl and fentanyl analogs
▪ heroin
▪ morphine
▪ hydro morphine (Dilaudid)
▪ opium
▪ oxycodone HCL
▪ hydrocodone bitartrate, acetaminophen
Stimulants
▪ amphetamine
▪ cocaine/crack
▪ MDMA (methylenedioxy-methamphetamine)
▪ methamphetamine
▪ methylphenidate (safe and effective for treatment of ADHD)
▪ *nicotine (excluded)*
Other Compounds (excluded)
▪ *anabolic steroids; Dextromethorphan (DXM); inhalants*

APPENDIX B. SCREENING QUESTIONS

LEVEL 1 TITLE SCREENING:

1. Please indicate if the citation/record is possibly related to prevention, treatment and/or a harm reduction for the use of any commonly abused drug(s)

   [Excluding nicotine, anabolic steroids, over-the-counter medications such as dextromethorphan, and inhalants]

   ☐ Pass to Level 2 – include
   ☐ Exclude – exclude

LEVEL 2 ABSTRACT SCREENING:

1. Is the citation related to prevention, treatment and/or a harm reduction for the use of a commonly abused drug?

   [Excluding nicotine, anabolic steroids, over-the-counter products such as dextromethorphan, and inhalants]

   ☐ Yes – include
   ☐ No – exclude
   ☐ Unclear – include

2. Is the citation a systematic review (SR)? [*Reports to have searched; reports selection criteria; Reports a method of quality assessment]

   ☐ Yes – include
   ☐ No – exclude
   ☐ Unclear – include

3. Is the citation an English-language report? (optional)

   ☐ Yes – include
   ☐ No – exclude
   ☐ Cannot tell – include

LEVEL 3 FULL-TEXT ARTICLES SCREENING:

1. This record reports searching at least one database/source & a search date:

   ☐ Yes – include
   ☐ No – exclude
   ☐ Cannot tell (excluded but to be flagged)

2. This record reports at least one eligibility criterion:

- ☐ Yes – include
- ☐ No – exclude
- ☐ Cannot tell (excluded but to be flagged)

3. This record reports to have assessed the quality of included studies (all reported methods are acceptable):

   - ☐ Yes – include
   - ☐ No – exclude
   - ☐ Cannot tell (excluded but to be flagged)

4. This record pertains to the prevention, treatment and/or a harm reduction for the use of one or more commonly abused drugs (NIDA List)?

   [Excluding nicotine, anabolic steroids, over-the-counter products such as dextromethorphan, and inhalants]

   - ☐ Yes – include
   - ☐ No – exclude
   - ☐ Cannot tell (excluded but to be flagged)

APPENDIX C: DATA EXTRACTION FORMS

GENERAL CHARACTERISTICS

1. **RefID: [text]**
2. **Country of the Corresponding Author:**
3. **Sources of Evidence (check all that apply) & Year:**
    - ☐ Databases & Search Dates (reported by range of years searched)
        - ☐ MEDLINE® [text box for years]
        - ☐ Cochrane Library (any database) [text box for years]
        - ☐ PsycINFO® (previous names PsycLit or Clinpsyc)[text box for years]
        - ☐ EMBASE [text box for years]
        - ☐ CINAHL® [text box for years]
        - ☐ ERIC [text box for years]
        - ☐ Other(s) (text) [please list] [text box for years]
4. **Absolute START Search Date (earliest reported year searched regardless of database)** [NOTE: Year only; NR = not reported] [text box]
5. **Absolute STOP Search Date (last reported year searched regardless of database)** [NOTE: Year only; NR = not reported] [text box]
6. **Other sources of evidence (check all that apply):**
    - ☐ Books
    - ☐ Websites
    - ☐ Hand searches
    - ☐ Cross check reference lists
    - ☐ Other (text) [please list]
7. **Funding sources reported:**
    - ☐ Yes

      If yes, type of funding provided:

- ☐ For Profit
- ☐ Non-profit
- ☐ Mixed

☐ No funding reported

☐ Can't Tell

8. Aim(s) of the SR (primary or secondary) – please select the most appropriate response below:

☐ Main intent of SR is directly related to the topic (Primary Aim)(i.e., prevention, treatment or harms reduction of commonly abused drug) [quote verbatim if explicitly stated; if not paraphrase in this text box]

☐ Intent of SR is indirectly related to the topic (Secondary)(i.e., prevention, treatment or harms reduction of commonly abused drugs)/reports some results related to the topic [quote verbatim if explicitly stated; if not paraphrase in this text box]

9. Regardless of the intent, does the SR exclusively focus on a particular drug type/category?

☐ Yes

☐ No

10. Number of studies specific to prevention, treatment and/or harm reduction: [text]

11. Drug(s) included in the SR using the NIDA List of Commonly Abused Drugs as a guide[8] (check all that apply):

☐ **Substance(s) – not otherwise specified** but reported separately from alcohol

☐ **Cannabinoids**

- ☐ hashish
- ☐ marijuana

☐ **Depressants**

- ☐ barbiturates
- ☐ benzodiazepines (other than flunitrazepam)
- ☐ flunitrazepam
- ☐ GHB
- ☐ methaqualone

- ☐ **Dissociative Anesthetics**
    - ☐ ketamine
    - ☐ PCP and analogs
- ☐ **Hallucinogens**
    - ☐ LSD
    - ☐ mescaline
    - ☐ psilocybin
- ☐ **Opioids and Morphine Derivatives**
    - ☐ codeine
    - ☐ fentanyl and fentanyl analogs
    - ☐ heroin
    - ☐ morphine
    - ☐ hydro morphine (Dilaudid)
    - ☐ opium
    - ☐ oxycodone HCL
    - ☐ hydrocodone bitartrate, acetaminophen
- ☐ **Stimulants**
    - ☐ amphetamine
    - ☐ cocaine/crack
    - ☐ MDMA (methylenedioxy-methamphetamine)
    - ☐ methamphetamine
    - ☐ methylphenidate (safe and effective for treatment of ADHD)
- ☐ **Other(s) (text) [please list]**

12. NOTES: [text]

SPECIFIC CHARACTERISTICS OF THE INTERVENTIONS

1. **RefID: [text]**
2. **Related Co-publications (please list all REFIDS below): [text]**
3. **Related Companion studies (please list all REFIDS below): [text]**

SECTION 1. FOR PREVENTION RELATED SRs

4. **If PREVENTION focused, please check below: [Note: It is assumed prevention pertains to non-users]**
   - ☐ Yes, SR is related to prevention intervention(s) for commonly abused drugs
5. **Please describe the intervention (one brief sentence summarizing the prevention)**
6. **Included populations (check all that apply):**
   - ☐ Adults (men only)
   - ☐ Adults (females only)
   - ☐ Adults (mixed)
   - ☐ Adults (not defined)
   - ☐ Adolescents
   - ☐ Children
   - ☐ Infants (exposed prenatally but given postnatal intervention)
   - ☐ Elderly
   - ☐ Injection drug users
   - ☐ Individuals with dual-diagnosis
   - ☐ Pregnant women
   - ☐ Other (text) [please state]
   - ☐ Not specified/unclear

SECTION 2. FOR TREATMENT RELATED SRs

7. Please specify Treatment Phase (check all that apply)

[Note: Please answer this question in terms of what is reported in the SR. If not clearly stipulated then indicate 'not specified']

- ☐ detoxification
- ☐ treatment
- ☐ relapse-prevention
- ☐ not specified

8. Please specify Treatment Type (check all that apply)

- ☐ Somatic-Pharmacological (A1)
- ☐ Somatic-Other (A2)
- ☐ Psychosocial (B)

9. If Somatic-Pharmacological (2A1) please check all the apply:

- ☐ **Medications to treat intoxication states:**
  - ☐ Intoxication
    - ☐ Naloxone (acute opioids overdose)
    - ☐ Flumazenil (acute benzodiazepine overdose)
    - ☐ Other(s) (text) [please list]
  - ☐ Overdose
    - ☐ Anticholinergics
    - ☐ Adrenergic pressor agents
    - ☐ Anti-arrythmics
    - ☐ Anticonvulsants
    - ☐ Other(s) (text) [please list]

- ☐ **Medications to decrease withdrawal syndromes:**
  - ☐ Methadone (opioids withdrawal)
  - ☐ Buprenorphine (opioids withdrawal)
  - ☐ Clonidine (opioids withdrawal symptoms)
  - ☐ Medications to treat non-specific withdrawal symptoms (e.g., upset stomach, headache)

    [Please list: (text)]
  - ☐ Medications to decrease withdrawal symptoms - Other(s) [please list]
- ☐ **Agonist maintenance therapies**
  - ☐ Opioids agonist maintenance therapies:
    - ☐Methadone
    - ☐Buprenorphine (alone)
    - ☐Buprenorphine (in combination with naloxone)
    - ☐LAAM (withdrawn)
    - ☐Other(s) (text) [please list]
- ☐ **Antagonist therapies**
  - ☐ Naltrexone [for opioids (heroin)]
  - ☐ Mecamylamine
  - ☐ Other(s) (text) [please list]
- ☐ **Medications to treat co-morbid psychiatric conditions**
  - ☐ Mood stabilizers
  - ☐ Antipsychotics
  - ☐ Antidepressants
  - ☐ Other(s) (text) [please list]

☐ ****Medications to treat dependence - Other (not covered above) [e.g., antidepressants to treat cocaine dependence] - please specify (other) [text]**

10. If Somatic-Other (2A2) please specify the intervention (e.g., physical exercise; acupuncture etc) [text]

11. If Psychosocial (2B) - please check all the apply

- ☐ Cognitive behavioural therapies (CBT e.g., relapse prevention, social skills training)
- ☐ Motivational interviewing (MI) (including Motivational enhancement therapy (MET)
- ☐ Behavioural therapies (e.g., community reinforcement, contingency management, cue exposure and relaxation training, aversion therapy)
- ☐ Psychodynamic therapy/interpersonal therapy (ITP)
- ☐ Group therapy
- ☐ Family therapies (may include the nuclear family, couples/marital therapy, concurrent for patients, spouses or partners, and siblings; multi-family parties; social networks)
- ☐ Self-help groups & 12-step facilitation (TSF)
- ☐ Brief therapies
- ☐ Self-guided therapies (guided by written, programmed, or Internet-based instruction; self help manuals; behavioural self-control)
- ☐ Case management
- ☐ Other (text) [please list]

12. Included populations (check all that apply):

- ☐ Adults (men only)
- ☐ Adults (females only)
- ☐ Adults (mixed)
- ☐ Adults (not defined)
- ☐ Adolescents
- ☐ Children
- ☐ Infants (exposed prenatally but given postnatal intervention)

- ☐ Elderly
- ☐ Injection drug users
- ☐ Individuals with dual-diagnosis
- ☐ Pregnant women
- ☐ Other (text) [please state]
- ☐ Not specified/unclear

SECTION 3. FOR HARMS REDUCTION RELATED SRs

13. If related HARMS REDUCTION focused (check all that apply):

- ☐ Substitution programs
- ☐ Needle & syringe exchange program
- ☐ Safe injection sites
- ☐ Programs preventing & managing overdoses
- ☐ DanceSafe/RaveSafe & related programs
- ☐ HIV/HCV Tx or Prevention (e.g., vaccines for hepatitis etc) Self-harm
- ☐ Other(s) (text) [please list]

14. Included populations (check all that apply):

- ☐ Adults (men only)
- ☐ Adults (females only)
- ☐ Adults (mixed)
- ☐ Adults (not defined)
- ☐ Adolescents
- ☐ Children
- ☐ Infants (exposed prenatally but given postnatal intervention)
- ☐ Elderly

- ☐ Injection drug users
- ☐ Individuals with dual-diagnosis
- ☐ Pregnant women
- ☐ Other (text) [please state]
- ☐ Not specified/unclear

SECTION 4. GENERIC QUESTIONS FOR ALL INTERVENTIONS

15. Regardless of intervention, does this SR refer to a specific setting?

- ☐ Yes
- ☐ No

16. If 'yes' to reporting a specific setting, please specify which setting from the list below:

- ☐ Hospitalization (regular and/or psychiatric hospitals)
- ☐ Partial hospitalization (day treatment/structured programming = 20 hours/week)
- ☐ Outpatient (intensive) treatment (e.g., day treatment outpatient/structured programming = 9 hours/week)
- ☐ Therapeutic Communities (TCs) (long-term residential)
- ☐ Community residential facilities (half-way houses – or 'sober houses')
- ☐ Aftercare
- ☐ Outpatient settings (e.g., include but are not limited to mental health clinics, integrated dual-diagnosis programs, private practice settings, primary care clinics, and substance abuse treatment centers including opioids treatment programs)
- ☐ Case management
- ☐ Legally mandated treatment
- ☐ Employee assistance programs (EAPs)
- ☐ Community-based (General) – please specify [text]
- ☐ Community-based (School-based)
- ☐ Other(s) – please specify [text]

17. Which of the following does the SR refer to (as reported in the SR)?

- ☐ Substance **use**
- ☐ Substance **misuse**
- ☐ Substance **abuse** (formal diagnostic category)
- ☐ Substance **dependence** (formal diagnostic category)
- ☐ Other(s) (text) [please list]
- ☐ Not specified

18. Does this SR report a meta-analysis?

- ☐ Yes
- ☐ No

LEVEL 6 SPECIFIC CHARACTERISTICS OF THE OUTCOMES

1. **Did the authors specify outcomes of interest/primary outcomes a priori?**
   - ☐ Yes
   - ☐ No
2. **Were more than 5 outcomes reported?**
3. **Outcome reported (please specify) (only list first five outcomes)**
4. **Outcome defined by the authors?**
   - ☐ Yes
   - ☐ No
5. **If defined, how was it measured and/or what definition was used?**
6. **Did the SR report outcomes for harms?**
   - ☐ Yes
   - ☐ No
7. **Were results provided for all pre-specified outcomes in the SR?**
   - ☐ Yes
   - ☐ No
8. **Additional comments**

APPENDIX D. AMSTAR FORM

AMSTAR: A MEASUREMENT TOOL TO ASSESS THE METHODOLOGICAL QUALITY OF SYSTEMATIC REVIEWS

1. Was an 'a priori' design provided?
The research question and inclusion criteria should be established before the conduct of the review.

Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."

□ Yes
□ No
□ Can't Answer
□ Not Applicable

2. Was there duplicate study selection and data extraction?
There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.

Note: 2 people do study selection, 2 people do data extraction, consensus process or one person check the other's work (e.g. if one verifies & 2nd checks, this scores a "yes")

□ Yes
□ No
□ Can't Answer
□ Not Applicable

3. Was a comprehensive literature search performed?
At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.

Note: if at least 2 sources & 1 supplementary strategy used, select "yes" (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary). If information is offered by contacting authors or through links, check "yes."

□ Yes
□ No
□ Can't Answer
□ Not Applicable

4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?
The authors should state that they searched for reports regardless of their publication status. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.

□ Yes

 No
 Can't Answer
 Not Applicable

5. Was a list of studies (included and excluded) provided?
A list of included and excluded studies should be provided.

Note: Acceptable if the excluded studies are referenced. If there is an electronic link to the list but the link is dead, select "no."

 Yes
 No
 Can't Answer
 Not Applicable

6. Were the characteristics of the included studies provided?
In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.

Note: acceptable if not in table format as long as they are described as above

 Yes
 No
 Can't Answer
 Not Applicable

7. Was the scientific quality of the included studies assessed and documented?
'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.

Note: Can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, etc. or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).
 Yes
 No
 Can't Answer
 Not Applicable

8. Was the scientific quality of the included studies used appropriately in formulating conclusions?
The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.

Note: Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7.

 Yes
 No
 Can't Answer
 Not Applicable

9. Were the methods used to combine the findings of studies appropriate?
For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?).

Note: Indicate "yes" if they mention or describe heterogeneity, i.e., if they explain that they cannot pool because of heterogeneity/variability between interventions.

 Yes
 No
 Can't Answer
 Not Applicable

10. Was the likelihood of publication bias assessed?
An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).

Note: If no test values or funnel plot included, score "no." Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.

 Yes
 No
 Can't Answer
 Not Applicable

11. Was the conflict of interest stated?
Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

Note: To get a "yes," must indicate source of funding or support for the systematic review AND for each of the included studies

 Yes
 No
 Can't Answer
 Not Applicable

APPENDIX E. LIST OF EXCLUDED STUDIES (FULL-TEXT)

Note: Appendix E is provided as a separate attachment (N=476)

Appendix F. Systematic Reviews (SRs) Identified with a Secondary Intent Related to the Prevention, Treatment and/or Harms Reduction for Illicit Drug Use (N=17).

1. Egg, R., Pearson, F. S., Cleland, C. M., and Lipton, D. S. **Evaluations of correctional treatment programs in Germany: a review and meta-analysis.** Subst.Use.Misuse. 2000. 35 (12-14) 1967-2009. RefID:566.

2. Stein, K., Dalziel, K., Walker, A., McIntyre, L., Jenkins, B., Horne, J., Royle, P., and Round, A. **Screening for hepatitis C among injecting drug users and in genitourinary medicine clinics: systematic reviews of effectiveness, modelling study and national survey of current practice.** Health Technol Assess 2002. 6 (31) 1-122. RefID:1952.

3. Dunn, C., Deroo, L., and Rivara, F. P. **The use of brief interventions adapted from motivational interviewing across behavioral domains: a systematic review.** Addiction 2001. 96 (12) 1725-1742. RefID:2386.

4. Wilens, T. E., Monuteaux, M. C., Snyder, L. E., Moore, H., Whitley, J., and Gignac, M. **The clinical dilemma of using medications in substance-abusing adolescents and adults with attention-deficit/hyperactivity disorder: what does the literature tell us?.** J Child Adolesc.Psychopharmacol. 2005. 15 (5) 787-798. RefID:2784.

5. Littell, J. H., Popa, M., and Forsythe, B. **Multisystemic Therapy for social, emotional, and behavioral problems in youth aged 10-17.** Cochrane Database Syst.Rev 2005. (3) CD004797. RefID:2957.

6. Lyles, C. M., Kay, L. S., Crepaz, N., Herbst, J. H., Passin, W. F., Kim, A. S., Rama, S. M., Thadiparthi, S., DeLuca, J. B., and Mullins, M. M. **Best-evidence interventions: findings from a systematic review of HIV behavioral interventions for US populations at high risk, 2000-2004.** Am J Public Health 2007. 97 (1) 133-143. RefID:4523.

7. Sword, W., Jack, S., Niccols, A., Milligan, K., Henderson, J., and Thabane, L. **Integrated programs for women with substance use issues and their children: a qualitative meta-synthesis of processes and outcomes.** Harm.Reduct.J 2009. 6 (#Issue#) 32. RefID:5186.

8. Probert, J. and Macnair, J. **Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. Bet 5: is dantrolene the best way to treat hyperthermia in patients with cocaine abuse?.** Emerg.Med J 2008. 25 (7) 442-443. RefID:6284.

9. Ost and L G. **Efficacy of the third wave of behavioral therapies: a systematic review and meta-analysis (DARE structured abstract).** Behaviour Research and Therapy 2008. 46; 296-321. RefID:6743.

10. Hogan, B. E., Linden, W., and Najarian, B. **Social support interventions: do they work? (DARE structured abstract).** Clinical Psychology Review 2002. 22; 381-440. RefID:7394.

11. Macdonald, Geraldine and Turner, William. **Treatment Foster Care for improving outcomes in children and young people. Cochrane Database of Systematic Reviews: Reviews.** RefID:7640.

12. Meader, Nicholas, Li, Ryan, Des Jarlais, Don C., and Pilling, Stephen. **Psychosocial interventions for reducing injection and sexual risk behaviour for preventing HIV in drug users. Cochrane Database of Systematic Reviews: Reviews 2010 Issue 1 John Wiley & Sons, Ltd Chichester, UK**

DOI: 10.1002/14651858.CD007192.pub2. RefID:7795.

13. **Evidence of benefits from telemental health: a systematic review.** RefID:9011.

14. **The effectiveness of mental health promotion, prevention and early intervention in children, adolescents and adults: a critical appraisal of the literature.** RefID:9015.

15. **Effectiveness of early interventions for preventing mental illness in young people.** RefID:9020.

16. Niccols, A., Milligan, K., Sword, W., Thabane, L., Henderson, J., Smith, A., Liu, J., and Jack, S. **Maternal mental health and integrated programs for mothers with substance abuse issues.** Psychol Addict.Behav 2010. 24 (3) 466-474. RefID:10008.

17. Colfax, G., Santos, G. M., Chu, P., Vittinghoff, E., Pluddemann, A., Kumar, S., and Hart, C. **Amphetamine-group substances and HIV.** Lancet 7-8-2010. 376 (9739) 458-474. RefID:10119.

Appendix G. Systematic Reviews (SRs) Identified But No Formal Risk of Bias Assessment Reported (N=34).

1. Levin, F. R. and Lehman, A. F. **Meta-analysis of desipramine as an adjunct in the treatment of cocaine addiction.** J Clin Psychopharmacol. 1991. 11 (6) 374-378. RefID:436.

2. Prendergast, M. L., Podus, D., and Chang, E. **Program factors and treatment outcomes in drug dependence treatment: an examination using meta-analysis.** Subst.Use.Misuse. 2000. 35 (12-14) 1931-1965. RefID:567.

3. Hulse, G. K., Milne, E., English, D. R., and Holman, C. D. **Assessing the relationship between maternal opiate use and neonatal mortality.** Addiction 1998. 93 (7) 1033-1042. RefID:1185.

4. Marsch, L. A. **The efficacy of methadone maintenance interventions in reducing illicit opiate use, HIV risk behavior and criminality: a meta-analysis.** Addiction 1998. 93 (4) 515-532. RefID:1204.

5. Skara, S. and Sussman, S. **A review of 25 long-term adolescent tobacco and other drug use prevention program evaluations.** Prev.Med 2003. 37 (5) 451-474. RefID:1684.

6. Das, D. and Ali, B. **Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. Conservative management [correction of management] of asymptomatic cocaine body packers.** Emerg.Med J 2003. 20 (2) 172-174. RefID:1920.

7. Werch, C. E. and Owen, D. M. **Iatrogenic effects of alcohol and drug prevention programs.** J Stud.Alcohol 2002. 63 (5) 581-590. RefID:2083.

8. **Report from the Swedish Council on Technology Assessment in Health Care (SBU). Treatment of alcohol and drug abuse: an evidence-based review.** Int J Technol Assess Health Care 2002. 18 (1) 145-154. RefID:2276.

9. Barnett, P. G., Rodgers, J. H., and Bloch, D. A. **A meta-analysis comparing buprenorphine to methadone for treatment of opiate dependence.** Addiction 2001. 96 (5) 683-690. RefID:2609.

10. Becker, W. C. and Fiellin, D. A. **Provider satisfaction with office-based treatment of opioid dependence: a systematic review.** Subst.Abus. 2005. 26 (1) 15-22. RefID:2696.

11. Waxmonsky, J. G. and Wilens, T. E. **Pharmacotherapy of adolescent substance use disorders: a review of the literature.** J Child Adolesc.Psychopharmacol. 2005. 15 (5) 810-825. RefID:2783.

12. Magura, S., Staines, G. L., Blankertz, L., and Madison, E. M. **The effectiveness of vocational services for substance users in treatment.** Subst.Use.Misuse. 2004. 39 (13-14) 2165-2213. RefID:3296.

13. West, S. L. and O'Neal, K. K. **Project D.A.R.E. outcome effectiveness revisited.** Am J Public Health 2004. 94 (6) 1027-1029. RefID:3516.

14. Page, R. L., Utz, K. J., and Wolfel, E. E. **Should beta-blockers be used in the treatment of cocaine-associated acute coronary syndrome?.** Ann Pharmacother 2007. 41 (12) 2008-2013. RefID:3889.

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APPENDIX H. LIST OF NON-ENGLISH CITATIONS (UNREVIEWED) (N=71)

Note: Appendix H is provided as a separate attachment (N=71)

APPENDIX I. OUTCOMES TABLES

PREVENTION INTERVENTIONS

TABLE A. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO PREVENTION INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Faggiano[122] (Italy) - Faggiano[51] (co-publication) A	Yes - specific outcomes provided	▪ Drug knowledge	Self reported, specific tests (NOS)	Yes – 7 outcomes categories; 19 sub-outcomes	Yes	No
		▪ Drug attitudes	Self reported, specific tests (NOS)			
		▪ Acquirement of personal skills	Self reported, specific tests (NOS)			
		▪ Peers/adults drug use	Self reported, specific tests (NOS)			
Fletcher[50] (UK) E	Yes - specific outcomes provided	▪ Drug use	-	Yes – 33 (as reported by primary studies)	Yes	No
		▪ Smoking	-			
		▪ Drinking	-			
		▪ Problem behaviours	-			
Gates[121] (UK) A	Yes - specific outcomes provided	▪ Drug use or initiation of drug use	Self reported; biologically validated or otherwise corroborated (NOS)	Yes - 6	Yes	No
		▪ Substance dependence	As defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM IV) criteria			
		▪ Death (all cause & drug related)	-			
		▪ Hospitalization	-			

TABLE A. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO PREVENTION INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
McBride[22] (Australia) A	Yes - but only a general reference/general class of outcomes mentioned *[drug-related behaviour change]*	-	-	N/A	N/A	No
Porath-Waller[135] (Canada) A	Yes - specific outcomes provided	▪ Reduction of cannabis use	Self report measures (NOS)	No	Yes	No
White[18] (UK) D	No	-	-	N/A	N/A	No

TREATMENT INTERVENTIONS

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Adi[64] (UK) B	Yes - specific outcomes provided	▪ Changes in illicit drug use	-	Yes - 12	Yes	Yes
		▪ Drug-related morbidity	-			
		▪ Drug-related mortality	-			
		▪ Health-related quality of life	-			
Alvarez[85] (Spain) B	Yes - specific outcomes provided	▪ Retention in the anticonvulsant treatment (compared to the placebo treatment)	Number of participants who did not complete the treatment	No	Yes	No
		▪ Subsequent cocaine use,	Detection/not detection of cocaine metabolite (benzoylecgonine) in urine samples			
Amato[38] (Italy) B	Yes - specific outcomes provided	▪ Completion of treatment	Number of participants completing the detoxification program	No	Yes	Yes
		▪ Acceptability of treatment	Duration and severity of signs/symptoms of withdrawal, including patient self-rating; side effects			
		▪ Use of primary substance of abuse	Number of participants that referred the use of opioid during treatment; number of participants with urine samples positive for opiate			
		▪ Results at follow-up	Number of participants abstinent in follow-up; naloxone challenge			

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Amato[59] (Italy) B	Yes - specific outcomes provided	▪ Completion of treatment	Described as number of participants completing the detoxification program	Yes - 6 including the 3 secondary outcomes	Yes	No
		▪ Use of opioid drugs	Measured as number of participants with positive urinalysis during the treatment			
		▪ Results at follow-up	Described as number of participants abstinent at follow up			
Amato[96] (Italy) B	Yes - specific outcomes provided	▪ Retention in treatment	Number of participants retained at the end of the study	Yes - 9	Yes	No
		▪ Use of primary substance	Number of participants with consecutive positive urinalysis for at least three weeks			
		▪ Results at follow-up	Number of participants in treatment at the end of follow-up, and number of participants abstinent at the end of follow-up			
Amato[97] (Italy) B	Yes - specific outcomes provided	▪ Dropouts from the treatment	Number of participants who did not complete treatment	Yes - 9	Yes	Yes
		▪ Acceptability of treatment	Number and type of side effects experienced during treatment			
		▪ Use of primary substance of abuse	Number of participants that reported the use of cocaine during the treatment, and/or number of participants with urine samples positive for cocaine			
		▪ Results at follow-up	Number of participants using cocaine at follow-up			

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Austin[113] (USA) B	Yes - but only a general reference/general class of outcomes mentioned [*evaluate the clinical significance of the changes in substance use associated with each intervention]*	-	-	N/A	N/A	No
Bale[16] (USA) B	No	- - - -	- - - -	N/A	N/A	No
Bosch-Capblanch[127] (Switzerland) B	Yes - specific outcomes provided	▪ Patient's adherence or change in behaviour related to adherence	Examples include patient's adherence to treatment regime; to undergo a diagnostic procedure; to participate in a health promotion program; consistency with agreed targets; attendance; participation number and rates; length or duration of participation; healthcare practitioners' adherence to agreed specifications	Yes - 9	Yes	Yes
		▪ Patient's participation in the contractual process	Qualitative statements or scales (NOS)			
		▪ Outcomes of agreed aims stated in the contracts	-			
		▪ Patient's satisfaction with the contracting process	Assessed either qualitatively or through scales (NOS)			

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Castells[53] (Spain) B	Yes - specific outcomes provided	▪ Study retention	-	No	Yes	Yes
		▪ Cocaine use	Assessed with urine analysis (UA)			
		▪ Cocaine craving	-			
Castells[130] (Spain) B	Yes - specific outcomes provided	▪ Sustained cocaine abstinence	Assessed by mean (SD) proportion of negative urine analysis across the study per patient	Yes - 17	Yes	Yes
		▪ Retention in treatment	Number of patients who achieved sustained cocaine abstinence			
		▪ Retention in treatment	Number of patients who finished the study			
Clark[29] (Australia) B	Yes - specific outcomes provided	▪ Retention in treatment	-	Yes - 14	Yes	Yes
		▪ Reduction in opiate use	-			
		▪ Continuous abstinence from opiate use	-			
		▪ Global assessments of health	-			
Cleary[95] (Australia)/ - Cleary[115] (companion) B	Yes - specific outcomes provided	▪ Substance use	-	No	Yes	No
		▪ Mental state	-			
		▪ Treatment retention	-			

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Cleary[110] (Australia) B	Yes - specific outcomes provided	▪ Attrition	Number of participants who did not continue with the treatment following randomization; numbers lost to evaluation	Yes - 10	Yes	No
		▪ Death	All causes; if reported, death recorded in a separate table but these cases were retained in the lost to treatment/lost to evaluation figures as it was often unclear when the death occurred or the cause of death was not stated as unlikely to be linked to the intervention			
		▪ Substance use	-			
		▪ Mental state	-			
Colantonio[17] (USA) B	Yes - but only a general reference/general class of outcomes mentioned *[program outcomes – NOS]*	-		N/A	N/A	No

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Connock[62] (UK) B	Yes – specific outcomes provided	▪ Drug use	Changes in illicit drug use; concordance with and retention in treatment (NOS)	No	Yes	Yes
		▪ Health of drug user	Drug-related mortality; drug-related morbidity (e.g. blood-borne virus infection rates); HRQoL; use of healthcare system; major adverse effects of treatment (i.e. drug interactions, liver disease, cardiac abnormality, exacerbation of co-morbidity)			
		▪ Social effects	Effects on employment; effects on family			
		▪ Effects on the CJS	Rates of crime; recidivism			
D'Alberto[45] (UK) B	No	-	-	N/A	N/A	Yes
Day[120] (UK) B	Yes – specific outcomes provided	▪ Completion of withdrawal	Measured by self-report data and urinary or saliva analysis	Yes – 6	Yes	Yes
		▪ Intensity and duration of signs and symptoms and overall withdrawal syndrome experienced	Measured by either objective or self-completed measures			
		▪ Nature and incidence of adverse effects experienced as a result of medication used in the detoxification procedure	Measured by either objective or self-completed measures			

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
		▪ Engagement in further treatment post-detoxification	Measured by attendance at treatment sessions			
de Lima[28] (Brazil) B	Yes – specific outcomes provided	▪ Retention in treatment	-	Yes - 7	Yes	Yes
		▪ Adverse effects	Number of people reporting adverse effects			
		▪ Efficacy	Urine samples positive for cocaine metabolites			
		▪ Self-reported craving	-			
Denis[70] (France) B	Yes - specific outcomes provided	▪ Use of benzodiazepine	Self-reported use of benzodiazepine with confirmation by urinalysis.	No	Yes	Yes
		▪ Retention in treatment	Measured by total number of dropouts at the end of the trial			
		▪ Treatment compliance	Measured by number of subjects who adhere to doses and frequency of administration of the treatment			
		▪ Severity of benzodiazepine withdrawal	Assessed by validated questionnaire			
Denis[71] (France) B	Yes - specific outcomes provided	▪ Severity of dependence/abuse	Measured with a standardized questionnaire (Addiction Severity Index or Severity of Dependence Scale)	No	Yes	No
		▪ Self-reported use of cannabis	Number of day/times per day with confirmation by biological analysis (urinalysis or hair/saliva analysis)			
		▪ Dropout from treatment	Measured as the absolute number of participants at the end of the follow up			

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Doggett[36] (Australia) B	Yes - specific outcomes provided *[4 categories of outcomes provided with sub outcomes for each]*	▪ Drug and alcohol related outcomes (e.g., 1. Continued alcohol or drug misuse in pregnancy and/or after birth; 2. Not stabilised on methadone if opiate dependent; 3. Maternal acquisition of HIV or hepatitis B or C; 4. Neonatal abstinence syndrome) ▪ Pregnancy and puerperium outcomes (e.g., 1. Not attending consistent or regular antenatal care before term gestation; 2. Placental abruption or antepartum haemorrhage; 3. Perinatal mortality (stillbirth or neonatal death)) ▪ Infant/child outcomes (e.g., 1. Neonatal mortality; 2. Established feeding regimen (e.g., established sole breastfeeding); 3. Excess weight loss (e.g., greater than 10% birth weight) ▪ Psychosocial outcome (e.g., 1. Infant not discharged in care of mother (foster, kinship or other care); 2. Infant failure to thrive, abuse, neglect, or removal from parents for these reasons; 3. Infant injury - accidental or non-accidental; 4. Continued domestic violence	- - - -	Yes - 39	Yes	Yes

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Donald[46] (Australia) B	Yes - but only a general reference/general class of outcomes mentioned [*outcomes for the spectrum of mental illnesses and substance use disorders are included]*	-	-	N/A	N/A	No
Doran[102] (Australia) B	No	-	-	N/A	N/A	No
Druss[118] (USA) B	Yes - specific outcomes provided	▪ Linkage with primary care ▪ Quality of primary care ▪ Medical outcomes ▪ Mental health and addictive outcomes	One or more visit with a general medical provider Medical care delivery consistent with evidence-based guidelines Change in health status and/or mortality Abstinence or symptom measures	No	Yes	No
Elliott[41] (UK) F	Yes - but only a general reference/general class of outcomes mentioned [*impact on drug use or the psychological or social problems associated with drug use - NOS*]	-	-	N/A	N/A	No

Faggiano[23] (Italy) B	Yes - specific outcomes provided	▪ Retention in treatment	Time a participant remains in treatment or retention rate at a given time	Yes - 13	Yes	Yes
		▪ Drug use during treatment	Use of opioid or cocaine, based on urinalysis or based on self report			
		▪ Long term abstinence after treatment	Abstinence from opioid, at a given time after the study beginning, based on urinalysis or based on self report			
		▪ Opioid amount used	Amount used per day or dollars spent per day			
Farre[32] (Spain) B	Yes - specific outcomes provided	▪ Retention in methadone treatment	-	No	Yes	No
		▪ Illicit opioid use	Based on analytical determination of drugs of abuse in urine samples as outcome variables			
Ferri[138] (Italy) - Ferri[119] (original review); [79] (co-publication) B	Yes - specific outcomes provided	▪ Retention in treatment	Number and proportion of patients in treatment at the end of the study for each arm out of the total number of patients allocated to each arm self-report	Yes – 8	Yes	Yes
		▪ Relapse to street heroin use	Number and proportion of people who self reported use of heroin during the study for each arm			
		▪ Use of other substances	Number and proportion of people who self reported use of other substances during the study for each arm			
		▪ Death	Number and proportion of people died during the study for each arm			
Fletcher[50] (UK) E	Yes - specific outcomes provided	▪ Drug use	-	Yes – 33 (as reported by primary studies)	Yes	No
		▪ Smoking	-			
		▪ Drinking	-			
		▪ Problem behaviours	-			

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Gates[77] (UK) B	Yes - specific outcomes provided	▪ Cocaine use	Biochemically validated	Yes - 6	Yes	Yes
		▪ Cocaine use	Self-report (NOS)			
		▪ Severity of dependence	Measured by Addiction Severity Index or similar measure			
		▪ Side effects of treatment	Pain, nausea			
Gowing[74] (Australia) B	Yes - specific outcomes provided	▪ Intensity of withdrawal	-	No	Yes	Yes
		▪ Duration of treatment	As an indication of the duration of withdrawal; and retention in treatment			
		▪ Nature and incidence of adverse events	Clinically significant signs/symptoms of opioid withdrawal (such as vomiting and diarrhoea) plus any incidents that are not typical components of the opioid withdrawal syndrome (delirium, hypotension)			
		▪ Completion of withdrawal treatment	-			

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Gowing[83] (Australia) B	Yes - specific outcomes provided	▪ Intensity of withdrawal	-	No	Yes	Yes
		▪ Duration of treatment	As an indication of the duration of withdrawal and retention in treatment			
		▪ Nature and incidence of adverse effects	Clinically significant signs and symptoms of opioid withdrawal (vomiting and diarrhoea) plus any incidents not typical of opioid withdrawal syndrome (delirium, hypotension, dry mouth)			
		▪ Completion of treatment	-			
Gowing[91] (Australia) - Gowing[31] (co-publication) B	Yes - specific outcomes provided	▪ Intensity of withdrawal/withdrawal syndrome	-	No	Yes	Yes
		▪ Duration of treatment	Described as an indication of the duration of withdrawal and retention in treatment			

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
		▪ Nature and incidence of adverse effects	Defined adverse effects as clinically significant signs and symptoms of opioid withdrawal (such as vomiting and diarrhoea) plus any incidents that are not typical components of the opioid withdrawal syndrome; also considered the occurrence of hypotension or symptoms of hypotension, withholding doses of medication and cessation of treatment because of adverse effects.			
		▪ Completion of treatment/withdrawal	Described with consideration also to completion of withdrawal which might not be the same as completion of treatment, depending on treatment setting and procedures for screening of drug use			
Gowing[106]. (Australia) B	Yes - specific outcomes provided	▪ Rates of HIV infection	-	Unclear	Yes	No
		▪ Prevalence & frequency of behaviours associated with high risk of HIV transmission (e.g.,): -Injecting drug use - Collective use of injecting equipment -Unprotected sex -Number of sex partners	-			
Gowing[125] (Australia) B	Yes - specific outcomes provided	▪ Intensity of withdrawal	-	No	Yes	Yes
		▪ Duration of withdrawal treatment or length of stay	When considered relative to the scheduled duration of treatment, the actual duration is an indication of retention in treatment			

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
		▪ Nature and incidence of adverse effects	Defined adverse effects as clinically significant signs and symptoms of opioid withdrawal (such as vomiting and diarrhea) plus any incidents that are not typical components of the opioid withdrawal syndrome (hypotension, dry mouth)			
		▪ Completion of treatment	With consideration also to completion of withdrawal which may not be the same as completion of treatment, depending on treatment setting and procedures for screening of drug use			
Harvey[114] (Australia) F	No *[However, SR included only outcome studies relevant to diversion or after for adult drug-involved offenders]*	-	-	N/A	N/A	No
Hesse[54] (Denmark) B	Yes - specific outcomes provided	▪ Drug use	Self-report; biological markers; problem severity measured by Addiction Severity Index (ASI), Drug Abuse Screening Test (DAST) or a similar scale	Yes - 12	Yes	No
		▪ Alcohol use	self-report, biological markers, problem severity measured by Addiction Severity Index (ASI), Alcohol Use Disorder Identification Test or a similar scale			
		▪ Employment and income	Number of days working; income from work; daily activities; problem severity as measured by ASI			
		▪ Physical health	Number of days hospitalized for physical problems; SF-36 Health Questionnaire; problem severity measured by Addiction Severity Index (ASI)			

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Hjorthoj[92] (Denmark) B	Yes - but only a general reference/general class of outcomes mentioned [*Cannabis reduction or cessation in patients with a diagnosis of schizophrenia spectrum disorders (SSD) or other psychoses according to either DSM or ICD criteria were kept]*	-	-	N/A	N/A	No
Hyde[100] (UK) B	Yes - but only a general reference/general class of outcomes mentioned [*Measures of self-efficacy pre- and post-intervention - NOS]*	-	-	N/A	N/A	No
Johansson[75] (Sweden) B	No	-	-	N/A	N/A	Yes
Kirchmayer[27] (Italy) B	Yes - specific outcomes provided	▪ Retention in treatment ▪ Heroin use under treatment ▪ Side/adverse effects ▪ Social behaviour	- Number of heroin positive urine tests - Changes in work or marital status	Yes - 7	Yes	Yes
Knapp[60] (Brazil) B	Yes - specific outcomes provided	▪ Efficacy	Urine samples positive for psycho stimulant metabolites; self-reported use of psycho stimulants/relapse; frequency of drug intake; changes in craving for the drug; severity of dependence using scales such as the Addiction Severity Index (ASI), Symptoms Checklist 90; any biological marker eventually provided in original studies.	Yes - 7	Yes	Yes

TABLE B. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO TREATMENT INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
		▪ Acceptability of treatment	Total number of dropouts at the end of the trial; side effects; number of subjects who dropped out because of lack of efficacy			
		▪ Death	-			
		▪ Medical problems	-			
Laker[52] (UK) F	Yes - but only a general reference/general class of outcomes mentioned [*reduction in the use of harmful substances in dually diagnosed patients - NOS]*	-	-	N/A	N/A	No
Larney[80] (Australia) B	Yes - specific outcomes provided	▪ Illicit opioid use ▪ Injecting drug use ▪ Sharing of needles and syringes ▪ HIV incidence	- - - -	No	Yes	No

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Lima[26] (Brazil) B	Yes - specific outcomes provided	▪ Dropouts from treatment	Number of participants who did not complete treatment	Yes - 11	Yes	Yes
		▪ Acceptability of treatment	Number and type of side effects experienced during treatment			
		▪ Use of primary substance of abuse	Number of participants that reported the use of cocaine during treatment, and/or number of participants with positive urine samples for cocaine			
		▪ Results at follow-up	number of participants using cocaine at follow-up			
Liu[94] (China) B	Yes - specific outcomes provided	▪ Total score for opioid-withdrawal symptoms	-	No	Yes	Yes
		▪ Relapse rate	-			
		▪ Side effects	-			
		▪ Medicine dosage needed to allay withdrawal	-			
Liu[99] (China) B	Yes - specific outcomes provided	▪ Opioid withdrawal symptoms	Total score on the opioid withdrawal symptoms scale (WWS)	No	Yes	Yes
		▪ Anxiety	Score measured by the Hamilton Anxiety Scale (HAMA)			
		▪ Rate of adverse effects	-			

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Lobmaier[105] (Norway) B	Yes - specific outcomes provided	▪ Opioid use during and after treatment	Use/no use; number of days with use, self-report; number of positive urine samples per participant	Yes - 9	Yes	Yes
		▪ Treatment adherence	Induction: started/not started; Compliance with protocol: days met for scheduled visits/not met; percentage met/not met; number of implants voluntarily removed			
		▪ Retention in treatment	Time to drop out			
		▪ Adverse effects (AEs) and severe AEs	Percentage with/without; time to AE			
Lussier[76] (USA) B	No	-	-	N/A	N/A	Yes
Mattick[86] (Australia) - Johannson[58] (companion) B	Yes - specific outcomes provided	▪ Retention in treatment	-	Yes - 8	Yes	No
		▪ Mortality	-			
		▪ Proportion of urine or hair analysis results positive for heroin (or morphine)	-			
		▪ Self-reported heroin use	-			

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Mattick[107] (Australia) B	Yes - specific outcomes provided	▪ Retention in treatment	Measured by the number of participants still in treatment at the end of the study	Yes - 8	Yes	Yes
		▪ Use of opioids	Measured by: a) urinalysis results positive for heroin metabolite (i.e., morphine); b) self reported heroin use			
		▪ Use of other substances of abuse	Measured by: a) urinalysis results positive for cocaine; b) urinalysis results positive for benzodiazepines			
		▪ Criminal activity	Measured by self report (NOS)			
Mayet[43] (UK) B	Yes - specific outcomes provided	▪ Use of primary substance of abuse	Urine samples positive for heroin or derivatives; self reported use of opioids; frequency of drug intake; any biological marker provided in original studies (e.g. hair analysis)	Yes - 8	Yes	No
		▪ Craving	Changing craving for the drug; severity of dependence (using scales such as Addiction Severity Index, Symptoms Checklist 90)			
		▪ Retention in treatment	Number of subjects who dropped out; number re-entered into treatment			
		▪ Compliance	Measured by attendance at sessions			

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McCarthy[124] (South Africa) B	Yes - specific outcomes provided	▪ Abstinence from methaqualone at three months, six months and twelve months following the completion of treatment	Urine samples positive for metabolites; self report data (NOS)	No	Yes	No
		▪ Completion of treatment	Number of participants who complete the specified treatment regime			
		▪ Quality of life (QoL)	Self report data; positive changes in scores on quality of life scales			
McGuire[24] (UK) B	Yes - specific outcomes provided	▪ Assisted ventilation in the neonatal period	-	Yes - 9	Yes	No
		▪ Duration of assisted ventilation	-			
		▪ Admission to neonatal unit or special baby care unit	-			
		▪ Duration of neonatal unit or special baby care unit admission	-			
McGuire[128] (Australia) B	Yes - specific outcomes provided	▪ Need for assisted ventilation in the neonatal period	Any form of mechanical ventilation including continuous positive airway pressure	Yes - 9	Yes	No
		▪ Duration of assisted ventilation	In days			
		▪ Admission to neonatal intensive care unit or special care baby unit in the neonatal period	-			
		▪ Duration of neonatal intensive care unit or special care baby unit admission	In days			

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Meader[81] (UK) B	Yes - specific outcomes provided	▪ Completion of treatment	Being retained in treatment up to the final day of its planned duration; ingestion of the final does of study medication; or reaching the point of zero dose of study medication	No	Yes	No
Milligan[134] (Canada) B	Yes - but only a general reference/general class of outcomes mentioned [*maternal substance use outcomes - NOS]*	-	-	N/A	N/A	No
Mills[42] (Canada) B	Yes - specific outcomes provided	▪ Frequency of cocaine use	Self-report (NOS)	No	No	Yes
		▪ Amount of cocaine use	Self-report (NOS)			
		▪ Biochemical confirmation of cocaine abstinence	Absence of the cocaine metabolite benzoylecognine in the urine			
Minozzi[78] (Italy) B	Yes - specific outcomes provided	▪ Retention in treatment	Measured as number of participants retained at the end of the study	No	Yes	Yes
		▪ Use of primary substance of abuse	Measured as number of participants with positive urinalysis at the end of the study and self report data (NOS)			
		▪ Results at follow up	Measured as number of participants relapsed at the end of follow up			

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Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Minozzi[88] (Italy) B	Yes - specific outcomes provided	▪ Dropouts	Measured as number of subjects that did not complete the maintenance treatment	Yes - 9	Yes	Yes
		▪ Use of primary substance	Measured as number of subjects with opiate positive urine analysis during and at the end of treatment or /and self reported data (NOS)			
		▪ Results at follow up	Measured as number of subjects relapsed at the end of follow up			
Minozzi[89] (Italy) B	Yes - specific outcomes provided	▪ Dropouts from the treatment	Measured as number of participants who did not complete the detoxification	Yes - 9	Yes	Yes
		▪ Use of primary substance	Measured as number of subjects with opiate positive urine analysis during and at the end of treatment or self reported data (NOS)			
		▪ Acceptability of the treatment	Measured as duration and severity of signs and symptoms of withdrawal, including patient self-rating; side effects			
		▪ .Results at follow up	Measured as number of subjects relapsed at the end of follow up			

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Minozzi[103] (Italy) B	Yes - specific outcomes provided	▪ Dropouts from the treatment	As number of participants who did not complete the treatment	Yes - 9	Yes	Yes
		▪ Acceptability of the treatment	As number and type of side effects experienced during the treatment			
		▪ Use of primary substance of abuse	As number of participants that reported the use of cocaine during the treatment, and/or number of participants with urine samples positive for cocaine.			
		▪ Results at follow-up	As number of participants using cocaine at follow-up			
Minozzi[104] (Italy) B	Yes - specific outcomes provided *[Note: Primary outcomes provided for the women & for the child]*	Women: ▪ Drop out from treatment	Measured by number of women dropped out at the end of the intervention	Yes - 9	Yes	Yes
		▪ Use of primary substance	Measured by number of women using heroin at the end of treatment confirmed by urine analysis			
		▪ Results at follow up	Measured by number of women using heroin at the end of follow up (after the childbirth); drop out from treatment at the end of follow up (after the childbirth)			
		Child: ▪ Health status	Measured as birth weight; APGAR score (Activity, Pulse, Grimace, Appearance, and Respiration score); Neonatal Abstinence Syndrome (NAS); prenatal and neonatal mortality			
Mitchell[87] (UK) B	No	-	-	N/A	N/A	No

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Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Mitchell[131] (USA) F	Yes - but only a general reference/general class of outcomes mentioned *[post-release criminal behavior – NOS; note this concept includes drug use*]	-	-	N/A	N/A	No
NICE[132] (UK) F	Yes - specific outcomes provided *[Examples taken from Section 7.4 referring to Brief Interventions & Reduction of Injection & Sexual Risk Behaviours]* *Other sections included: Psychological Interventions; Residential, Prison and Inpatient Care*	▪ HIV seroconversion	Refers to the production of specific antibodies to antigens present in the body, resulting in a change of a serologic test from negative to positive and indicating the development of antibodies in response to infection (Macpherson, 2002).	Yes – 15 unique outcomes across the various three report sections	Yes	Yes
		▪ Injection risk behaviour	Includes the frequency of injection drug use, sharing needles and reusing needles (Darke et al., 1991)			
		▪ Sexual risk behaviour	Refers to unsafe sexual practices, including not using condoms, either with a regular or casual partner, having multiple sexual partners and anal sex (Darke et al., 1991)			

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NICE[133] (UK) B	Yes – specific outcomes provided [Examples taken from Section referring to *Pharmacological Interventions in Opioid Detoxification]* *Other report sections included: Physical Interventions In Opioid Detoxification & Psychosocial Interventions In Opioid Detoxification*	▪ Abstinence	Refers to evidence for the absence of opioid use at a particular time point (for example, at the end of treatment or at 3-month follow-up). Measures based on urinalysis or other forms of chemical testing were preferred, but self-report measures were not excluded	No – 4 unique outcomes repeatedly assessed across the two report sections	Yes	Yes
		▪ Treatment completion	Regarded as an important proxy measure of detoxification success. Completion has typically been defined as being retained in treatment up to the final day of its planned duration, ingestion of the final dose of study medication, or reaching the point of zero dose of study medication			
		▪ Safety/adverse events	Categorized broadly as due to opioid withdrawal itself or to side effects of the medication given for the detoxification regimen. During the latter stages of detoxification and in early abstinence, some signs and symptoms such as anxiety or insomnia might be the emergence of the person's 'natural state'			
		▪ Severity of withdrawal	Most frequently used scales were the Subjective Opiate Withdrawal Scale and Short Opiate Withdrawal Scale. Subjective rather than objective measures of withdrawal also used, as the former were judged by the GDG as more representative of service-user acceptability			

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Nolte[139] (Canada) B	Yes - specific outcomes provided	▪ Clinically significant response in global state ▪ Clinically significant response in general behaviour ▪ Hospital admission/relapse -Service utilization outcomes ▪ Clinically significant change in composite functioning	As defined by each of the studies (NOS) As defined by each of the studies (NOS) - As defined by each of the studies (NOS)	Yes - > 50	Yes	Yes
Nunes[48] (USA) B	Yes - but only a general reference/general class of outcomes mentioned *[Depression (symptoms) and substance use outcomes were extracted - NOS]*	-	-	N.A	N/A	No
O'Campo[84] (Canada) B	Yes - but only a general reference/general class of outcomes mentioned [*For the purposes of this realist review, we focused on research that presented evaluative program data on outcomes related to mental health and substance use disorders among homeless clients with CDs]*	-	-	N/A	N/A	Yes

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O'Connor[19] (USA) B	Yes - specific outcomes provided	▪ Clinical outcomes (NOS) ▪ Length of follow-up ▪ Adverse effects (NOS)	- - -	No	No	Yes
Osborn[39] (Australia) B	Yes - specific outcomes provided	▪ Treatment failure ▪ Seizures ▪ Neonatal and infant mortality ▪ Neurodevelopmental outcome	Including failure to achieve control defined as a failure to reduce a standardized score of NAS from a clinically significant level to a clinically safe level defined by author of trial, or the use of additional pharmacological treatments for control of NAS in the neonatal period, - - -	Yes - 13	Yes	No

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Osborn[40] (Australia) B	Yes - specific outcomes provided	▪ Treatment failure	Including failure to achieve control defined as a failure to reduce a standardized score of NAS from a clinically significant level to a clinically safe level defined by author of trial; or the use of additional pharmacological treatments for control of NAS in the neonatal period	Yes - 13	Yes	Yes
		▪ Seizures	-			
		▪ Neonatal and infant mortality	-			
		▪ Neurodevelopmental outcome	-			
O'Shea[65] (NR) B	Yes - specific outcomes provided	▪ Mortality from treatment failure	-	Yes - 15	Yes	Yes
		▪ Proportion of drug-free days	-			
		▪ Proportion of drug metabolite-free urine samples	-			
		▪ Retention in the trial	-			

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Pani[126] (Italy) B	Yes - specific outcomes provided	▪ Dropouts from treatment	Number of participants who did not complete the treatment	Yes - 9	Yes	Yes
		▪ Acceptability of treatment	Number and type of side effects experienced during the treatment			
		▪ Use of primary substance of abuse	Number of participants that reported the use of cocaine during the treatment, and/or number of participants with urine samples positive for cocaine			
		▪ Results at follow-up	Number of participants using cocaine at follow-up			
Parr[117] (Australia) B	Yes - specific outcomes provided	▪ Proportions of participants ceasing benzodiazepine use in each condition	-	No	Yes	No

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Perry[72] (UK) - Perry[93] (co-publication) F	Yes - specific outcomes provided	▪ Drug use	Measured by: self-report drug use (unspecified drug, not including alcohol); self-report drug use (specific drug); Addiction Severity Index (ASI drug use); drug testing by urine analysis; drug testing by hair analysis; saliva analysis; any other additional tools (e.g., MAP or ISS)	No	Yes	No
		▪ Criminal activity	Arrest for any offence (self-report/official records); arrest for a drug offence (self-report/official records); arrest for a technical violation (self-report/official records); conviction for any offence (self-report/official records); conviction for a drug offence (self-report/official records); incarceration for any offence (self-report/official records); Incarceration for a drug offence (self-report/official records); recidivism (self-report/official records); criminal activity (self-report/official records)			
Petrie[69] (UK) B	Yes - specific outcomes provided	▪ Smoking, drinking or drug use by child	Objective or self-reported measure (NOS)	No	Yes	No
		▪ Intention of child to participate in smoking, drinking or using drugs	Objective or self-reported measure (NOS)			
		▪ Alcohol and drug-related risk behaviours in child	Such as criminal offending, antisocial behaviour, risky sexual behaviour using an objective or self-reported measure (NOS)			
		▪ Antecedent behaviours	Such as truancy, conduct disorders, or poor academic performance by objective or self-reported measure (NOS)			

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Prendergast[30] (USA) F	No	-	-	N/A	N/A	No
Prendergast[66] (USA) B	Yes - but only a general reference/general class of outcomes mentioned *[Measures of drug use - NOS]*	-	-	N/A	N/A	No

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Rathbone[98] (UK) B	Yes - specific outcomes provided	▪ Death (suicide or natural causes)	-	Yes – >12 outcomes categories (with sub outcomes listed)	Yes	Yes
		▪ Mental state	No clinically important change in general mental state; not any change in general mental state; average endpoint general mental state score; average change in general mental state scores; etc.			
		▪ General functioning	No clinically important change in general functioning; not any change in general functioning; average endpoint general functioning score; average change in general functioning scores; no clinically important change in specific aspects of functioning, such as social or life skills; etc.			
		▪ Global state	relapse/time to relapse; no clinically important change in global state; not any change in global state; average endpoint global state score; average change in global state scores			

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Roozen[35] (The Netherlands) B	Yes - specific outcomes provided	▪ Relapse rates	Defined as drinking at least 4 alcoholic drinks for women, 5 for men, on an occasion or single day	No	Yes	No
		▪ Continuous abstinence	Confirmed by urine tests, blood samples or self report OR abstinence percentage (the proportion of participants abstinent during follow-up period)			
		▪ Frequency of substance abuse	Percentage of drinking days or days using drugs			
		▪ Time to first relapse	-			
Roozen[49] (The Netherlands) B	Yes - specific outcomes provided	▪ Continuous abstinence	Determined by urine samples, blood samples or self-reports.	No	Yes	No
		▪ Addiction severity	Measured for example according to the Addiction Severity Index (ASI)			
		▪ Frequency of substance abuse	Measured for example according to the number of (heavy) drinking days			
		▪ Time to relapse	-			

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Shoptaw[90] (USA) B	Yes - specific outcomes provided	▪ Discontinuation rate	Measured as number of participants who did not complete the treatment	Yes - 7	Yes	Yes
		▪ Average score in global state	Measured by global psychiatric rating scales, e.g. Clinical Global Impression			
		▪ Average score in withdrawal symptoms	Measured by withdrawal symptomatology assessments, e.g. Amphetamine Withdrawal Questionnaire			
		▪ Average score in craving	Measured by craving rating scales, e.g. Questionnaire for Evaluating Cocaine Craving and Related Responses, Visual Analog Scale, Brief Substance Craving Scale			
Simoens[44] (Belgium) B	Yes - specific outcomes provided	▪ Abstinence from illicit opiate use	-	Yes - 12	Yes	No
		▪ Reduction in illicit opiate use	-			
		▪ Withdrawal severity	-			
		▪ Retention in treatment	-			
Smith[123] (UK) B	Yes - specific outcomes provided	▪ Illicit drug use	Measured by self-report or urinalysis during treatment or follow-up	Yes - 10	No	Yes
		▪ Alcohol use	Measured by self-report or urinalysis during treatment or follow-up			
		▪ Retention in treatment	-			
		▪ Reasons for withdrawal from treatment	-			

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Soares[25] (Brazil) B	Yes - specific outcomes provided	▪ Acceptability of the treatment	Measured by the number of people reporting adverse events and dropping out during the trial/ post randomization exclusions	Yes – 5 primary outcomes (with 7 secondary outcomes noted)	Yes	Yes
		▪ Efficacy - Abstinence from using cocaine	Measured by urine samples positive for cocaine metabolite (dichotomous); self-report			
		▪ Efficacy - Severity of dependence	Measured by using scales such as the Addiction Severity Index (ASI); retention time in treatment (continuous)			
		▪ Efficacy - Amount of cocaine use	Measured by grams used or dollars spent			
Srisurapanont[33] (Thailand) B	Yes - specific outcomes provided	▪ Number of people who relapse to amphetamine dependence or abuse	-	Yes - 16	Yes	Yes
		▪ Number of people who return to amphetamine use	Defined as those that do not meet the priori criteria for amphetamine dependence or abuse			
		▪ Discontinuation rate	-			
		▪ Death	-			
Stoffel[47] (USA) B	No	-	-	N/A	N/A	No
Tait[21] (Australia) B	No	-	-	N/A	N/A	No

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Terplan[55] (UK) B	Yes - specific outcomes provided	▪ Obstetrical outcomes ▪ Neonatal outcomes ▪ Use of primary substance abuse ▪ Retention in treatment	Birth weight; gestational age at birth; placental abruption Neonatal abstinence syndrome; admission to and length of time spent in neonatal intensive care unit Maternal toxicology; maternal self-report; newborn toxicology; any biological marker eventually provided in original studies Number of subjects retained at the end of the study	Yes - 7	Yes	No
Theis[20] (Canada) B	No	-	-	N/A	N/A	No
Vanderplasschen[61] (Belgium) B	No	-	-	N/A	N/A	No
Vaughn[111] (USA) B	Yes - but only a general reference/general class of outcomes mentioned [*Substance use treatment outcomes (as opposed to compliance, safety, other problem behaviors, or prevention-only outcomes); drug use outcomes – NOS] were examined]*	-	-	N/A	N/A	No
Voshaar[68] (NR) B	No	-	-	N/A	N/A	No

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Waldron[101] (USA) B	No	-	-	N/A	N/A	No
Watkins[37] (USA) B	No	-	-	N/A	N/A	No
White[18] (UK) D	No	-	-	N/A	N/A	No
Wobrock[109] (Germany) B	No	-	-	N/A	N/A	Yes
Wright[73] (UK) B	Yes - specific outcomes provided	▪ Reduction in sexual risk behaviour ▪ Reduction in drug taking risk behaviour ▪ Changes in self esteem and coping ▪ Changes in awareness and knowledge of risk factors	As evidenced by an Increased frequency of condom use; or a reduction in number of sexual partners - - -	No	Yes	No
Zgierska[82] (USA) B	No	-	-	N/A	N/A	Yes

HARMS REDUCTION INTERVENTIONS

TABLE C. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO HARMS REDUCTION INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Baral[56] (USA) C	No	-	-	N/A	N/A	No
Elliott[41] (UK) F	Yes - but only a general reference/general class of outcomes mentioned [*impact on drug use or the psychological or social problems associated with drug use - NOS*]	-	-	N/A	N/A	No
Gibson[116] (USA) C	No	-	-	N/A	N/A	No
Harvey[114] (Australia) F	No *[However, SR included only outcome studies relevant to diversion or after for adult drug-involved offenders]*	-	-	N/A	N/A	No
Holloway[63] (UK) C	Yes - but only a general reference/general class of outcomes mentioned [*must include a measure of criminal behaviour - NOS*]	-	-	N/A	N/A	No

TABLE C. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO HARMS REDUCTION INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Jones[137] (UK) C	Yes - specific outcomes provided	▪ Changes in drug injecting behaviours (NOS) ▪ Incidence and prevalence of blood borne viral infections	- -	No	Yes	No
Laker[52] (UK) F	Yes - but only a general reference/general class of outcomes mentioned [*reduction in the use of harmful substances in dually diagnosed patients - NOS]*	-	-	N/A	N/A	No
Meader[129] (UK) C	Yes - specific outcomes provided	▪ Reduction in injection risk behaviour ▪ Reduction in sexual risk behaviour ▪ HIV seroconversion	- - -	No	Yes	No
Mitchell[131] (USA) F	Yes - but only a general reference/general class of outcomes mentioned *[post-release criminal behavior – NOS; note this concept includes drug use*]	-	-	N/A	N/A	No

TABLE C. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO HARMS REDUCTION INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
NICE Report 51[132] (UK) F	Yes - specific outcomes provided *[Examples taken from Section 7.4 referring to Brief Interventions & Reduction of Injection & Sexual Risk Behaviours]* *Other sections included: Psychological Interventions; Residential, Prison and Inpatient Care*	▪ HIV seroconversion ▪ Injection risk behaviour ▪ Sexual risk behaviour	Refers to the production of specific antibodies to antigens present in the body, resulting in a change of a serologic test from negative to positive and indicating the development of antibodies in response to infection (Macpherson, 2002). Includes the frequency of injection drug use, sharing needles and reusing needles (Darke et al., 1991) Refers to unsafe sexual practices, including not using condoms, either with a regular or casual partner, having multiple sexual partners and anal sex (Darke et al., 1991)	Yes – 15 unique outcomes across the various three report sections	Yes	Yes
Novick[108] (USA) C	No	-	-	N/A	N/A	Yes

TABLE C. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO HARMS REDUCTION INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Perry[72] (UK) - Perry[93] (co-publication) F	Yes - specific outcomes provided	▪ Drug use	Measured by: self-report drug use (unspecified drug, not including alcohol); self-report drug use (specific drug); Addiction Severity Index (ASI drug use); drug testing by urine analysis; drug testing by hair analysis; saliva analysis; any other additional tools (e.g., MAP or ISS)	No	Yes	No
		▪ Criminal activity	Arrest for any offence (self-report/official records); arrest for a drug offence (self-report/official records); arrest for a technical violation (self-report/official records); conviction for any offence (self-report/official records); conviction for a drug offence (self-report/official records); incarceration for any offence (self-report/official records); Incarceration for a drug offence (self-report/official records); recidivism (self-report/official records); criminal activity (self-report/official records)			

TABLE C. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO HARMS REDUCTION INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
Pendergast[30] (USA) F	No	-	-	N/A	N/A	No
Prendergast[34] (USA) C	Yes - but only a general reference/general class of outcomes mentioned *[General mention of dependent variables – injection practices; sexual behaviour – NOS]*	-	-	N/A	N/A	No
Sorensen[112] (USA) C	No	-	-	N/A	N/A	No
Starrels[136] (USA) C	Yes - specific outcomes provided	▪ Opioid misuse	Behaviours described as aberrant or indicative of abuse, misuse, or diversion, consistent with the terminology recommended by Ballantyne and LaForge. Could have been measured from patients, providers, medical charts, or lab tests. Urine drug testing confirmed with gas or liquid chromatography and mass spectrometry.	No	Yes	No

TABLE C. OUTCOMES FOR SYSTEMATIC REVIEWS (SRS) RELATED TO HARMS REDUCTION INTERVENTIONS (*NOS – NOT OTHERWISE SPECIFIED)

Author (Country of 1st Author)	Pre-specified outcomes of interest provided?	Pre-specified outcomes *A max. of 4 listed below	Reported Outcome measurements/ Definitions	>5 outcomes pre-specified?	All pre-specified outcomes reported in SR results?	Any outcomes for harms reported?
White[18] (USA) D	No	-	-	N/A	N/A	No
Wright[67] (UK) C	Yes - specific outcomes provided	▪ Prevalence of hepatitis C infection ▪ Incidence of hepatitis C infection	- -	No	Yes	No
Yung[57] (Canada) C	Yes - specific outcomes provided	▪ Complete cure (both clinical and microbiological, after completion of therapy until the end of the follow-up period)	Clinical cure was defined as the disappearance of clinical signs or symptoms of infection including improvement on radiographic assessment. Microbiological cure was specified in the presence of negative blood cultures.	No	Yes	Yes
		▪ Failure	Defined for all patients not achieving clinical or microbiological cure, therefore requiring modification or discontinuation of the assigned therapy or resulting in death.			

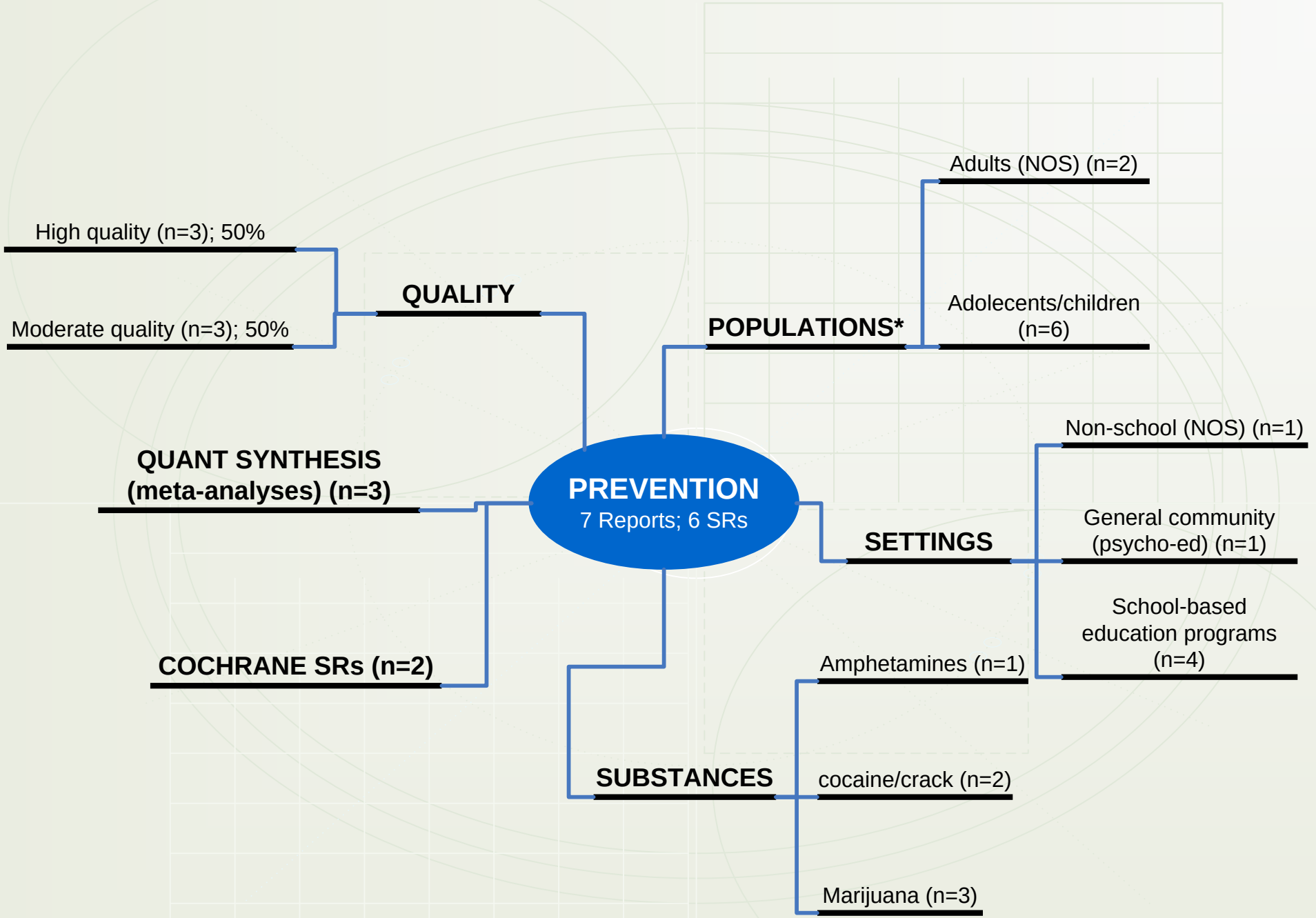
APPENDIX J. AMSTAR RESPONSES (N=117)

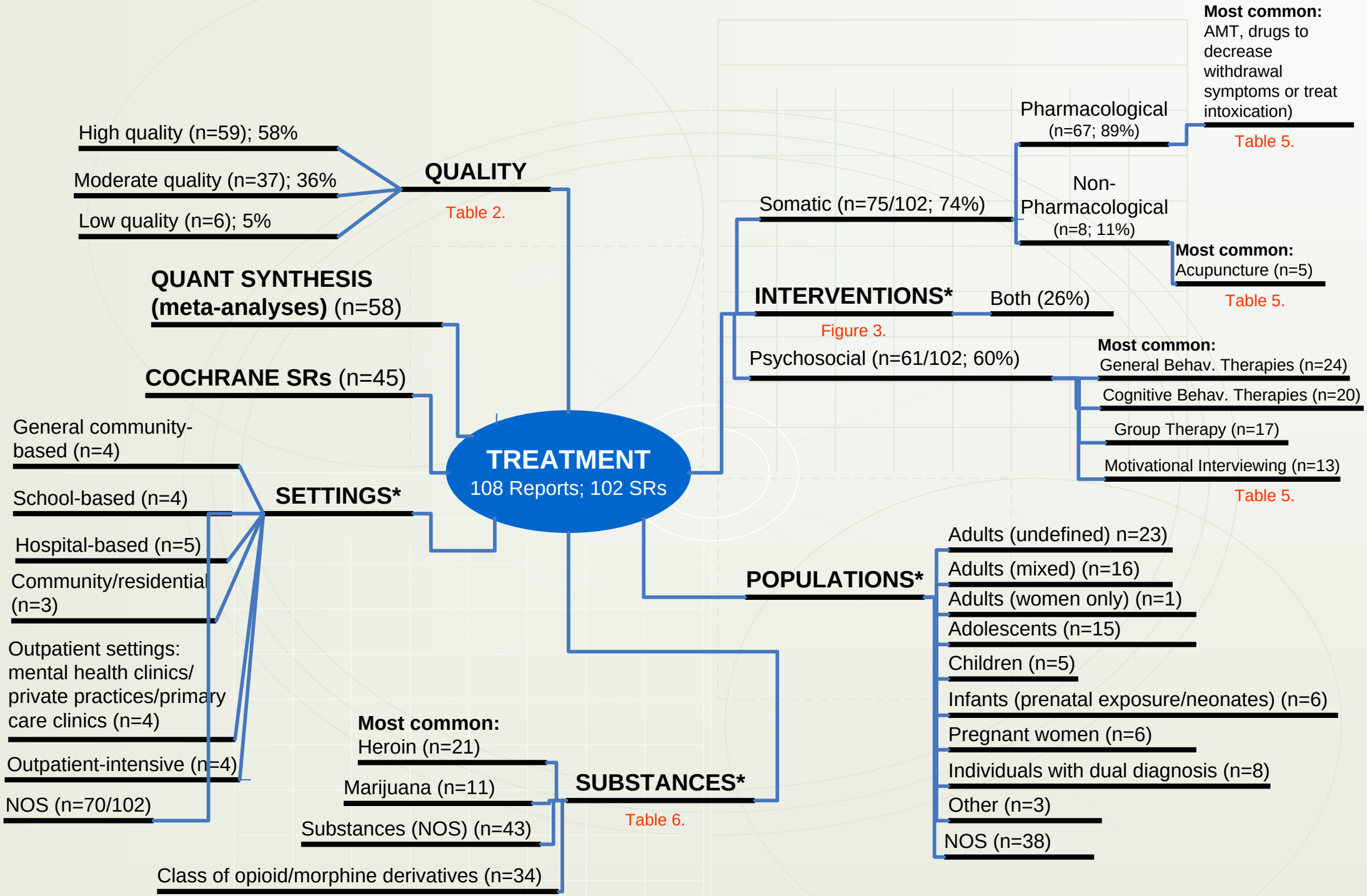
Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total Scores
Adi[64]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	8/11
Alvarez[85]	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7/11
Amato[38]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Amato[59]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Amato[96]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
Amato[97]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Austin[113]	Yes	No	No	No	No	Yes	Yes	Yes	No	No	No	4/11
Bale[16]	No	No	No	Yes	No	No	No	No	No	No	No	1/11
Baral[56]	No	Yes	Yes	No	No	Yes	No	No	No	No	No	3/11
Bosch-Capblanch[127]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
Castells[53]	No	No	No	No	No	No	No	No	No	No	Yes	1/11
Castells[130]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Clark[29]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Cleary*[95;115]	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	6/11
Cleary[110]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Colantonio[17]	No	No	Yes	Yes	No	Yes	Yes	Yes	No	No	No	5/11
Connock[62]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
D'Alberto[45]	No	No	Yes	Yes	No	Yes	Yes	Yes	No	No	No	5/11
Day[120]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
de Lima[28]	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8/11
Denis[70]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
Denis[71]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
Doggett[36]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Donald[46]	No	No	Yes	No	No	Yes	No	No	N/A	No	No	2/10
Doran[102]	No	No	Yes	Yes	No	Yes	Yes	Yes	No	No	No	5/11
Druss[118]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	7/11
Elliott[41]	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	6/11
Faggiano*[51;122]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
Faggiano[23]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Farre[32]	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	6/11
Ferri*[79;119;138]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Fletcher[50]	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7/11
Gates[77]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
* Denotes more than one citation (i.e., co-publication, companion record) was used to inform the assessment of the AMSTAR items												

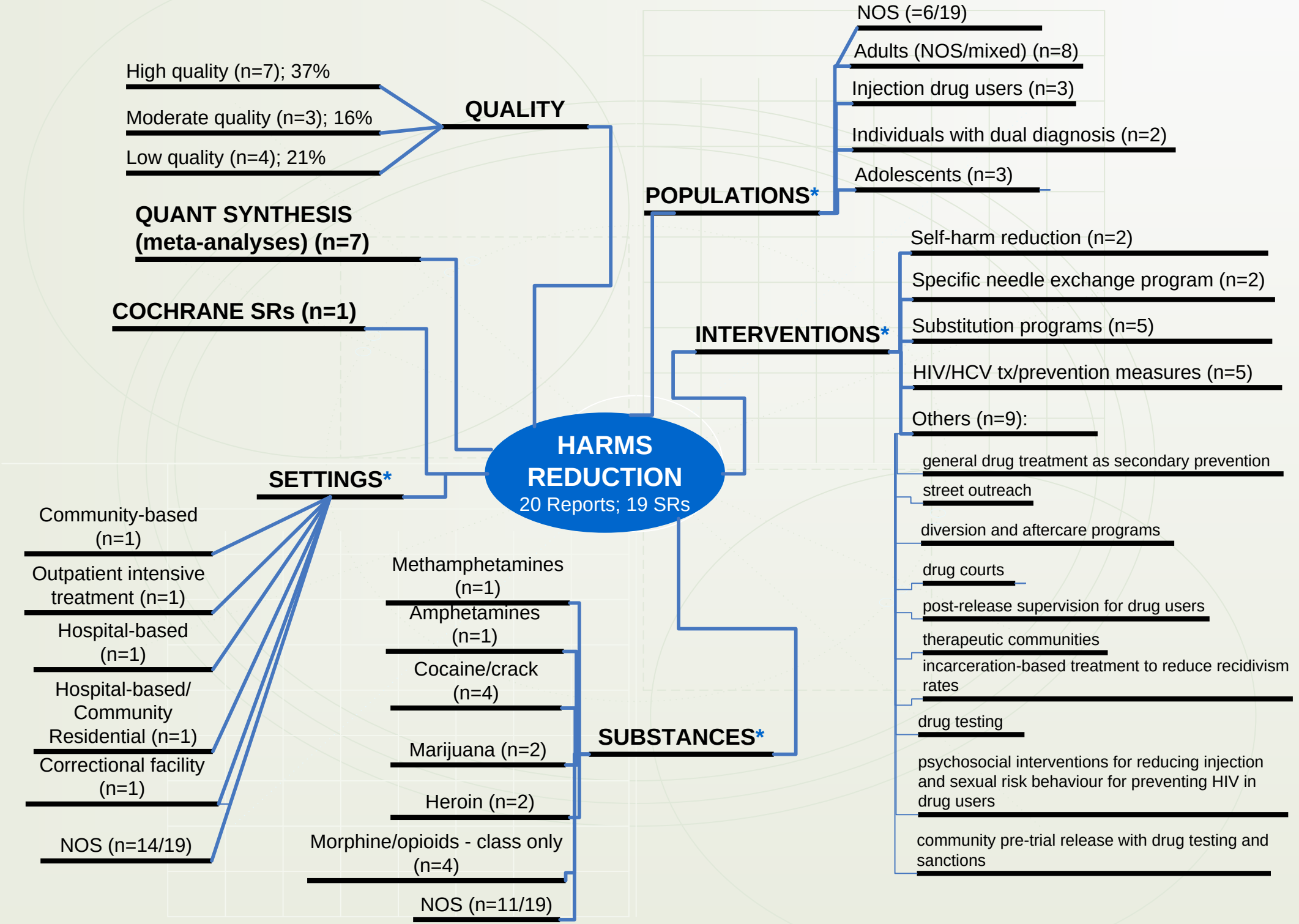
Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total Scores
Gates[121]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	8/11
Gibson[116]	No	Yes	No	No	No	Yes	No	No	Yes	No	No	3/11
Gowing*[31;91]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
Gowing[74]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	8/11
Gowing[83]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	8/11
Gowing[106]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
Gowing[125]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	8/11
Harvey[114]	No	No	Yes	No	No	Yes	Yes	Yes	Yes	No	No	5/11
Hesse[54]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Hjorthoj[92]	No	No	Yes	C/A	No	Yes	Yes	Yes	N/A	No	C/A	4/10
Holloway[63]	No	No	No	Yes	No	Yes	Yes	Yes	Yes	No	No	5/11
Hyde[100]	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	7/11
Johansson[75]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	8/11
Jones[137]	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	6/11
Kirchmayer[27]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	8/11
Knapp[60]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
Laker[52]	No	No	No	No	No	No	Yes	Yes	No	No	No	2/11
Larney[80]	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	6/11
Lima[26]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Liu[94]	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8/11
Liu[99]	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7/11
Lobmaier[105]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
Lussier[76]	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	7/11
Mattick[86]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
Mattick[107]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
Mayet[43]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
McBride[22]	No	No	Yes	Yes	No	Yes	No	Yes	No	No	No	4/11
McCarthy[124]	Yes	Yes	Yes	Yes	N/A	N/A	N/A	N/A	N/A	N/A	N/A	4/11
McGuire[24]	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7/11
McGuire[128]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	8/11
Meader[81]	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	6/11
Meader[129]	No	No	Yes	No	No	Yes	Yes	Yes	Yes	No	No	5/11
Milligan[134]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11/11
Mills[42]	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7/11
Minozzi[78]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7/11
* Denotes more than one citation (i.e., co-publication, companion record) was used to inform the assessment of the AMSTAR items												

Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total Scores
Minozzi[88]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Minozzi[89]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Minozzi[103]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Minozzi[104]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Mitchell[87]	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	7/11
Mitchell[131]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
NICE clinical guideline 51[132]	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	8/11
NICE clinical guideline 52[133]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	10/11
Nolte[139]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Novick[108]	No	No	Yes	No	Yes	Yes	No	No	No	No	No	3/11
Nunes[48]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	9/11
O'Campo[84]	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	No	No	6/11
O'Connor[19]	Yes	No	No	No	No	Yes	Yes	Yes	Yes	No	No	5/11
Osborn[39]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
Osborn[40]	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	7/11
O'Shea[65]	No	No	No	Yes	No	Yes	Yes	Yes	No	No	No	4/11
Pani[126]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Parr[117]	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	6/11
Perry[72;93]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11/11
Petrie[69]	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7/11
Porath-Waller[135]	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8/11
Prendergast[30]	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	9/11
Prendergast[34]	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	9/11
Prendergast[66]	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	8/11
Rathbone[98]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	9/11
Roozen[35]	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	7/11
Roozen[49]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	8/11
Shoptaw[90]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	9/11
Simoens[44]	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	7/11
Smith[123]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	N/A	No	No	7/10
Soares[25]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Sorensen[112]	No	No	Yes	Yes	No	Yes	No	No	Yes	No	No	4/11
Srisurapanont[33]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	9/11
Starrels[136]	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	7/11
Stoffel[47]	No	No	Yes	No	No	No	Yes	Yes	No	No	No	3/11
* Denotes more than one citation (i.e., co-publication, companion record) was used to inform the assessment of the AMSTAR items												

Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total Scores
Tait[21]	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	6/11
Terplan[55]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
Theis[20]	No	No	No	No	No	Yes	Yes	Yes	Yes	No	No	4/11
Vanderplasschen[61]	No	No	Yes	Yes	No	Yes	No	No	No	Yes	No	4/11
Vaughn[111]	No	No	Yes	No	No	Yes	Yes	Yes	Yes	No	No	5/11
Voshaar[68]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	8/11
Waldron[101]	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	6/11
Watkins[37]	No	No	Yes	No	No	No	No	No	No	No	No	1/11
White[18]	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	7/11
Wobrock[109]	No	No	Yes	No	No	Yes	Yes	Yes	No	No	No	4/11
Wright[67]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	8/11
Wright[73]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	8/11
Yung[57]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	9/11
Zgierska[82]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	8/11
* Denotes more than one citation (i.e., co-publication, companion record) was used to inform the assessment of the AMSTAR items												


PREVENTION
7 Reports; 6 SRs
QUALITY
High quality (n=3); 50%
Moderate quality (n=3); 50%
QUANT SYNTHESIS (meta-analyses) (n=3)
COCHRANE SRs (n=2)
POPULATIONS*
Adults (NOS) (n=2)
Adolecents/children (n=6)
SETTINGS
Non-school (NOS) (n=1)
General community (psycho-ed) (n=1)
School-based education programs (n=4)
SUBSTANCES
Amphetamines (n=1)
cocaine/crack (n=2)
Marijuana (n=3)


TREATMENT
108 Reports; 102 SRs
QUALITY
Table 2.
High quality (n=59); 58%
Moderate quality (n=37); 36%
Low quality (n=6); 5%
QUANT SYNTHESIS (meta-analyses) (n=58)
COCHRANE SRs (n=45)
SETTINGS*
General community-based (n=4)
School-based (n=4)
Hospital-based (n=5)
Community/residential (n=3)
Outpatient settings: mental health clinics/ private practices/primary care clinics (n=4)
Outpatient-intensive (n=4)
NOS (n=70/102)
SUBSTANCES*
Table 6.
Most common:
Heroin (n=21)
Marijuana (n=11)
Substances (NOS) (n=43)
Class of opioid/morphine derivatives (n=34)
INTERVENTIONS*
Figure 3.
Somatic (n=75/102; 74%)
Psychosocial (n=61/102; 60%)
Both (26%)
Pharmacological (n=67; 89%)
Non-Pharmacological (n=8; 11%)
Most common:
AMT, drugs to decrease withdrawal symptoms or treat intoxication)
Table 5.
Most common:
Acupuncture (n=5)
Table 5.
Most common:
General Behav. Therapies (n=24)
Cognitive Behav. Therapies (n=20)
Group Therapy (n=17)
Motivational Interviewing (n=13)
Table 5.
POPULATIONS*
Adults (undefined) n=23)
Adults (mixed) (n=16)
Adults (women only) (n=1)
Adolescents (n=15)
Children (n=5)
Infants (prenatal exposure/neonates) (n=6)
Pregnant women (n=6)
Individuals with dual diagnosis (n=8)
Other (n=3)
NOS (n=38)


HARMS REDUCTION
20 Reports; 19 SRs
QUALITY
High quality (n=7); 37%
Moderate quality (n=3); 16%
Low quality (n=4); 21%
QUANT SYNTHESIS (meta-analyses) (n=7)
COCHRANE SRs (n=1)
SETTINGS*
Community-based (n=1)
Outpatient intensive treatment (n=1)
Hospital-based (n=1)
Hospital-based/ Community Residential (n=1)
Correctional facility (n=1)
NOS (n=14/19)
SUBSTANCES*
Methamphetamines (n=1)
Amphetamines (n=1)
Cocaine/crack (n=4)
Marijuana (n=2)
Heroin (n=2)
Morphine/opioids - class only (n=4)
NOS (n=11/19)
POPULATIONS*
NOS (=6/19)
Adults (NOS/mixed) (n=8)
Injection drug users (n=3)
Individuals with dual diagnosis (n=2)
Adolescents (n=3)
INTERVENTIONS*
Self-harm reduction (n=2)
Specific needle exchange program (n=2)
Substitution programs (n=5)
HIV/HCV tx/prevention measures (n=5)
Others (n=9):
general drug treatment as secondary prevention
street outreach
diversion and aftercare programs
drug courts
post-release supervision for drug users
therapeutic communities
incarceration-based treatment to reduce recidivism rates
drug testing
psychosocial interventions for reducing injection and sexual risk behaviour for preventing HIV in drug users
community pre-trial release with drug testing and sanctions