Drug use disorder module - evidence profile DRU3: Psychosocial interventions for adults with stimulant dependence/subjects with moderate or severe stimulant use disorder

WHO mhGAP guideline update: Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders

2023

World Health Organization

Contents

Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders, available at: https://www.who.int/publications/i/item/9789240084278

1. Background

Cocaine and amphetamines are the most commonly abused stimulants in people aged 15–64 years. New psychoactive substances such as amphetamine-type stimulants, methamphetamine, and ecstasy have benne also widespread used in the recent years. Patients addicted to stimulants experience a range of psychological and physical sequelae including psychosis and other mental illnesses, neurological disorders and cognitive deficits, cardiovascular dysfunctions, sexually transmitted diseases, and blood-borne viral infections such as HIV and hepatitis B and C, and are at increased risk of all-cause mortality. Moreover, the social burden of stimulant abuse is worsened by its association with crime, violence, and sexual abuse.

At the present time, there is no widely accepted treatment for psychostimulant disorders. No evidence for efficacy has been found for pharmacological treatments. Currently, international clinical guidelines recommend the use of psychosocial interventions for cocaine and/or amphetamine addiction as first-line treatment. In the absence of approved pharmacotherapies, several structured psychosocial and self-help approaches are available, such as contingency management (CM) (a behavioural approach that consists in providing stimulant users with rewards upon drug-free urine samples), community reinforcement approach (a multi-layered intervention involving functional analysis, coping-skills training, and social, familial, recreational, and vocational reinforcements), and 12-step programme (a set of guiding principles outlining a course of action for self-help recovery from addiction). However, there is not clear evidence on which is the most effective approach both in the short and long term.

With the present review, we aim to assess the effectiveness of psychosocial treatments for psychostimulant abuse and dependence in adults to help health decision makers, therapists and patients to take decision informed by the best available evidence from the scientific literature.

2. Methodology

2.1. PICO question

Population (P): Adults (18 years and older) with stimulant dependence according to DSM-III (APA 1980), DSM- III-R (APA 1987), DSM-IV-TR (APA 2000), or ICD-10 (WHO 1992; WHO 2010) or subjects with moderate or severe stimulant use disorder according to DSM-5 (APA 2013),

Intervention (I): Psychosocial interventions. We will consider any of the following psychosocial treatments.

- Cognitive behavioural approach, including: cognitive therapy, community reinforcement approach, coping skills training (CST), relapse prevention.
- Contingency management approach.
- Motivational interviewing approach (motivational interviewing, motivational enhancement).
- Interpersonal therapy approach.
- Psychodynamic therapy and supportive expressive therapy.
- 12-step approach.

We will include studies if they consider the above treatments alone or in combination with other types of treatment.

We will not include other eclectic approaches. We will only include structured and standardized interventions.

Case management and counselling are usually provided in standard care (treatment as usual), so we will not consider them among the experimental interventions.

We will exclude studies that compared the same type of intervention as a different modality or at a different intensity (e.g. intensive versus standard, group versus individual, long versus short)

Comparator (C):
•No treatment
• Treatment as usual (including counselling, case management, clinical management, pharmacotherapy or other active intervention also provided to the experimental group)
• Other psychosocial treatment
• Pharmacological treatment

Types of comparisons foreseen
• Any psychosocial approach versus no treatment (including studies where any psychosocial intervention was given in addition to any other treatment , included treatment as usual, which was received by both groups)
• Any psychosocial approach versus treatment as usual
• Any psychosocial approach versus an alternative psychosocial approach

Outcomes (O):

<u>List critical outcomes:</u>
•Dropouts from treatment: number of participants who did not complete the study protocol
• Use of primary substance of abuse, measured as:
* Point abstinence (number of participants abstinent at the end of treatment, self reported);
* Point abstinence (number of participants with negative urine samples at the end of treatment);
* Continuous abstinence (number of participants with continuous abstinence during treatment, self reported);
* Continuous abstinence (number of participants with negative urine during treatment);
* Frequency of drug intake;
* Longest period of abstinence

<u>List important outcomes:</u>
•Craving, as measured by validated scales (e.g. Brief Substance Craving Scale (BSCS), visual analogue scale [VAS]).
• Adverse events.
• Severity of dependence, as measured by validated scales (e.g. Addiction Severity Index [ASI], Clinical Global Impression scale (CGI-S), Clinical Global Impression - Observer Scale [CGI-O]).
• Depression, as measured by validated scales (Hamilton Depression Rating Scale, Beck Depression Inventory).

Subgroups:
no subgroups analyses planned

3. Methodology. Phase 1. Search for relevant systematic reviews

3.1. Search strategy

The Cochrane Drugs and Alcohol review group published in 2016 a systematic review on the effect of psychosocial treatments for people with psychostimulant use disorders. Therefore, We searched for systematic reviews on the effectiveness of psychological treatments for the management of psychostimulant use disorders on MEDLINE, Embase, PsycInfo, Web of Science Core Collection, Epistemonikos and PROSPERO from 2015 to 14 January 2022. The detailed search strategy for each database is provided in Appendix IIa. The inclusion criteria were: systematics reviews of randomized controlled trials that assessed the effect of psychosocial treatments listed in our inclusion criteria compared to no treatment, usual care, pharmacological treatments to achieve and maintain abstinence or reduce psychostimulant consumption in adults with psychostimulant use disorders.

3.2. Data collection and analysis

As the first stage in selecting relevant studies, records retrieved from the bibliographic databases and from other sources were recorded and assessed for eligibility by examining their titles and abstracts only. This assessment was performed in accordance with the inclusion and exclusion criteria developed a priori. The full text of articles found to be potentially relevant on the basis of their titles and abstracts were retrieved and examined in light of the same inclusion criteria in the second stage of study selection. Two reviewers independently screened records retrieved with the search and evaluated full text of potentially relevant reviews.

3.3. Selection and coding of identified records

We used EndNote X7 as reference management software

3.4. Quality assessment

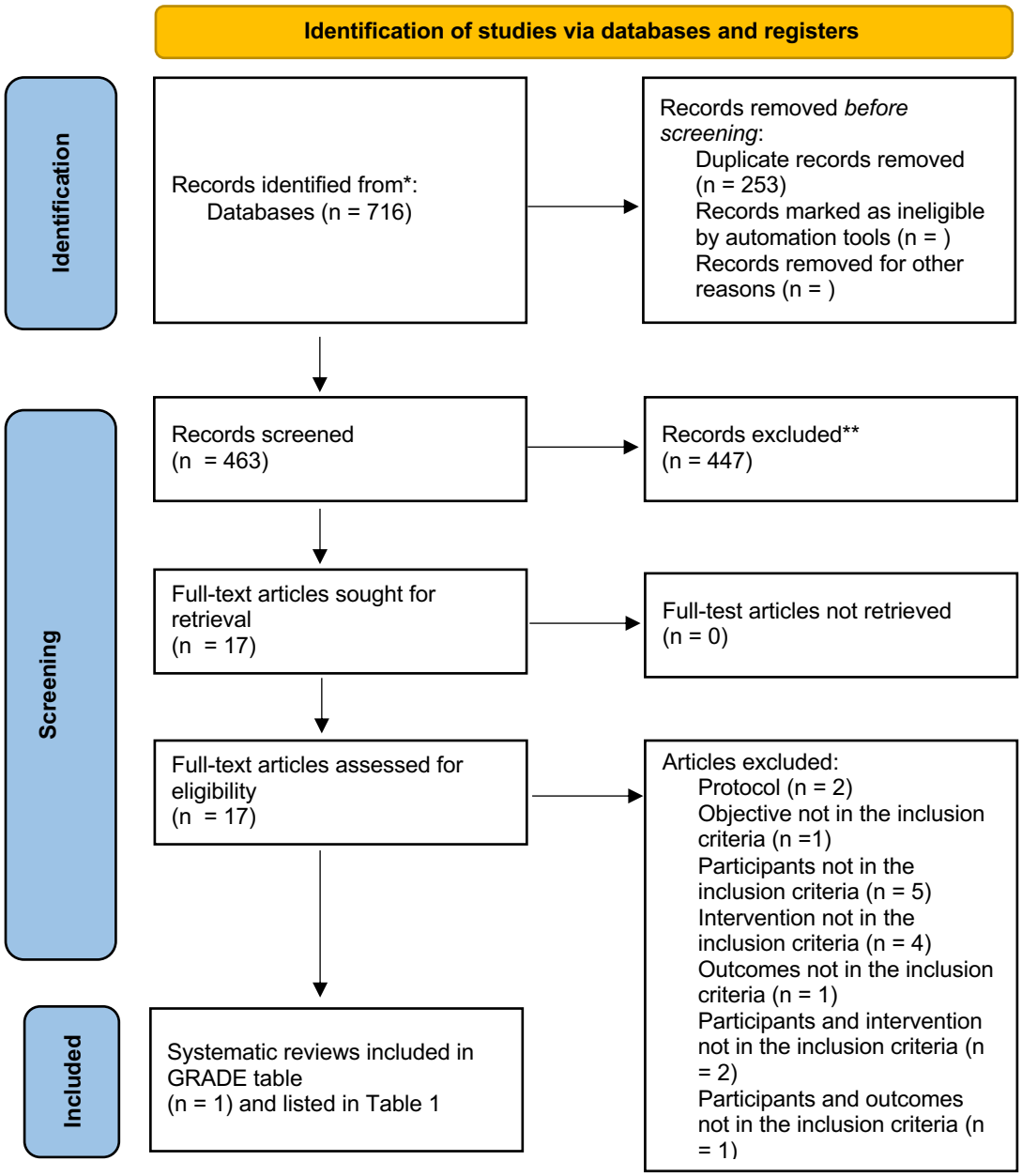
We assessed the methodological quality of retrieved reviews with AMSTAR 2 checklist (https://amstar.ca/Amstar_Checklist.php

3.5. Analysis of subgroups or subsets

No subgroup analysis was undertaken in phase 1

4. Results. Phase 1.

Fig. 1. PRISMA 2020 flow diagram for systematic review of reviews which includes searches of databases and registers only



4.1. Systematic reviews and/or studies identified by the search process

After removing duplicates, we screened 463 titles and abstracts. Seventeen reviews were judged as potentially relevant and acquired in full text. Sixteen reviews were excluded for the following reasons:

Protocol of systematic review (Hamel 2020, Stuart 2017).

Objective not in the inclusion criteria: description of the intervention, efficacy not assessed (De Giorgi 2018).

Participants not in the inclusion criteria: only methamphetamine use disorder (AshaRani 2020, Stuart 2020), only cocaine use disorders (Bentzley 2021), only amphetamine types stimulants (Tran 2021), only women (De Giorgi 2017)

Intervention not in the inclusion criteria: only cognitive behavioural therapy (Harada 2018), Contingency management combined with pharmacological interventions (Tardelli 2018), pharmacological interventions alone or combined with cognitive behavioural therapy (Khoramizadeh 2019), only contingency management and cognitive behavioural therapy (Ronslley 2020),

Outcomes not in the inclusion criteria: only abstinence and dropout of treatment assessed (De Crescenzo 2018),

Participants and intervention not in the inclusion criteria: only contingency management for methamphetamines use (Brown 2020), only 12 steps approach considered, no separate data provided for stimulant use participants (Bøg 2017)

Participants and outcomes not in the inclusion criteria (only anxiety in subjects with methamphetamines use (Hellem 2016).

We evaluated the methodological quality of Minozzi 2016 that was judged of high quality. The details of methodological quality of the retrieved revies are shown in appendix II b.

References of excluded reviews are reported in Appendix IIc

Therefore, we decided that the most appropriate approach will be to update the existing Cochrane Minozzi S, Saulle R, De Crescenzo F, Amato L. Psychosocial interventions for psychostimulant misuse. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD011866. DOI: 10.1002/14651858.CD011866.pub2

5. Methodology. Phase 2. Update of Cochrane systematic review "Minozzi S, Saulle R, De Crescenzo F, Amato L. Psychosocial interventions for psychostimulant misuse. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD011866. DOI: 10.1002/14651858.CD011866.pub2.

5.1. Search strategy

We searched the Cochrane Drugs and Alcohol Group (CDAG) Specialized Register via CRS live), MEDLINE Ovid, Embase Ovid; PsycInfo, Web of Science, CINAHL from January 2015 to 29 April 2022 without language restriction. We searched the following trials registries on 29 April 2022:

ClinicalTrials.gov (www.clinicaltrials.gov); World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (apps.who.int/trialsearch/). Details of the search strategies are reported in Appendix IIc.

The inclusion criteria were: randomized controlled trials that assessed the effect of psychosocial treatments listed in our inclusion criteria compared to no treatment, usual care, pharmacological treatments to achieve and maintain abstinence or reduce psychostimulant consumption in adults with psychostimulant use disorders.

5.2. Data collection and analysis

As the first stage in selecting relevant studies, records retrieved from the bibliographic databases and other sources are recorded and assessed for eligibility by examining their titles and abstracts only. This assessment is performed in accordance with the inclusion and exclusion criteria developed a priori. The full text of articles found to be potentially relevant on the basis of their titles and abstracts is retrieved and examined in light of the same inclusion criteria in the second stage of study selection. Two reviewers independently screened the records retrieved with the search and evaluated full text of potentially relevant reviews. Two authors independently extracted relevant data from the included studies.

5.3. Selection and coding of identified records

We used EndNote X7 as reference management software.

5.4. Quality assessment

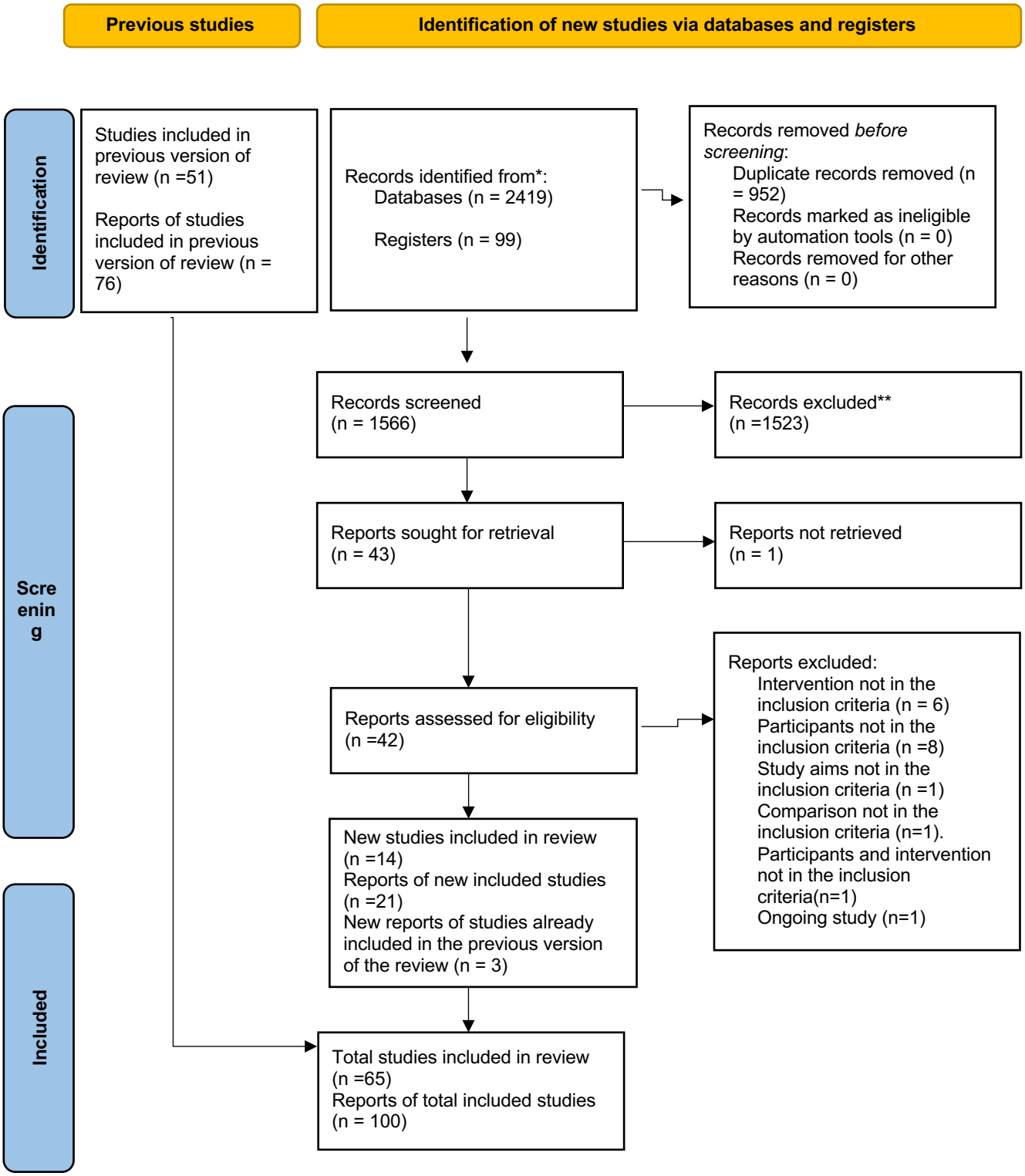
Two authors independently assessed the risk of bias of the included studies. We used the criteria recommended in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2017). The recommended approach for assessing risk of bias in studies included in Cochrane Reviews is a two-part tool, addressing the following specific domains: sequence generation and allocation concealment (selection bias), blinding of participants and providers (performance bias), blinding of outcome assessors (detection bias), incomplete outcome data (attrition bias), and selective outcome reporting (reporting bias). The first part of the tool involves describing what was reported to have happened in the study.

5.5. Analysis of subgroups or subsets

Subgroup analysis for type for psychosocial treatment was performed.

6. Results. Phase 2.

Fig. 2. PRISMA 2020 flow diagram for updated systematic reviews which included searches of databases and registers only



6.1. List of studies identified by the search process

After removing duplicates, we screened 1 566 titles and abstracts. Forty-three records were judged as potentially relevant; for one study, written in Chinese, we were unable to retrieve the full text. Forty-two records were acquired in full text. Seventeen studies were excluded as not fulfilling the inclusion criteria. Three records were secondary publication of studies already included in the previous update. One record was an ongoing study. Fourteen new studies, reported in 21 reports were finally included.

Overall, 65 studies involving a total of 8 351 participants were included in this update. See figure 2.

6.1.1. Studies included in GRADE tables/footnotes

Alammehrjerdi Z, Briggs NE, Biglarian A, Mokri A, Dolan K. A Randomized Controlled Trial of Brief Cognitive Behavioral Therapy for Regular Methamphetamine Use in Methadone Treatment. Journal of psychoactive drugs. 2019;51(3):280-9.

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Carrol KM, Rounsaville BJ, Gawin FH. A comparative trial of psychotherapies for ambulatory cocaine abusers: relapse prevention and interpersonal psychotherapy. American Journal of Dug and Alcohol Abuse. 1991;17(3):229-47.

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Carroll KM, Kiluk BD, Nich C, Gordon MA, Portnoy GA, Marino DR, et al. Computer-assisted delivery of cognitive-behavioral therapy: efficacy and durability of CBT4CBT among cocaine-dependent individuals maintained on methadone. The American Journal of Psychiatry. 2014;171(4):436-44.

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Carroll KM, Nich C, Petry NM, Eagan DA, Shi JM, Ball SA. A randomized factorial trial of disulfiram and contingency management to enhance cognitive behavioral therapy for cocaine dependence. Drug and alcohol dependence. 2016;160:135-42.

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Dursteler-MacFarland KM, Farronato NS, Strasser J, Boss J, Kuntze MF, Petitjean SA, et al. A randomized, controlled, pilot trial of methylphenidate and cognitive-behavioral group therapy for cocaine dependence in heroin prescription. Journal of Clinical Pharmacology. 2013;33(1):104-8.

Festinger DS, Dugosh KL, Kirby KC, Seymour BL. Contingency management for cocaine treatment: cash vs. vouchers. Journal of Substance Abuse Treatment. 2014;47(2):168-74.

García-Fernández G, Secades-Villa R, García-Rodríguez O, Sánchez-Hervás E, Fernández-Hermida JR, Higgins ST. Adding voucher-based incentives to community reinforcement approach improves outcomes during treatment for cocaine dependence. The American Journal on Addictions. 2011;20(5):456-61.

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Landovitz RJ, Fletcher JB, Shoptaw S, Reback CJ. Contingency management facilitates the use of postexposure prophylaxis among stimulant-using men who have sex with men. Open Forum Infectious Diseases. 2015;2(1):1-9.

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Marsden J, Stillwell G, Barlow H, Boys A, Taylor C, Hunt N, et al. An evaluation of a brief motivational intervention among young ecstasy and cocaine users: no effect on substance and alcohol use outcomes. Addiction. 2006;101:1014-26.

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6.1.2. Studies excluded from GRADE tables/footnotes

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Table 1. PICO Table

N.	Intervention/ Comparison	Outcomes	Systematic reviews (Name, Year)	Justification/Explanation for systematic review
1	Any psychosocial intervention versus no treatment	Dropout from treatment	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (point abstinence at the end of treatment)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (point abstinence at the longest follow up)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (continuous abstinence at the end of treatment)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (continuous abstinence at the longest follow up)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (frequency of drug intake at the longest follow up)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (longest period of abstinence)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Craving	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi

N.	Intervention/ Comparison	Outcomes	Systematic reviews (Name, Year)	Justification/Explanation for systematic review
				et al 2016. Update not yet published
		Adverse events	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Severity of dependence	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Depression	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
2	Any psychosocial treatments versus treatment as usual (TAU)	Dropout from treatment	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (point abstinence at the end of treatment)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (point abstinence at the longest follow up)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (continuous abstinence at the end of treatment)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (continuous abstinence at the longest follow up)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (frequency of drug	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published

N.	Intervention/ Comparison	Outcomes	Systematic reviews (Name, Year)	Justification/Explanation for systematic review
		intake at the longest follow up)		
		Use of primary substance of abuse (longest period of abstinence)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Craving	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Adverse events	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Severity of dependence	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Depression	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
3	Any psychosocial approach versus an alternative psychosocial approach	Dropout from treatment	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (point abstinence at the end of treatment)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (point abstinence at the longest follow up)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (continuous abstinence at the end of treatment)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published

N.	Intervention/ Comparison	Outcomes	Systematic reviews (Name, Year)	Justification/Explanation for systematic review
		Use of primary substance of abuse (continuous abstinence at the longest follow up)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (frequency of drug intake at the longest follow up)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Use of primary substance of abuse (longest period of abstinence)	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Craving	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Adverse events	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Severity of dependence	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published
		Depression	-	No available recent meta-analytic evidence on this outcome (N/A). We updated the Cochrane systematic review Minozzi et al 2016. Update not yet published

6.2. Narrative description of studies that contributed to GRADE analysis

We included 65 randomized controlled trials (RCTs), involving a total of 8 351 participants. The study size ranged from 19 (Petry 2013) to 487 participants (Crits-Christoph 1999). Twenty-seven studies recruited fewer than 100 participants. The mean age of participants was 36.5 years, and there were more men (77.7%) than women. Forty-seven studies took place in the United States, four in Spain, three in Australia, three in the UK, two in Switzerland, two in Brazil, two in Iran, and one each in The Netherlands and South Africa.

Most trials enrolled outpatients with a diagnosis of cocaine or amphetamine dependence based on DSM-III, DSM- IV, DSM-TR-IV, DSM-5 or ICD-10 criteria, and most included patients with alcohol consumption or comorbid alcohol dependence. In 19 studies, all of the patients had comorbid opioid dependence and were in opioid maintenance therapy (Alammehrjerdi 2019; Carroll 2012; Carroll 2014; Carroll 2018; Dursteler-MacFarland 2013; Festinger 2014; Ghitza 2007; Knealing 2006; Mitcheson 2007; Peirce 2006; Petry 2005b; Petry 2007; Petry 2012a; Petry 2018; Poling 2006; Rawson 2002; Silverman 1996; Silverman 1998; Blanken 2016). In five studies, the proportion of participants with comorbid opioid dependence and methadone maintenance ranged from 26% to 67% (Baker 2001; Ledgerwood 2006; Marsden 2018; Petitjean 2014; Petry 2013).

The mean duration of the interventions was 3.9 months (range one to twelve months); two interventions lasted only one session. The mean duration of follow-up was 7.8 months (range 2 to 36 months).

6.2.1. Types of interventions

The included studies considered the psychosocial interventions of cognitive behavioural therapy (CBT), contingency management (CM), motivational interviewing (MI), a combination of CBT and MI, interpersonal therapy, positive affect intervention, psychodynamic therapy, and 12-step facilitation.

CBT: Eleven studies compared CBT versus no intervention (Alammehrjerdi 2019; Baker 2001; Baker 2005; Carroll 2014; Carroll 2018; Crits-Christoph 1999; Higgins 2003; Milby 2008; Mimiaga 2019; Rawson 2002; Shoptaw 2005), seven versus treatment as usual (TAU) (Carroll 1994; Dursteler-MacFarland 2013; Higgins 1993**;** Marsden 2018; Rawson 2002; Sanchez-Hervas 2010; Shoptaw 2008), three versus 12-step facilitation (Carroll 1998; Maude-Griffin 1998; Schottenfeld 2011), three versus interpersonal therapy (Carroll 1991; Carroll 2004; Crits-Christoph 1999), two versus CM (Rawson 2002; Shoptaw 2005), one versus individual counselling (Crits-Christoph 1999), and one versus acceptance and commitment therapy (Smout 2010).

CM: Twenty-nine studies compared CM versus no intervention (Blanken 2016; Carroll 2015; Festinger 2014; Garcia-Fernandez 2011; Ghitza 2007; Hagedorn 2013; Higgins 1994; Higgins 2000; Kirby 1998a; Ledgerwood 2006; McDonell 2013; Menza 2010; Miguel 2017; Miguel 2022; Peirce 2006; Petitjean 2014; Petry 2005a; Petry 2005b; Petry 2007; Petry 2013; Petry 2012a; Petry 2012b; Petry 2015; Petry 2018; Pirnia 2016; Rawson 2002; Roll 2013; Secades Villa 2013; Shoptaw 2005), two versus TAU (Rawson 2002, Garcia-Rodriguez 2007), six versus non-contingent reinforcements (Landovitz 2015; McDonell 2013; Poling 2006; Schottenfeld 2011; Silverman 1996; Silverman 1998), and two versus CBT (Rawson 2002; Shoptaw 2005).

MI: Five studies compared MI versus no intervention (Ingersoll 2011; Marsden 2006; McKee 2007; Mitcheson 2007; Stein 2009), and one study versus TAU (Sorsdahl 2021). One study compared a combination of CBT and MI versus TAU (Parsons 2018).

Interpersonal therapy: One study compared interpersonal therapy versus individual counselling (Crits-Christoph 1999), and three compared it to CBT (Carroll 1991; Carroll 2004; Crits-Christoph 1999).

Positive affect intervention: One study compared positive affect intervention versus no intervention (Carrico 2018).

Psychodynamic therapy: One study compared psychodynamic therapy versus no intervention (Crits-Christoph 1999).

12-step facilitation: One study compared 12-step facilitation versus no intervention (Carroll 2012), and three compared it with CBT (Carroll 1998; Maude-Griffin 1998; Schottenfeld 2011).

Three included studies did not provide useful data for inclusion in the quantitative analyses (Carroll 2004; Ghitza 2007; Ledgerwood 2006).

Ten studies added pharmacological interventions to the psychosocial ones: disulphiram (Carroll 1998; Carroll 2004; Carroll 2012; Carrol 2015, Higgins 1993; Higgins 1994), bupropion (Poling 2006), desipramine hydrochloride (Carroll 1994), methylphenidate (Dursteler-MacFarland 2013), and galantamine (Carroll 2018).

6.2.2. Types of comparisons

We grouped the studies into three main comparisons.

Any psychosocial intervention versus no intervention (50 studies included), including studies where the psychosocial interventions were given in addition to TAU or another intervention which was received by both groups.

Any psychosocial intervention versus TAU (10 studies included).

Any psychosocial intervention versus an alternative psychosocial intervention (16 studies included).

6.3. Grading the Evidence

Table 2a. Evidence profile Any psychosocial intervention vs no intervention
Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,
Date:
Question: Should any psychosocial intervention versus no intervention be used for psychostimulant misuse?
Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any psychosocial treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
Dropouts												
33	randomized trials	serious[a]	not serious	not serious	not serious	none	713/2490 (28.6%)	710/2081 (34.1%)	**RR 0.81** (0.73 to 0.91)	**65 fewer per 1000** (from 92 fewer to 31 fewer)	⨁⨁⨁◯ Moderate	
Point abstinence, end of treatment												
8	randomized trials	not serious	not serious	not serious	not serious	none	356/772 (46.1%)	221/572 (38.6%)	**RR 1.11** (0.91 to 1.35)	**43 more per 1000** (from 35 fewer to 135 more)	⨁⨁⨁⨁ High	
Point abstinence, longest follow-up												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any psychosocial treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
7	randomized trials	serious[b]	serious[c]	not serious	not serious	none	400/797 (50.2%)	229/499 (45.9%)	**RR 1.09** (0.81 to 1.46)	**41 more per 1000** (from 87 fewer to 211 more)	⨁⨁◯◯ Low	
Continuous abstinence, end of treatment												
10	randomized trials	serious[d]	not serious	not serious	not serious	publication bias strongly suspected[e]	180/724 (24.9%)	72/680 (10.6%)	**RR 2.41** (1.47 to 3.93)	**149 more per 1000** (from 50 more to 310 more)	⨁⨁◯◯ Low	
Continuous abstinence, longest follow-up												
5	randomized trials	serious[f]	not serious	not serious	serious[g]	none	91/198 (46.0%)	61/167 (36.5%)	**RR 1.22** (0.88 to 1.69)	**80 more per 1000** (from 44 fewer to 252 more)	⨁⨁◯◯ Low	
Frequency of drug intake, longest follow-up												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any psychosocial treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
14	randomized trials	serious[h]	not serious	not serious	not serious	none	1 030	944	-	SMD **0.63 lower** (0.96 lower to 0.3 lower)	⊕⊕⊕◯ Moderate	
Longest period of abstinence												
15	randomized trials	serious[i]	not serious	not serious	not serious	none	1 171	917	-	SMD **0.51 higher** (0.39 higher to 0.62 higher)	⊕⊕⊕◯ Moderate	
Craving												
3	randomized trials	serious[j]	not serious	not serious	not serious	none	246	210	-	SMD **0.39 lower** (0.72 lower to 0.06 lower)	⊕⊕⊕◯ Moderate	
Severity of dependence												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any psychosocial treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
7	randomized trials	serious[k]	serious[l]	not serious	not serious	none	211	202	-	SMD **0.76 lower** (1.66 lower to 0.14 higher)	⊕⊕◯◯ Low	
Depression												
2	randomized trials	serious[m]	not serious	not serious	very serious[n]	none	41	37	-	SMD **0.41 lower** (0.86 lower to 0.04 higher)	⊕◯◯◯ Very low	

a. Downgraded of one level for risk of bias because twenty studies were at unclear risk and two at high risk for selection bias
b. Downgraded of one level for risk of bias because tree studies were at unclear risk for selection bias, one study at high risk for attrition bias
c. Downgraded of one level for inconsistency because I^2 = 78%
d. Downgraded of one level for risk of bias because five studies were at unclear risk for selection bias and tree studies were at high risk of attrition bias
e. Downgraded of one level for suspected publication bias
f. Downgraded of one level for risk of bias because four studies were at unclear risk and one at high risk for selection bias and one study at high risk for attrition bias.
g. Downgraded of one level for imprecision because OIS not met.
h. Downgraded of one level for risk of bias because nine studies were at unclear risk and one at high risk for selection bias
i. Downgraded of one level for risk of bias because thirteen were at unclear risk for selection bias
j. Downgraded of one level for risk of bias because two were at unclear risk for selection bias and attrition bias
k. Downgraded of one level for risk of bias because four studies were at unclear risk and one at high risk for selection bias, two at high risk for attrition bias
l. Downgraded of one level for inconsistency because I^2 = 94%
m. Downgraded of one level for risk of bias because one study was at unclear risk for selection bias and one at high risk for attrition bias
n. Downgraded of two levels for imprecision because < 100 participants and wide IC

6.3.1. Subgroup analyses for type of psychosocial treatment versus no intervention

Table 2aa. Evidence profile Cognitive Behavioural Therapy (CBT) vs no intervention
Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,
Date:
Question: Should CBT versus no intervention be used for psychostimulant misuse?
Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
Dropouts – CBT												
8	randomized trials	serious[a]	not serious	not serious	not serious	none	177/534 (33.1%)	184/468 (39.3%)	**RR 0.89** (0.67 to 1.19)	**43 fewer per 1000** (from 130 fewer to 75 more)	⊕⊕⊕◯ Moderate	
Point abstinence, end of treatment – CBT												
3	randomized trials	serious[f]	not serious	not serious	not serious	none	129/248 (52.0%)	136/253 (53.8%)	**RR 0.97** (0.80 to 1.18)	**16 fewer per 1000** (from 108 fewer to 97 more)	⊕⊕⊕◯ Moderate	
Point abstinence, longest follow-up – CBT												
3	randomized trials	not serious	not serious	not serious	not serious	none	128/283 (45.2%)	85/225 (37.8%)	**RR 1.65** (0.85 to 3.24)	**246 more per 1000** (from 57 fewer to 846 more)	⊕⊕⊕⊕ High	
Continuous abstinence, end of treatment – CBT												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[b]	not serious[c]	not serious	serious[e]	none	17/47 (36.2%)	9/54 (16.7%)	**RR 2.17** (1.07 to 4.40)	**195 more per 1000** (from 12 more to 567 more)	⨁⨁◯◯ Low	
Continuous abstinence, longest follow-up - CBT												
1	randomized trials	serious[b]	not serious[c]	not serious	very serious[d]	none	38/45 (84.4%)	29/40 (72.5%)	**RR 1.16** (0.93 to 1.46)	**116 more per 1000** (from 51 fewer to 333 more)	⨁◯◯◯ Very low	
Frequency of drug intake, longest follow-up - CBT												
3	randomized trials	serious[g]	not serious	not serious	serious[h]	none	114	113	-	SMD **1.96 lower** (4.78 lower to 0.85 higher)	⨁⨁◯◯ Low	
Longest period of abstinence - CBT												
4	randomized trials	serious[i]	not serious	not serious	not serious	none	211	219	-	SMD **0.5 higher** (0.16 higher to 0.84 higher)	⨁⨁⨁◯ Moderate	

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
Severity of dependence - CBT												
1	randomized trials	not serious	not serious[c]	not serious	serious[h]	none	60	60	-	SMD **2.17 lower** (2.62 lower to 1.71 lower)	⨁⨁⨁◯ Moderate	
Depression - CBT												
1	randomized trials	serious[b]	not serious[c]	not serious	very serious[j]	none	21	20	-	SMD **0.28 lower** (0.90 lower to 0.34 higher)	⨁◯◯◯ Very low	

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardized mean difference

a. Downgraded of one level for risk of bias because five studies at unclear risk of selection bias

b. Downgraded of one level for risk of bias because the only included study was at unclear risk of selection bias

c. Not applicable because one study included

d. Downgraded of two levels for imprecision because < 100 events

e. Downgraded of one level for imprecision because OIS not met

f. Downgraded of one level for risk of bias because two studies at unclear risk for selection bias

g. Downgraded of one level for risk of bias because two studies at unclear risk of selection bias

h. Downgraded of one level for imprecision because < 400 participants

i. Downgraded of one level for risk of bias because all studies at unclear risk of selection bias

j. Downgraded of two levels for imprecision because < 100 participants

Table 2ab. Evidence profile Contingency Management (CM) vs no intervention
Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,
Date:
Question: Should CM versus no intervention be used for psychostimulant misuse?
Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
Dropouts - CM												
17	randomized trials	serious[a]	not serious	not serious	not serious	publication bias strongly suspected[b]	362/1306 (27.7%)	406/1051 (38.6%)	**RR 0.77** (0.68 to 0.87)	**89 fewer per 1000** (from 124 fewer to 50 fewer)	⨁⨁◯◯ Low	
Point abstinence, end of treatment - CM												
5	randomized trials	serious[f]	not serious	not serious	serious[e]	none	94/262 (35.9%)	66/263 (25.1%)	**RR 1.45** (0.86 to 2.43)	**113 more per 1000** (from 35 fewer to 359 more)	⨁⨁◯◯ Low	
Point abstinence, longest follow-up - CM												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
2	randomized trials	not serious	not serious	not serious	serious[e]	none	39/84 (46.4%)	54/75 (72.0%)	**RR 0.63** (0.49 to 0.83)	**266 fewer per 1000** (from 367 fewer to 122 fewer)	⨁⨁⨁◯ Moderate	

Continuous abstinence, end of treatment - CM

9	randomized trials	serious[g]	not serious	not serious	not serious	none	163/677 (24.1%)	63/626 (10.1%)	**RR 2.51** (1.43 to 4.43)	**152 more per 1000** (from 43 more to 345 more)	⨁⨁⨁◯ Moderate	

Continuous abstinence, longest follow-up - CM

3	randomized trials	serious[h]	not serious	not serious	very serious[d]	none	50/136 (36.8%)	31/115 (27.0%)	**RR 2.06** (0.62 to 6.82)	**286 more per 1000** (from 102 fewer to 1.000 more)	⨁◯◯◯ Very low	

Frequency of drug intake, longest follow-up - CM

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
6	randomized trials	serious[j]	not serious	not serious	not serious	none	516	391	-	SMD **0.36 lower** (0.51 lower to 0.22 lower)	⨁⨁⨁◯ Moderate	
Longest period of abstinence - CM												
12	randomized trials	serious[k]	not serious	not serious	not serious	none	1000	698	-	SMD **0.54 higher** (0.4 higher to 0.69 higher)	⨁⨁⨁◯ Moderate	
Severity of dependence - CM												
4	randomized trials	serious[f]	not serious	not serious	serious[i]	none	116	108	-	SMD **0.75 lower** (1.83 lower to 0.34 higher)	⨁⨁◯◯ Low	
Depression - CM												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[m]	not serious[c]	not serious	very serious[l]	none	20	17	-	SMD **0.56 lower** (1.22 lower to 0.10 higher)	⨁◯◯◯ Very low	

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardized mean difference

a. Downgraded of one level for risk of bias because eleven studies at unclear risk and one at high risk of selection bias; four studies at high risk of attrition bias

b. Downgraded because asymmetric funnel plot suggesting for publication bias

c. Not applicable because one study included

d. Downgraded of two levels for imprecision because < 100 events

e. Downgraded of one level for imprecision because OIS not met

f. Downgraded of one level for risk of bias because three studies at unclear risk of selection bias; one study at high risk of attrition bias

g. Downgraded of one level for risk of bias because four studies at unclear risk; three studies at high risk of attrition bias

h. Downgraded of one level for risk of bias because all three studies at unclear risk of selection bias

i. Downgraded of one level for imprecision because < 400 participants

j. Downgraded of one level for risk of bias because five studies at unclear risk of selection bias

k. Downgraded of one level for risk of bias because nine studies at unclear risk of selection bias

l. Downgraded of two levels for imprecision because < 100 participants

m. Downgraded of one level for risk of bias because the only included study was at high risk of attrition bias

Table 2ac. Evidence profile Motivational Interview (MI) vs no intervention
Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,
Date:
Question: Should MI versus no intervention be used for psychostimulant misuse?
Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
Dropouts - MI												
5	randomized trials	serious[a]	not serious	not serious	serious[b]	none	52/345 (15.1%)	58/351 (16.5%)	**RR 0.91** (0.65 to 1.27)	**15 fewer per 1000** (from 58 fewer to 45 more)	⊕⊕◯◯ Low	
Point abstinence, longest follow-up - MI												
2	randomized trials	not serious	not serious	not serious	not serious	none	97/185 (52.4%)	90/199 (45.2%)	**RR 1.16** (0.95 to 1.42)	**72 more per 1000** (from 23 fewer to 190 more)	⊕⊕⊕⊕ High	
Continuous abstinence, longest follow-up - MI												
1	randomized trials	very serious[e]	not serious[c]	not serious	very serious[d]	none	3/17 (17.6%)	1/12 (8.3%)	**RR 2.12** (0.25 to 17.98)	**93 more per 1000** (from 63 fewer to 1.000 more)	⊕◯◯◯ Very low	
Frequency of drug intake, longest follow-up - MI												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
2	randomized trials	not serious	not serious	not serious	serious[f]	none	183	188	-	SMD **0.18 lower** (0.38 lower to 0.03 higher)	⨁⨁⨁◯ Moderate	
Severity of dependence - MI												
2	randomized trials	very serious[g]	not serious	not serious	very serious[h]	none	35	34	-	SMD **0.01 higher** (0.71 lower to 0.73 higher)	⨁◯◯◯ Very low	

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardized mean difference

a. Downgraded of one level for risk of bias because three studies at unclear risk and one at high risk of selection bias; two studies at high risk of attrition bias

b. Downgraded of one level because OIS not meet and because CI include important benefits and important harms

c. Not applicable because one study included

d. Downgraded of two levels for imprecision because < 100 events

e. Downgraded of two level for risk of bias because the only study included was at high risk of selection bias

f. Downgraded of one level for imprecision because < 400 participants

g. Downgraded of one level for risk of bias because one study at unclear risk and one at high risk of selection bias

h. Downgraded of two levels for imprecision because < 100 participants

Table 2ad. Evidence profile 12 steps facilitation vs no intervention

Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,

Date:

Question: Should 12 steps facilitation versus no intervention be used for psychostimulant misuse?

Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
Dropouts - 12-step facilitation												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	none	19/56 (33.9%)	12/56 (21.4%)	**RR 1.58** (0.85 to 2.94)	**124 more per 1000** (from 32 fewer to 416 more)	⨁◯◯◯ Very low	
Point abstinence, end of treatment - 12-step facilitation												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	none	16/56 (28.6%)	19/56 (33.9%)	**RR 0.84** (0.48 to 1.46)	**54 fewer per 1000** (from 176 fewer to 156 more)	⨁◯◯◯ Very low	

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardized mean difference

a. Downgraded of one level for risk of bias because the only included study was at unclear risk of selection bias

b. Not applicable because one study included

c. Downgraded of two levels for imprecision because < 100 events

Table 2ae. Evidence profile psychodynamic therapy vs no intervention

Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,

Question: Should psychodynamic therapy versus no intervention be used for psychostimulant misuse?

Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
Dropouts - Psychodynamic therapy												
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	none	83/124 (66.9%)	95/123 (77.2%)	**RR 0.87** (0.74 to 1.01)	**100 fewer per 1000** (from 201 fewer to 8 more)	⊕⊕⊕◯ Moderate	
Point abstinence, end of treatment - Psychodynamic therapy												
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	none	62/124 (50.0%)	59/123 (48.0%)	**RR 1.04** (0.81 to 1.34)	**19 more per 1000** (from 91 fewer to 163 more)	⊕⊕⊕◯ Moderate	
Point abstinence, longest follow-up – psychodynamic therapy												
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	none	64/124 (51.6%)	66/123 (53.7%)	**RR 0.96** (0.76 to 1.22)	**21 fewer per 1000** (from 129 fewer to 118 more)	⊕⊕⊕◯ Moderate	

a. Not applicable because one study included

b. Downgraded of one level for imprecision because OIS not met

Table 2af. Evidence profile individual counselling vs no intervention

Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,

Date:

Question: Should individual counselling versus no intervention be used for psychostimulant misuse?

Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
Point abstinence, end of treatment - Individual counselling												
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	none	73/121 (60.3%)	59/123 (48.0%)	**RR 1.26** (1.00 to 1.59)	**125 more per 1000** (from 0 fewer to 283 more)	⨁⨁⨁◯ Moderate	
Point abstinence, longest follow-up - individual counselling												
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	none	72/121 (59.5%)	66/123 (53.7%)	**RR 1.11** (0.89 to 1.38)	**59 more per 1000** (from 59 fewer to 204 more)	⨁⨁⨁◯ Moderate	

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardized mean difference

a. Not applicable because one study included

b. Downgraded of one level for imprecision because OIS not met

Table 2ag. Evidence profile positive affect intervention vs no intervention

Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,

Date:

Question: Should positive affect intervention versus no intervention be used for psychostimulant misuse?

Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	no intervention	Relative (95% CI)	Absolute (95% CI)		
Frequency of drug intake, longest follow-up - positive affect intervention												
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	none	107	107	-	SMD **0.29 lower** (0.56 lower to 0.02 lower)	⊕⊕⊕◯ Moderate	
Craving - positive affect intervention												
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	none	107	107	-	SMD **0.31 lower** (0.58 lower to 0.04 lower)	⊕⊕⊕◯ Moderate	

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardized mean difference

a. Not applicable because one study included

b. Downgraded of one level for imprecision because <400 participants

Table 2b. Evidence profile Any psychosocial intervention vs treatment as usual (TAU)

Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,

Date:

Question: Should any psychosocial intervention versus no intervention be used for psychostimulant misuse?

Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any psychosocial treatment	TAU	Relative (95% CI)	Absolute (95% CI)		
Dropouts												
8	randomized trials	serious[a]	not serious	not serious	not serious	none	125/310 (40.3%)	154/296 (52.0%)	**RR 0.76** (0.61 to 0.96)	**125 fewer per 1000** (from 203 fewer to 21 fewer)	⊕⊕⊕◯ Moderate	
Point abstinence, end of treatment												
3	randomized trials	serious[b]	not serious	not serious	very serious[c]	none	43/135 (31.9%)	15/105 (14.3%)	**RR 1.93** (1.14 to 3.28)	**133 more per 1000** (from 20 more to 326 more)	⊕◯◯◯ Very low	
Point abstinence, longest follow up												
2	randomized trials	serious[d]	not serious	not serious	very serious[c]	none	51/102 (50.0%)	16/62 (25.8%)	**RR 1.89** (1.18 to 3.02)	**230 more per 1000** (from 46 more to 521 more)	⊕◯◯◯ Very low	
Continuous abstinence, end of treatment												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any psychosocial treatment	TAU	Relative (95% CI)	Absolute (95% CI)		
3	randomized trials	serious[e]	not serious	not serious	serious[f]	none	61/140 (43.6%)	49/124 (39.5%)	**RR 1.15** (0.91 to 1.46)	**59 more per 1000** (from 36 fewer to 182 more)	⨁⨁◯◯ Low	
Longest period of abstinence												
2	randomized trials	serious[g]	very serious[h]	not serious	serious[i]	none	74	66	-	SMD **0.4 SD higher** (0.8 lower to 1.59 higher)	⨁◯◯◯ Very low	
Severity of dependence												
2	randomized trials	serious[d]	not serious	not serious	serious[i]	none	75	74	-	SMD **0.24 lower** (0.56 lower to 0.08 higher)	⨁⨁◯◯ Low	
frequency of drug intake, end of teratment												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any psychosocial treatment	TAU	Relative (95% CI)	Absolute (95% CI)		
4	randomized trials	serious[j]	serious[k]	not serious	not serious	none	196	193	-	SMD **0.02 lower** (0.22 lower to 0.18 higher)	⨁⨁◯◯ Low	
Craving												
2	randomized trials	serious[l]	not serious	not serious	very serious[m]	none	33	36	-	SMD **0.7 lower** (1.21 lower to 0.2 lower)	⨁◯◯◯ Very low	
Depression (HAM)												
1	randomized trials	serious[n]	not serious[o]	not serious	very serious[m]	none	17	22	-	SMD **0 16 lower** (0.8 lower to 0.47 higher)	⨁◯◯◯ Very low	
N.subjects with adverse events												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any psychosocial treatment	TAU	Relative (95% CI)	Absolute (95% CI)		
2	randomized trials	serious[l]	not serious	not serious	very serious[c]	none	5/46 (10.9%)	1/44 (2.3%)	**RR 4.38** (0.58 to 33.10)	**77 more per 1.000** (from 10 fewer to 730 more)	⨁◯◯◯ Very low	

a. Downgraded one level for risk of bias because all but one was at unclear risk for selection bias and one at high risk, two studies were at high risk for attrition bias
b. Downgraded one level for risk of bias because all but one was at unclear risk for selection bias and one at high risk
c. Downgraded of two levels for imprecision because < 100 events
d. Downgraded of one level for risk of bias because all studies were at unclear risk for selection bias and one at high risk for attrition bias
e. Downgraded of one level for risk of bias because all were at unclear risk for selection bias
f. Downgraded of one level for imprecision because OIS not met
g. Downgraded one level for risk of bias because one study was at unclear and one at high risk for selection bias and one at high risk for attrition bias
h. Downgraded of two levels for inconsistency because I^2 = 85%
i. Downgraded of one level for imprecision because < 400 participants
j. Downgraded one level for risk of bias because all but one was at unclear risk for selection bias and one at high risk, one study was at high risk for attrition bias
k. Downgraded of one level for inconsistency because I^2 = 71%
l. Downgraded of one level for risk of bias because one study was at unclear risk and one at high risk for selection bias
m. Downgraded of two levels for imprecision because < 100 participants
n. Downgraded of one level for risk of bias because the only study included was at unclear risk of bias and at high risk for attrition
o. Not applicable because one study included

6.3.2. Subgroup analyses for type of psychosocial treatment versus treatment as usual (TAU)

Table 2ba. Evidence profile CBT vs treatment as usual (TAU)

Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,
Date:
Question: Should CBT versus no intervention be used for psychostimulant misuse?
Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	TAU	Relative (95% CI)	Absolute (95% CI)		
Dropouts - CBT												
6	randomized trials	very serious[a]	not serious	not serious	not serious	none	96/236 (40.7%)	113/214 (52.8%)	**RR 0.78** (0.64 to 0.94)	**116 fewer per 1000** (from 190 fewer to 32 fewer)	⨁⨁◯◯ Low	
Point abstinence, end of treatment - CBT												
3	randomized trials	very serious[d]	not serious	not serious	very serious[e]	none	27/108 (25.0%)	15/105 (14.3%)	**RR 1.73** (0.99 to 3.02)	**104 more per 1000** (from 1 fewer to 289 more)	⨁◯◯◯ Very low	
Point abstinence, longest follow up - CBT												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	TAU	Relative (95% CI)	Absolute (95% CI)		
2	randomized trials	serious[g]	not serious	not serious	serious[f]	none	37/75 (49.3%)	16/62 (25.8%)	**RR 1.94** (1.20 to 3.14)	**243 more per 1000** (from 52 more to 552 more)	⨁⨁◯◯ Low	
Continuous abstinence, end of treatment - CBT												
1	randomized trials	serious[c]	not serious[b]	not serious	very serious[e]	none	45/64 (70.3%)	38/64 (59.4%)	**RR 1.18** (0.92 to 1.53)	**107 more per 1000** (from 47 fewer to 315 more)	⨁◯◯◯ Very low	
Longest period of abstinence - CBT												
2	randomized trials	very serious[h]	not serious	not serious	serious[i]	none	74	66	-	SMD **0.4 SD higher** (0.8 lower to 1.59 higher)	⨁◯◯◯ Very low	
Severity of dependence (ASI) - CBT												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	TAU	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[j]	not serious[b]	not serious	serious[i]	none	58	52	-	SMD **0.22 SD lower** (0.59 lower to 0.16 higher)	⨁⨁◯◯ Low	
frequency of drug intake, end of treatment - CBT												
1	randomized trials	serious[l]	not serious[b]	not serious	very serious[k]	none	16	14	-	SMD **1.21 lower** (1.99 lower to 0.42 lower)	⨁◯◯◯ Very low	
craving - CBT												
1	randomized trials	very serious[l]	not serious[b]	not serious	very serious[k]	none	16	14	-	SMD **1.63 SD lower** (2.47 lower to 0.79 lower)	⨁◯◯◯ Very low	
N subjects with adverse events – CBT												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	TAU	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[l]	not serious[b]	not serious	very serious[e]	none	5/16 (31.3%)	1/14 (7.1%)	**RR 4.38** (0.58 to 33.10)	**241 more per 1000** (from 30 fewer to 1.000 more)	⨁◯◯◯ Very low	

a. Downgraded of two levels for risk of bias because the five studies were at unclear and one at high risk of selection bias; two studies at high risk of bias
b. Not applicable because one study included
c. Downgraded of one level for risk of bias because the study was at unclear of selection bias
d. Downgraded of two levels for risk of bias because two studies at unclear risk and one at high risk of selection bias
e. Downgraded of two levels because < 100 events
f. Downgraded of one level because OIS not met
g. Downgraded of one level for risk of bias because two studies at unclear of selection bias and one at high risk of attrition bias
h. Downgraded of two levels for risk of bias because one study at unclear risk and one at high risk of selection bias and one study at high risk of attrition bias
i. Downgraded of one level for imprecision because < 400 participants
j. Downgraded of two levels for risk of bias because the study was at unclear of selection bias and one at high risk of attrition bias
k. Downgraded of one level for imprecision because < 100 participants
l. Downgraded of two levels for risk of bias because the only study included was at high risk of selection bias

Table 2bb. Evidence profile CM vs treatment as usual (TAU)
Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,
Date:
Question: Should CM versus no intervention be used for psychostimulant misuse?
Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	TAU	Relative (95% CI)	Absolute (95% CI)		
Dropouts – CM												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	none	21/47 (44.7%)	21/35 (60.0%)	**RR 0.74** (0.49 to 1.13)	**156 fewer per 1000** (from 306 fewer to 78 more)	⊕◯◯◯ Very low	
Point abstinence, end of treatment - CM												
1	randomized trials	serious[d]	not serious[b]	not serious	serious[f]	none	16/27 (59.3%)	6/27 (22.2%)	**RR 2.67** (1.23 to 5.77)	**371 more per 1000** (from 51 more to 1.000 more)	⊕⊕◯◯ Low	
Point abstinence, longest follow up - CM												
1	randomized trials	serious[d]	not serious[b]	not serious	very serious[e]	none	14/27 (51.9%)	7/27 (25.9%)	**RR 2.00** (0.96 to 4.17)	**259 more per 1000** (from 10 fewer to 822 more)	⊕◯◯◯ Very low	

a. Downgraded of one level for risk of bias because the study was at unclear of selection bias and at high risk of attrition bias
b. Not applicable because one study included
c. Downgraded of two levels for risk imprecision because OIS not met and wide CI
d. Downgraded of one level for risk of bias because the study was at unclear of selection bias
e. Downgraded of two levels because < 100 events
f. Downgraded of one level because OIS not met

Table 2bc. Evidence profile interpersonal therapy vs treatment as usual (TAU)
Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,
Date:
Question: Should interpersonal therapy versus no intervention be used for psychostimulant misuse?
Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	TAU	Relative (95% CI)	Absolute (95% CI)		
frequency of drug intake, end of treatment - interpersonal therapy												
1	randomized trials	very serious[c]	not serious[a]	not serious	serious[b]	none	58	52	-	SMD **0.15 higher** (0.22 lower to 0.53 higher)	⨁◯◯◯ Very low	

a. Not applicable because one study included
b. Downgraded of one level for imprecision because < 400 participants
c. Downgraded of two levels for risk of bias because the study at unclear risk of selection bias and high risk of attrition bias

Table 2bd. Evidence profile motivational interview vs treatment as usual (TAU)
Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,
Date:
Question: Should motivational interview versus no intervention be used for psychostimulant misuse?
Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	TAU	Relative (95% CI)	Absolute (95% CI)		
Dropouts - MI												
1	randomized trials	serious[b]	not serious[a]	not serious	very serious[c]	none	13/30 (43.3%)	8/30 (26.7%)	**RR 1.63** (0.79 to 3.34)	**168 more per 1000** (from 56 fewer to 624 more)	⊕◯◯◯ Very low	
Severity of dependence (ASI) - MI												
1	randomized trials	serious[b]	not serious[a]	not serious	very serious[d]	none	17	22	-	SMD **0.31 SD lower** (0.95 lower to 0.32 higher)	⊕◯◯◯ Very low	
frequency of drug intake, end of treatment - MI												
1	randomized trials	not serious	not serious[a]	not serious	very serious[d]	none	17	22	-	SMD **0.25 lower** (0.89 lower to 0.38 higher)	⊕⊕◯◯ Low	

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	TAU	Relative (95% CI)	Absolute (95% CI)		
craving – MI												
1	randomized trials	not serious	not serious[a]	not serious	very serious[d]	none	17	22	-	SMD **0.18 SD lower** (0.81 lower to 0.45 higher)	⨁⨁◯◯ Low	
depression - MI												
1	randomized trials	not serious	not serious[a]	not serious	very serious[d]	none	17	22	-	SMD **0.16 SD lower** (0.8 lower to 0.47 higher)	⨁⨁◯◯ Low	
N subjects with adverse events - MI												
1	randomized trials						0/30 (0.0%)	0/30 (0.0%)	not estimable		-	

a. Not applicable because one study included
b. Downgraded of one level for risk of bias because the study was at unclear of selection bias
c. Downgraded of two levels for imprecision because OIS not met and CI include important benefits and important harms
d. Downgraded of one level for imprecision because < 100 participants

Table 2be. Evidence profile motivational interview + cognitive behavioural therapy (MI+CBT) vs treatment as usual (TAU)

Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,

Date:

Question: Should motivational interview + cognitive behavioural therapy (MI+CBT) versus no intervention be used for psychostimulant misuse?

Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single treatment	TAU	Relative (95% CI)	Absolute (95% CI)		
frequency of drug intake, end of treatment - MI+CBT												
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	none	105	105	-	SMD **0.07 higher** (0.2 lower to 0.34 higher)	⊕⊕⊕◯ Moderate	

a. Not applicable because one study included

b. Downgraded of one level for imprecision because < 400 participants

6.3.3. Single treatments versus each other

Table 2c. Evidence profile Cognitive Behavioural Therapy (CBT) vs 12 step facilitation
Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,
Date:
Question: Should any Cognitive Behavioural Therapy (CBT) vs 12 step facilitation be used for psychostimulant misuse?
Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	12-step facilitation	Relative (95% CI)	Absolute (95% CI)		
Dropouts												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	none	31/71 (43.7%)	37/74 (50.0%)	**RR 0.87** (0.62 to 1.24)	**65 fewer per 1000** (from 190 fewer to 120 more)	⊕◯◯◯ Very low	
Continuous abstinence, end of treatment												
2	randomized trials	serious[d]	not serious	not serious	very serious[c]	none	46/106 (43.4%)	42/119 (35.3%)	**RR 1.22** (0.88 to 1.69)	**78 more per 1000** (from 42 fewer to 244 more)	⊕◯◯◯ Very low	
Continuous abstinence, longest follow-up												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	12-step facilitation	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[e]	not serious[b]	not serious	very serious[c]	none	14/24 (58.3%)	8/27 (29.6%)	**RR 1.97** (1.00 to 3.86)	**287 more per 1000** (from 0 fewer to 847 more)	⨁◯◯◯ Very low	

a. Downgraded of one level for risk of bias because one study was at unclear risk for selection bias and one at high risk for attrition bias
b. Not applicable because one study included
c. Downgraded of two levels for imprecision because less than 100 events
d. Downgraded of one level for risk of bias because all were at unclear risk for selection bias
e. Downgraded of one level for risk of bias because one study was at unclear risk for selection bias

Table 2d. Evidence profile Cognitive Behavioural Therapy (CBT) vs acceptance and commitment therapy (ACT)

Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,

Date:

Question: Should any Cognitive Behavioural Therapy (CBT) vs acceptance and commitment therapy (ACT be used for psychostimulant misuse?

Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	ACT	Relative (95% CI)	Absolute (95% CI)		
Dropouts												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	none	36/53 (67.9%)	37/51 (72.5%)	**RR 0.94** (0.73 to 1.20)	**44 fewer per 1000** (from 196 fewer to 145 more)	⊕◯◯◯ Very low	
Point abstinence, end of treatment												
1	randomized trials	serious[a]	not serious	not serious	very serious[c]	none	6/14 (42.9%)	4/12 (33.3%)	**RR 1.29** (0.47 to 3.51)	**97 more per 1000** (from 177 fewer to 837 more)	⊕◯◯◯ Very low	
Point abstinence, longest follow-up												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	ACT	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[a]	not serious	not serious	very serious[c]	none	4/11 (36.4%)	4/8 (50.0%)	**RR 0.73** (0.26 to 2.07)	**135 fewer per 1000** (from 370 fewer to 535 more)	⨁◯◯◯ Very low	

a. Downgraded of one level for risk of bias because the study was at high risk for selection bias
b. Not applicable because one study
c. Downgraded of two levels for risk of bias because less than 100 events

Table 2e. Evidence profile Cognitive Behavioural Therapy (CBT) vs Contingency Management (CM)

Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,

Date:

Question: Should any Cognitive Behavioural Therapy (CBT) vs Contingency Management (CM be used for psychostimulant misuse?

Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	CM	Relative (95% CI)	Absolute (95% CI)		
Point abstinence, end of treatment												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	none	11/28 (39.3%)	16/27 (59.3%)	**RR 0.66** (0.38 to 1.16)	**201 fewer per 1000** (from 367 fewer to 95 more)	⊕◯◯◯ Very low	
Point abstinence, longest follow-up												
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[c]	none	17/28 (60.7%)	14/27 (51.9%)	**RR 1.17** (0.73 to 1.87)	**88 more per 1000** (from 140 fewer to 451 more)	⊕◯◯◯ Very low	
Frequency of drug intake, longest follow-up (days/months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	CM	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[a]	not serious[b]	not serious	very serious[d]	none	40	42	-	SMD **0.09 lower** (0.53 lower to 0.34 higher)	⨁◯◯◯ Very low	

a. Downgraded of one level for risk of bias because one study was at unclear risk for selection bias
b. Not applicable because one study included
c. Downgraded of two levels for imprecision because less than 100 events
d. Downgraded of two levels for imprecision because less than 100 participants

Table 2f. Evidence profile Cognitive Behavioural Therapy (CBT) vs Individual Counselling

Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,

Date:

Question: Should any Cognitive Behavioural Therapy (CBT) vs Individual Counselling be used for psychostimulant misuse?

Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	individual counselling	Relative (95% CI)	Absolute (95% CI)		
Dropouts												
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	none	79/119 (66.4%)	93/121 (76.9%)	**RR 0.86** (0.74 to 1.01)	**108 fewer per 1000** (from 200 fewer to 8 more)	⨁⨁⨁◯ Moderate	
Point abstinence, end of treatment												
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	none	50/119 (42.0%)	73/121 (60.3%)	**RR 0.70** (0.54 to 0.90)	**181 fewer per 1000** (from 278 fewer to 60 fewer)	⨁⨁⨁◯ Moderate	
Point abstinence, longest follow-up												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	individual counselling	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	none	64/119 (53.8%)	72/121 (59.5%)	**RR 0.90** (0.72 to 1.13)	**60 fewer per 1000** (from 167 fewer to 77 more)	⨁⨁⨁◯ Moderate	

a. Not applicable because one study included

b. Downgraded of one level for imprecision because OIS not met

Table 2 g. Evidence profile Cognitive Behavioural Therapy (CBT) vs interpersonal therapy

Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,

Date:

Question: Should any Cognitive Behavioural Therapy (CBT) vs interpersonal therapy be used for psychostimulant misuse?

Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	interpersonal therapy	Relative (95% CI)	Absolute (95% CI)		
Dropouts												
2	Randomized trials	serious[a]	not serious	not serious	serious[b]	none	86/140 (61.4%)	96/145 (66.2%)	**RR 0.80** (0.45 to 1.43)	**132 fewer per 1000** (from 364 fewer to 285 more)	⨁⨁◯◯ Low	
Point abstinence, end of treatment												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT	interpersonal therapy	Relative (95% CI)	Absolute (95% CI)		
2	randomized trials	serious[a]	serious[c]	not serious	serious[b]	none	62/140 (44.3%)	67/145 (46.2%)	**RR 1.12** (0.59 to 2.15)	**55 more per 1000** (from 189 fewer to 531 more)	⊕◯◯◯ Very low	
Continuous abstinence, end of treatment												
1	randomized trials	serious[a]	not serious[d]	not serious	very serious[e]	none	9/21 (42.9%)	4/21 (19.0%)	**RR 2.25** (0.82 to 6.18)	**238 more per 1000** (from 34 fewer to 987 more)	⊕◯◯◯ Very low	
Point abstinence, longest follow-up												
1	randomized trials	not serious	not serious[d]	not serious	serious[b]	none	64/119 (53.8%)	64/124 (51.6%)	**RR 1.04** (0.82 to 1.32)	**21 more per 1000** (from 93 fewer to 165 more)	⊕⊕⊕◯ Moderate	

a. Downgraded of one level for risk of bias because one study was at unclear risk for selection bias and one at high risk for attrition bias
b. Downgraded of one level for imprecision because OIS not met
c. Downgraded of one level for inconsistency because $I^2 = 67\%$
d. Not applicable because one study included
e. Downgraded of two levels for imprecision because less than 100 events

Table 2h. Evidence profile interpersonal therapy vs individual counselling

Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,

Date:

Question: Should any interpersonal therapy vs individual counselling be used for psychostimulant misuse?

Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Interpersonal	individual counselling	Relative (95% CI)	Absolute (95% CI)		
Dropouts												
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	None	83/124 (66.9%)	93/121 (76.9%)	**RR 0.87** (0.74 to 1.02)	**100 fewer per 1000** (from 200 fewer to 15 more)	⊕⊕⊕◯ Moderate	
Point abstinence, end of treatment												
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	None	62/124 (50.0%)	73/121 (60.3%)	**RR 0.83** (0.66 to 1.04)	**103 fewer per 1000** (from 205 fewer to 24 more)	⊕⊕⊕◯ Moderate	
Point abstinence, longest follow-up												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Interpersonal	individual counselling	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	not serious	not serious[a]	not serious	serious[b]	None	64/124 (51.6%)	72/121 (59.5%)	**RR 0.87** (0.69 to 1.09)	**77 fewer per 1000** (from 184 fewer to 54 more)	⨁⨁⨁◯ Moderate	

a. Not applicable because one study included

b. Downgraded of one level for risk of bias because OIS not met

Table 2i. Evidence profile contingency management reinforcement (CM) vs no contingency management reinforcement (no CM)
Author(s): Minozzi S, Traccis F, Saulle R , Agabio R,
Date:
Question: Should any contingency management reinforcement (CM vs no contingency management reinforcement (no CM) be used for psychostimulant misuse?
Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CM reinforcement	no CM reinforcement	Relative (95% CI)	Absolute (95% CI)		
Dropouts												
5	randomized trials	serious[a]	serious[b]	not serious	serious[c]	none	118/305 (38.7%)	140/329 (42.6%)	**RR 0.84** (0.50 to 1.42)	**68 fewer per 1000** (from 213 fewer to 179 more)	⊕◯◯◯ Very low	
Point abstinence, longest follow-up												
1	randomized trials	not serious	not serious[d]	not serious	serious[e]	none	42/91 (46.2%)	30/35 (85.7%)	**RR 0.54** (0.42 to 0.70)	**394 fewer per 1000** (from 497 fewer to 257 fewer)	⊕⊕⊕◯ Moderate	
Continuous abstinence, end of treatment												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CM reinforcement	no CM reinforcement	Relative (95% CI)	Absolute (95% CI)		
2	randomized trials	not serious	not serious	not serious	serious[e]	none	16/59 (27.1%)	1/37 (2.7%)	**RR 8.11** (1.62 to 40.55)	**192 more per 1000** (from 17 more to 1.000 more)	⊕⊕⊕◯ Moderate	
Frequency of drug intake, longest follow-up												
1	randomized trials	not serious	not serious[d]	not serious	serious[f]	none	52	55	-	SMD **0.29 SD lower** (0.57 lower to 0.09 higher)	⊕⊕⊕◯ Moderate	

a. Downgraded of one level for risk of bias because three studies at high risk of attrition bias
b. Downgraded of one level for inconsistency because I^2 = 83%
c. Downgraded of one level for imprecision because CI include important benefits and important harms
d. Not applicable because one study included
e. Downgraded of one level for imprecision because OIS not met
f. Downgraded of one level for imprecision because < 400 participants
[1]4 categories of quality of evidence: ⊕⊕⊕⊕ (High), ⊕⊕⊕◯Moderate), ⊕⊕◯ ◯ (Low), ⊕◯◯◯ (Very low).
[2]Recommendation: 2 grades – conditional or strong (for or against an intervention). Examples are provided in the table. Note: an alternative categorization of standard or strong is used for the conditions related to stress module.

6.4. Additional evidence not mentioned in GRADE tables

There is no additional evidence not mentioned in GRADE tables.

7. From Evidence to Recommendations

7.1. Summary of findings

Table 3a. Summary of findings table any psychosocial treatment versus no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no intervention	**Risk with Any psychosocial treatment**			
Dropouts	341 per 1000	**276 per 1000** (249 to 310)	**RR 0.81** (0.73 to 0.91)	4 571 (33 RCTs)	⨁⨁⨁◯ Moderate[a]
Point abstinence, end of treatment	386 per 1000	**429 per 1000** (352 to 522)	**RR 1.11** (0.91 to 1.35)	1 344 (8 RCTs)	⨁⨁⨁⨁ High
Point abstinence, longest follow-up	459 per 1000	**500 per 1000** (372 to 670)	**RR 1.09** (0.81 to 1.46)	1 296 (7 RCTs)	⨁⨁◯◯ Low[b,c]
Continuous abstinence, end of treatment	106 per 1000	**255 per 1000** (156 to 416)	**RR 2.41** (1.47 to 3.93)	1 404 (10 RCTs)	⨁⨁◯◯ Low[d,e]
Continuous abstinence, longest follow-up	365 per 1000	**446 per 1000** (321 to 617)	**RR 1.22** (0.88 to 1.69)	365 (5 RCTs)	⨁⨁◯◯ Low[f,g]
Frequency of drug intake, longest follow-up	-	SMD **0.63 lower** (0.96 lower to 0.3 lower)	-	1 974 (14 RCTs)	⨁⨁⨁◯ Moderate[h]
Longest period of abstinence	-	SMD **0.51 higher** (0.39 higher to 0.62 higher)	-	2 088 (15 RCTs)	⨁⨁⨁◯ Moderate[i]

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no intervention	**Risk with Any psychosocial treatment**			
Craving	-	SMD **0.39 lower** (0.72 lower to 0.06 lower)	-	456 (3 RCTs)	⨁⨁⨁◯ Moderate[j]
Severity of dependence	-	SMD **0.76 lower** (1.66 lower to 0.14 higher)	-	413 (7 RCTs)	⨁⨁◯◯ Low[k,l]
Depression	-	SMD **0.41 lower** (0.86 lower to 0.04 higher)	-	78 (2 RCTs)	⨁◯◯◯ Very low[m,n]

a. Downgraded of one level for risk of bias because twenty studies were at unclear risk and two at high risk for selection bias
b. Downgraded of one level for risk of bias because tree studies were at unclear risk for selection bias, one study at high risk for attrition bias
c. Downgraded of one level for inconsistency because I^2 = 78%
d. Downgraded of one level for risk of bias because five studies were at unclear risk for selection bias and tree studies were at high risk of attrition bias
e. Downgraded of one level for suspected publication bias
f. Downgraded of one level for risk of bias because four studies were at unclear risk and one at high risk for selection bias and one study at high risk for attrition bias.
g. Downgraded of one level for imprecision because OIS not met.
h. Downgraded of one level for risk of bias because nine studies were at unclear risk and one at high risk for selection bias
i. Downgraded of one level for risk of bias because thirteen were at unclear risk for selection bias
j. Downgraded of one level for risk of bias because two were at unclear risk for selection bias and attrition bias
k. Downgraded of one level for risk of bias because four studies were at unclear risk and one at high risk for selection bias, two at high risk for attrition bias
l. Downgraded of one level for inconsistency because I^2 = 94%
m. Downgraded of one level for risk of bias because one study was at unclear risk for selection bias and one at high risk for attrition bias
n. Downgraded of two levels for imprecision because < 100 participants and wide IC

7.1.1. Subgroup analyses single treatment versus no treatment

Table 3aa. Summary of findings table Cognitive behavioural therapy (CBT) versus no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no intervention	**Risk with Single treatment**			
Dropouts - CBT	393 per 1000	**350 per 1000** (263 to 468)	**RR 0.89** (0.67 to 1.19)	1 002 (8 RCTs)	⊕⊕⊕◯ Moderate[a]
Point abstinence, end of treatment - CBT	538 per 1000	**521 per 1000** (430 to 634)	**RR 0.97** (0.80 to 1.18)	501 (3 RCTs)	⊕⊕⊕◯ Moderate[f]
Point abstinence, longest follow-up - CBT	378 per 1000	**623 per 1000** (321 to 1.000)	**RR 1.65** (0.85 to 3.24)	508 (3 RCTs)	⊕⊕⊕⊕ High
Continuous abstinence, end of treatment - CBT	167 per 1000	**362 per 1000** (178 to 733)	**RR 2.17** (1.07 to 4.40)	101 (1 RCT)	⊕⊕◯◯ Low[b,c,e]
Continuous abstinence, longest follow-up - CBT	725 per 1000	**841 per 1000** (674 to 1.000)	**RR 1.16** (0.93 to 1.46)	85 (1 RCT)	⊕◯◯◯ Very low[b,c,d]
Frequency of drug intake, longest follow-up - CBT	-	SMD **1.96 lower** (4.78 lower to 0.85 higher)	-	227 (3 RCTs)	⊕⊕◯◯ Low[g,h]
Longest period of abstinence - CBT	-	SMD **0.5 higher** (0.16 higher to 0.84 higher)	-	430 (4 RCTs)	⊕⊕⊕◯ Moderate[i]
Severity of dependence - CBT	-	SMD **2.17 lower** (2.62 lower to 1.71 lower)	-	120 (1 RCT)	⊕⊕⊕◯ Moderate[c,h]
Depression - CBT	The mean depression - CBT was **0**	SMD **0.28 lower** (0.90 lower to 0.34 higher)	-	41 (1 RCT)	⊕◯◯◯ Very low[b,c,j]

a. Downgraded of one level for risk of bias because five studies at unclear risk of selection bias
b. Downgraded of one level for risk of bias because the only included study was at unclear risk of selection bias

c. Not applicable because one study included
d. Downgraded of two levels for imprecision because < 100 events
e. Downgraded of one level for imprecision because OIS not met
f. Downgraded of one level for risk of bias because two studies at unclear risk for selection bias
g. Downgraded of one level for risk of bias because two studies at unclear risk of selection bias
h. Downgraded of one level for imprecision because < 400 participants
i. Downgraded of one level for risk of bias because all studies at unclear risk of selection bias
j. Downgraded of two levels for imprecision because < 100 participants

Table 3ab. Summary of findings table Contingency Management (CM) versus no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no intervention	**Risk with Single treatment**			
Dropouts - CM	386 per 1000	**297 per 1000** (263 to 336)	**RR 0.77** (0.68 to 0.87)	2 357 (17 RCTs)	⊕⊕◯◯ Low[a,b]
Point abstinence, end of treatment - CM	251 per 1000	**364 per 1000** (216 to 610)	**RR 1.45** (0.86 to 2.43)	525 (5 RCTs)	⊕⊕◯◯ Low[e,f]
Point abstinence, longest follow-up - CM	720 per 1000	**454 per 1000** (353 to 598)	**RR 0.63** (0.49 to 0.83)	159 (2 RCTs)	⊕⊕⊕◯ Moderate[e]
Continuous abstinence, end of treatment - CM	101 per 1000	**253 per 1000** (144 to 446)	**RR 2.51** (1.43 to 4.43)	1303 (9 RCTs)	⊕⊕⊕◯ Moderate[g]
Continuous abstinence, longest follow-up - CM	270 per 1000	**555 per 1000** (167 to 1.000)	**RR 2.06** (0.62 to 6.82)	251 (3 RCTs)	⊕◯◯◯ Very low[d,h]
Frequency of drug intake, longest follow-up - CM	-	SMD **0.36 lower** (0.51 lower to 0.22 lower)	-	907 (6 RCTs)	⊕⊕⊕◯ Moderate[j]
Longest period of abstinence - CM	-	SMD **0.54 higher** (0.4 higher to 0.69 higher)	-	1698 (12 RCTs)	⊕⊕⊕◯ Moderate[k]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no intervention	**Risk with Single treatment**			
Craving - CM	-	SMD **0.52 lower** (1.26 lower to 0.22 higher)	-	242 (2 RCTs)	⨁⨁◯◯ Low[i,l]
Severity of dependence - CM	-	SMD **0.75 lower** (1.83 lower to 0.34 higher)	-	224 (4 RCTs)	⨁⨁◯◯ Low[f,i]
Depression - CM	The mean depression - CM was **0**	SMD **0.56 lower** (1.22 lower to 0.10 higher)	-	37 (1 RCT)	⨁◯◯◯ Very low[c,m,n]

a. Downgraded of one level for risk of bias because eleven studies at unclear risk and one at high risk of selection bias; four studies at high risk of attrition bias
b. Downgraded because asymmetric funnel plot suggesting for publication bias
c. Not applicable because one study included
d. Downgraded of two levels for imprecision because < 100 events
e. Downgraded of one level for imprecision because OIS not met
f. Downgraded of one level for risk of bias because three studies at unclear risk of selection bias; one study at high risk of attrition bias
g. Downgraded of one level for risk of bias because four studies at unclear risk; three studies at high risk of attrition bias
h. Downgraded of one level for risk of bias because all three studies at unclear risk of selection bias
i. Downgraded of one level for imprecision because < 400 participants
j. Downgraded of one level for risk of bias because five studies at unclear risk of selection bias
k. Downgraded of one level for risk of bias because nine studies at unclear risk of selection bias
l. Downgraded of one level for risk of bias because all studies at unclear risk of selection bias
m. Downgraded of two levels for imprecision because < 100 participants
n. Downgraded of one level for risk of bias because the only included study was at high risk of attrition bias

Table 3ac. Summary of findings table Motivational Interview (MI) versus no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no intervention	**Risk with Single treatment**			
Dropouts - MI	165 per 1000	**150 per 1000** (107 to 210)	**RR 0.91** (0.65 to 1.27)	696 (5 RCTs)	⨁⨁◯◯ Low[a,b]
Point abstinence, longest follow-up - MI	452 per 1000	**525 per 1000** (430 to 642)	**RR 1.16** (0.95 to 1.42)	384 (2 RCTs)	⨁⨁⨁⨁ High
Continuous abstinence, longest follow-up - MI	83 per 1000	**177 per 1000** (21 to 1.000)	**RR 2.12** (0.25 to 17.98)	29 (1 RCT)	⨁◯◯◯ Very low[c,d,e]
Frequency of drug intake, longest follow-up - MI	-	SMD **0.18 lower** (0.38 lower to 0.03 higher)	-	371 (2 RCTs)	⨁⨁⨁◯ Moderate[f]
Severity of dependence – MI	-	SMD **0.01 higher** (0.71 lower to 0.73 higher)	-	69 (2 RCTs)	⨁◯◯◯ Very low[g,h]

a. Downgraded of one level for risk of bias because three studies at unclear risk and one at high risk of selection bias; two studies at high risk of attrition bias
b. Downgraded of one level because OIS not meet and because CI include important benefits and important harms
c. Not applicable because one study included
d. Downgraded of two levels for imprecision because < 100 events
e. Downgraded of two level for risk of bias because the only study included was at high risk of selection bias
f. Downgraded of one level for imprecision because < 400 participants
g. Downgraded of one level for risk of bias because one study at unclear risk and one at high risk of selection bias
h. Downgraded of two levels for imprecision because < 100 participants

Table 3ad. Summary of findings table 12 steps facilitation versus no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no intervention	**Risk with Single treatment**			
Dropouts - 12-step facilitation	214 per 1000	**339 per 1000** (182 to 630)	**RR 1.58** (0.85 to 2.94)	112 (1 RCT)	⊕◯◯◯ Very low[a,b,c]
Point abstinence, end of treatment - 12-step facilitation	339 per 1000	**285 per 1000** (163 to 495)	**RR 0.84** (0.48 to 1.46)	112 (1 RCT)	⊕◯◯◯ Very low[a,b,c]

a. Downgraded of one level for risk of bias because the only included study was at unclear risk of selection bias
b. Not applicable because one study included
c. Downgraded of two levels for imprecision because < 100 events

Table 3ae. Summary of findings table psychodynamic therapy versus no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no intervention	**Risk with Single treatment**			
Dropouts - Psychodynamic therapy	772 per 1000	**672 per 1000** (572 to 780)	**RR 0.87** (0.74 to 1.01)	247 (1 RCT)	⊕⊕⊕◯ Moderate[a,b]
Point abstinence, end of treatment - Psychodynamic therapy	480 per 1000	**499 per 1000** (389 to 643)	**RR 1.04** (0.81 to 1.34)	247 (1 RCT)	⊕⊕⊕◯ Moderate[a,b]
Point abstinence, longest follow-up - psychodynamic	537 per 1000	**515 per 1000** (408 to 655)	**RR 0.96** (0.76 to 1.22)	247 (1 RCT)	⊕⊕⊕◯ Moderate[a,b]

a. Not applicable because one study included
b. Downgraded of one level for imprecision because OIS not met

Table 3af. Summary of findings table individual counselling versus no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no intervention	**Risk with Single treatment**			
Point abstinence, end of treatment - Individual counselling	480 per 1000	**604 per 1000** (480 to 763)	**RR 1.26** (1.00 to 1.59)	244 (1 RCT)	⨁⨁⨁◯ Moderate[a,b]
Point abstinence, longest follow-up - individual counselling	537 per 1000	**596 per 1000** (478 to 740)	**RR 1.11** (0.89 to 1.38)	244 (1 RCT)	⨁⨁⨁◯ Moderate[a,b]

a. Not applicable because one study included
b. Downgraded of one level for imprecision because OIS not met

Table 3ag. Summary of findings table positive affect intervention versus no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no intervention	**Risk with Single treatment**			
Frequency of drug intake, longest follow-up - positive affect intervention	-	SMD **0.29 lower** (0.56 lower to 0.02 lower)	-	214 (1 RCT)	⨁⨁⨁◯ Moderate[a,b]
Craving - positive affect intervention	-	SMD **0.31 lower** (0.58 lower to 0.04 lower)	-	214 (1 RCT)	⨁⨁⨁◯ Moderate[a,b]

a. Not applicable because one study included
b. Downgraded of one level for imprecision because <400 participants

Table 3b. Summary of findings table any psychosocial treatment versus treatment as usual (TAU)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with TAU	**Risk with Any psychosocial treatment**			
Dropouts	520 per 1000	**395 per 1000** (317 to 499)	**RR 0.76** (0.61 to 0.96)	606 (8 RCTs)	⊕⊕⊕◯ Moderate[a]
Point abstinence, end of treatment	143 per 1000	**276 per 1000** (163 to 469)	**RR 1.93** (1.14 to 3.28)	240 (3 RCTs)	⊕◯◯◯ Very low[b,c]
Point abstinence, longest follow up	258 per 1000	**488 per 1000** (305 to 779)	**RR 1.89** (1.18 to 3.02)	164 (2 RCTs)	⊕◯◯◯ Very low[c,d]
Continuous abstinence, end of treatment	395 per 1000	**454 per 1000** (360 to 577)	**RR 1.15** (0.91 to 1.46)	264 (3 RCTs)	⊕⊕◯◯ Low[e,f]
Longest period of abstinence	-	SMD **0.4 SD higher** (0.8 lower to 1.59 higher)	-	140 (2 RCTs)	⊕◯◯◯ Very low[g,h,i]
Severity of dependence	-	SMD **0.24 lower** (0.56 lower to 0.08 higher)	-	149 (2 RCTs)	⊕⊕◯◯ Low[d,i]
frequency of drug intake, end of treatment	-	SMD **0.02 lower** (0.22 lower to 0.18 higher)	-	389 (4 RCTs)	⊕⊕◯◯ Low[j,k]
craving	-	SMD **0.7 lower** (1.21 lower to 0.2 lower)	-	69 (2 RCTs)	⊕◯◯◯ Very low[l,m]
Depression (HAM)	The mean depression (HAM) was **0**	SMD **0.16 lower** (0.80 lower to 0.47 higher)	-	39 (1 RCT)	⊕◯◯◯ Very low[m,n,o]

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with TAU	**Risk with Any psychosocial treatment**			
N.subjects with adverse events	23 per 1.000	**100 per 1000** (13 to 752)	**RR 4.38** (0.58 to 33.10)	90 (2 RCTs)	⨁◯◯◯ Very low[c,l]

a. Downgraded one level for risk of bias because all but one was at unclear risk for selection bias and one at high risk, two studies were at high risk for attrition bias
b. Downgraded one level for risk of bias because all but one was at unclear risk for selection bias and one at high risk
c. Downgraded of two levels for imprecision because < 100 events
d. Downgraded of one level for risk of bias because all studies were at unclear risk for selection bias and one at high risk for attrition bias
e. Downgraded of one level for risk of bias because all were at unclear risk for selection bias
f. Downgraded of one level for imprecision because OIS not met
g. Downgraded one level for risk of bias because one study was at unclear and one at high risk for selection bias and one at high risk for attrition bias
h. Downgraded of two levels for inconsistency because I^2 = 85%
i. Downgraded of one level for imprecision because < 400 participants
j. Downgraded one level for risk of bias because all but one was at unclear risk for selection bias and one at high risk, one study was at high risk for attrition bias
k. Downgraded of one level for inconsistency because I^2 = 71%
l. Downgraded of one level for risk of bias because one study was at unclear risk and one at high risk for selection bias
m. Downgraded of two levels for imprecision because < 100 participants
n. Downgraded of one level for risk of bias because the only study included was at unclear risk of bias and at high risk for attrition
o. Not applicable because one study included

7.1.2. Subgroup analyses for type of psychosocial treatment versus treatment as usual (TAU)

Table 3ba. Cognitive Behavioural Therapy (CBT) versus TAU

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with TAU	**Risk with Single treatment**			
Dropouts - CBT	528 per 1000	**412 per 1000** (338 to 496)	**RR 0.78** (0.64 to 0.94)	450 (6 RCTs)	⨁⨁◯◯ Low[a]
Point abstinence, end of treatment - CBT	143 per 1000	**247 per 1000** (141 to 431)	**RR 1.73** (0.99 to 3.02)	213 (3 RCTs)	⨁◯◯◯ Very low[d,e]
Point abstinence, longest follow up - CBT	258 per 1000	**501 per 1000** (310 to 810)	**RR 1.94** (1.20 to 3.14)	137 (2 RCTs)	⨁⨁◯◯ Low[f,g]
Continuous abstinence, end of treatment - CBT	594 per 1000	**701 per 1000** (546 to 908)	**RR 1.18** (0.92 to 1.53)	128 (1 RCT)	⨁◯◯◯ Very low[b,c,e]
Longest period of abstinence - CBT	-	SMD **0.4 SD higher** (0.8 lower to 1.59 higher)	-	140 (2 RCTs)	⨁◯◯◯ Very low[h,i]
Severity of dependence (ASI) - CBT	-	SMD **0.22 SD lower** (0.59 lower to 0.16 higher)	-	110 (1 RCT)	⨁⨁◯◯ Low[b,i,j]
frequency of drug intake, end of treatment - CBT	-	SMD **1.21 lower** (1.99 lower to 0.42 lower)	-	30 (1 RCT)	⨁◯◯◯ Very low[b,k,l]
craving - CBT	-	SMD **1.63 SD lower** (2.47 lower to 0.79 lower)	-	30 (1 RCT)	⨁◯◯◯ Very low[b,k,l]
N subjects with adverse events - CBT	71 per 1000	**313 per 1000** (41 to 1.000)	**RR 4.38** (0.58 to 33.10)	30 (1 RCT)	⨁◯◯◯ Very low[b,e,l]

a. Downgraded of two levels for risk of bias because the five studies were at unclear and one at high risk of selection bias; two studies at high risk of bias
b. Not applicable because one study included
c. Downgraded of one level for risk of bias because the study was at unclear of selection bias
d. Downgraded of two levels for risk of bias because two studies at unclear risk and one at high risk of selection bias
e. Downgraded of two levels because < 100 events
f. Downgraded of one level because OIS not met
g. Downgraded of one level for risk of bias because two studies at unclear of selection bias and one at high risk of attrition bias
h. Downgraded of two levels for risk of bias because one study at unclear risk and one at high risk of selection bias and one study at high risk of attrition bias
i. Downgraded of one level for imprecision because < 400 participants
j. Downgraded of two levels for risk of bias because the study was at unclear of selection bias and one at high risk of attrition bias
k. Downgraded of one level for imprecision because < 100 participants
l. Downgraded of two levels for risk of bias because the only study included was at high risk of selection bias

Table 3bb. Contingency management (CM) versus TAU

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with TAU	**Risk with Single treatment**			
Dropouts - CM	600 per 1000	**444 per 1000** (294 to 678)	**RR 0.74** (0.49 to 1.13)	82 (1 RCT)	⨁◯◯◯ Very low[a,b,c]
Point abstinence, end of treatment - CM	222 per 1000	**593 per 1000** (273 to 1.000)	**RR 2.67** (1.23 to 5.77)	54 (1 RCT)	⨁⨁◯◯ Low[b,d,f]
Point abstinence, longest follow up - CM	259 per 1000	**519 per 1000** (249 to 1.000)	**RR 2.00** (0.96 to 4.17)	54 (1 RCT)	⨁◯◯◯ Very low[b,d,e]

a. Downgraded of one level for risk of bias because the study was at unclear of selection bias and at high risk of attrition bias
b. Not applicable because one study included
c. Downgraded of two levels for risk imprecision because OIS not met and wide CI
d. Downgraded of one level for risk of bias because the study was at unclear of selection bias
e. Downgraded of two levels because < 100 events
f. Downgraded of one level because OIS not met

Table 3bc. Interpersonal therapy versus TAU

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with TAU	**Risk with Single treatment**			
frequency of drug intake, end of treatment - interpersonal therapy	-	SMD **0.15 higher** (0.22 lower to 0.53 higher)	-	110 (1 RCT)	⨁◯◯◯ Very low[a,b,c]

a. Not applicable because one study included
b. Downgraded of one level for imprecision because < 400 participants
c. Downgraded of two levels for risk of bias because the study at unclear risk of selection bias and high risk of attrition bias

Table 3bd. Motivational interview versus TAU

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with TAU	**Risk with Single treatment**			
Dropouts - MI	267 per 1000	**435 per 1000** (211 to 891)	**RR 1.63** (0.79 to 3.34)	60 (1 RCT)	⨁◯◯◯ Very low[a,b,c]
Severity of dependence (ASI) - MI	-	SMD **0.31 SD lower** (0.95 lower to 0.32 higher)	-	39 (1 RCT)	⨁◯◯◯ Very low[a,b,d]
frequency of drug intake, end of treatment - MI	-	SMD **0.25 lower** (0.89 lower to 0.38 higher)	-	39 (1 RCT)	⨁⨁◯◯ Low[a,d]
craving - MI	-	SMD **0.18 SD lower** (0.81 lower to 0.45 higher)	-	39 (1 RCT)	⨁⨁◯◯ Low[a,d]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with TAU	**Risk with Single treatment**			
N subjects with adverse events - MI	0 per 1000	**0 per 1.000** (0 to 0)	not estimable	60 (1 RCT)	-

a. Not applicable because one study included
b. Downgraded of one level for risk of bias because the study was at unclear of selection bias
c. Downgraded of two levels for imprecision because OIS not met and CI include important benefits and important harms
d. Downgraded of one level for imprecision because < 100 participants

Table 3be. Motivational interview + Cognitive behavioural therapy (MI+CBT) versus TAU

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with TAU	**Risk with Single treatment**			
frequency of drug intake, end of treatment - MI+CBT	-	SMD **0.07 higher** (0.2 lower to 0.34 higher)	-	210 (1 RCT)	⨁⨁⨁◯ Moderate[a,b]

a. Not applicable because one study included
b. Downgraded of one level for imprecision because < 400 participants

7.1.3. Single treatments vs each other

Table 3c. Summary of findings table Cognitive Behavioural Therapy (CBT) versus 12 step facilitation

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with 12-step facilitation	**Risk with CBT**			
Dropouts	500 per 1000	**435 per 1000** (310 to 620)	**RR 0.87** (0.62 to 1.24)	145 (1 RCT)	⨁◯◯◯ Very low[a,b,c]
Continuous abstinence, end of treatment	353 per 1000	**431 per 1000** (311 to 596)	**RR 1.22** (0.88 to 1.69)	225 (2 RCTs)	⨁◯◯◯ Very low[c,d]
Continuous abstinence, longest follow-up	296 per 1000	**584 per 1000** (296 to 1.000)	**RR 1.97** (1.00 to 3.86)	51 (1 RCT)	⨁◯◯◯ Very low[b,c,e]

a. Downgraded of one level for risk of bias because one study was at unclear risk for selection bias and one at high risk for attrition bias
b. Not applicable because one study included
c. Downgraded of two levels for imprecision because less than 100 events
d. Downgraded of one level for risk of bias because all were at unclear risk for selection bias
e. Downgraded of one level for risk of bias because one study was at unclear risk for selection bias

Table 3d. Summary of findings table Cognitive Behavioural Therapy (CBT) versus Acceptance Commitment Therapy (ACT)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with ACT	**Risk with CBT**			
Dropouts	725 per 1000	**682 per 1000** (530 to 871)	**RR 0.94** (0.73 to 1.20)	104 (1 RCT)	⨁◯◯◯ Very low[a,b,c]
Point abstinence, end of treatment	333 per 1000	**430 per 1000** (157 to 1.000)	**RR 1.29** (0.47 to 3.51)	26 (1 RCT)	⨁◯◯◯ Very low[a,c]
Point abstinence, longest follow-up	500 per 1000	**365 per 1000** (130 to 1.000)	**RR 0.73** (0.26 to 2.07)	19 (1 RCT)	⨁◯◯◯ Very low[a,c]

a. Downgraded of one level for risk of bias because the study was at high risk for selection bias
b. Not applicable because one study
c. Downgraded of two levels for risk of bias because less than 100 events

Table 3e. Summary of findings table Cognitive Behavioural Therapy (CBT) versus Contingency Management (CM)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with CM	**Risk with CBT**			
Point abstinence, end of treatment	593 per 1000	**391 per 1000** (225 to 687)	**RR 0.66** (0.38 to 1.16)	55 (1 RCT)	⨁◯◯◯ Very low[a,b,c]
Point abstinence, longest follow-up	519 per 1000	**607 per 1000** (379 to 970)	**RR 1.17** (0.73 to 1.87)	55 (1 RCT)	⨁◯◯◯ Very low[a,b,c]
Frequency of drug intake, longest follow-up (days/months)	The mean frequency of drug intake, longest follow-up (days/months) was **0**	SMD **0.09 lower** (0.53 lower to 0.34 higher)	-	82 (1 RCT)	⨁◯◯◯ Very low[a,b,d]

a. Downgraded of one level for risk of bias because one study was at unclear risk for selection bias
b. Not applicable because one study included
c. Downgraded of two levels for imprecision because less than 100 events
d. Downgraded of two levels for imprecision because less than 100 participants

Table 3f. Summary of findings table Cognitive Behavioural Therapy (CBT) versus Individual Counselling

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with individual counselling	**Risk with CBT**			
Dropouts	769 per 1000	**661 per 1000** (569 to 776)	**RR 0.86** (0.74 to 1.01)	240 (1 RCT)	⨁⨁⨁◯ Moderate[a,b]
Point abstinence, end of treatment	603 per 1000	**422 per 1000** (326 to 543)	**RR 0.70** (0.54 to 0.90)	240 (1 RCT)	⨁⨁⨁◯ Moderate[a,b]
Point abstinence, longest follow-up	595 per 1000	**536 per 1000** (428 to 672)	**RR 0.90** (0.72 to 1.13)	240 (1 RCT)	⨁⨁⨁◯ Moderate[a,b]

a. Not applicable because one study included
b. Downgraded of one level for imprecision because OIS not met

Table 3g. Summary of findings table Cognitive Behavioural Therapy (CBT) versus interpersonal therapy

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with interpersonal therapy	**Risk with CBT**			
Dropouts	662 per 1000	**530 per 1000** (298 to 947)	**RR 0.80** (0.45 to 1.43)	285 (2 RCTs)	⊕⊕◯◯ Low[a,b]
Point abstinence, end of treatment	462 per 1000	**518 per 1000** (273 to 993)	**RR 1.12** (0.59 to 2.15)	285 (2 RCTs)	⊕◯◯◯ Very low[a,b,c]
Continuous abstinence, end of treatment	190 per 1000	**429 per 1000** (156 to 1.000)	**RR 2.25** (0.82 to 6.18)	42 (1 RCT)	⊕◯◯◯ Very low[a,d,e]
Point abstinence, longest follow-up	516 per 1000	**537 per 1000** (423 to 681)	**RR 1.04** (0.82 to 1.32)	243 (1 RCT)	⊕⊕⊕◯ Moderate[b,d]

a. Downgraded of one level for risk of bias because one study was at unclear risk for selection bias and one at high risk for attrition bias
b. Downgraded of one level for imprecision because OIS not met
c. Downgraded of one level for inconsistency because $I^2 = 67\%$
d. Not applicable because one study included
e. Downgraded of two levels for imprecision because less than 100 events

Table 3h. Summary of findings table interpersonal therapy versus individual counselling

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with individual counselling	**Risk with Interpersonal**			
Dropouts	769 per 1000	**669 per 1000** (569 to 784)	**RR 0.87** (0.74 to 1.02)	245 (1 RCT)	⊕⊕⊕◯ Moderate[a,b]
Point abstinence, end of treatment	603 per 1000	**501 per 1000** (398 to 627)	**RR 0.83** (0.66 to 1.04)	245 (1 RCT)	⊕⊕⊕◯ Moderate[a,b]
Point abstinence, longest follow-up	595 per 1000	**518 per 1000** (411 to 649)	**RR 0.87** (0.69 to 1.09)	245 (1 RCT)	⊕⊕⊕◯ Moderate[a,b]

a. Not applicable because one study included
b. Downgraded of one level for risk of bias because OIS not met

Table 3i. Summary of findings Contingency reinforcement management (CM) versus no contingency reinforcement management (no CM)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no CM reinforcement	**Risk with CM reinforcement**			
Dropouts	426 per 1000	**357 per 1000** (213 to 604)	**RR 0.84** (0.50 to 1.42)	634 (5 RCTs)	⊕◯◯◯ Very low[a,b,c]
Point abstinence, longest follow-up	857 per 1000	**463 per 1000** (360 to 600)	**RR 0.54** (0.42 to 0.70)	126 (1 RCT)	⊕⊕⊕◯ Moderate[d,e]
Continuous abstinence, end of treatment	27 per 1000	**219 per 1000** (44 to 1.000)	**RR 8.11** (1.62 to 40.55)	96 (2 RCTs)	⊕⊕⊕◯ Moderate[e]
Frequency of drug intake, longest follow-up	-	SMD **0.29 SD lower** (0.57 lower to 0.09 higher)	-	107 (1 RCT)	⊕⊕⊕◯ Moderate[d,f]

a. Downgraded of one level for risk of bias because three studies at high risk of attrition bias
b. Downgraded of one level for inconsistency because I^2 = 83%
c. Downgraded of one level for imprecision because CI include important benefits and important harms
d. Not applicable because one study included
e. Downgraded of one level for imprecision because OIS not met
f. Downgraded of one level for imprecision because < 400 participants

7.2. Evidence to decision

Table 4. Evidence to decision table

Please note * indicates evidence from overarching qualitative review by Gronholm et al, 2023

	CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Priority of the problem	Is the problem a priority? The more serious a problem is, the more likely it is that an option that addresses the problem should be a priority (e.g. diseases that are fatal or disabling are likely to be a higher priority than diseases that only cause minor distress). The more people who are affected, the more likely it is that an option that addresses the problem should be a priority.			
	• Are the consequences of the problem serious (that is, severe or important in terms of the potential benefits or savings)? • Is the problem urgent? • Is it a recognized priority (such as based on a political or policy decision)? [Not relevant when an individual patient perspective is taken]	☐ No ☐ Probably no ☐ Probably yes ☒ **Yes** ☐ Varies ☐ Don't know	Drug use and drug use disorders constitute a public health, developmental and security problem both in developed and developing countries worldwide. According to the latest global estimates, about 5.5 per cent of the population aged between 15 and 64 years have used drugs at least once in the past year, while 36.3 million people, or 13 per cent of the total number of persons who use drugs, suffer from drug use disorders (UNODC, 2021). Approximately 0.5 million deaths annually attributable to drug use (UNODC, 2021).	
Desirable Effects	How substantial are the desirable anticipated effects? The larger the benefit, the more likely it is that an option should be recommended.			
	• Judgements for each outcome for which there is a desirable effect • How substantial (large) are the desirable anticipated effects (including health and other benefits) of the option (taking into account the severity or importance of the desirable consequences and the number of people affected)?	☐ Trivial ☐ Small ☐ Moderate ☐ Large ☒ **Varies** ☐ Don't know	**Compare to no treatment:** **Effect:** • **any psychosocial intervention** probably decreases dropouts from study and frequency of drug intake and longest period of abstinence (moderate certainty); may increase continuous abstinence at the end of treatment (low certainty) • **CBT** may increase Continuous	**Head to head comparisons**: • **CBT versus 12 step facilitation** We are uncertain whether CBT makes little or no difference compared to 12 steps) in dropout from study, continuous abstinence and of treatment and longest FU

CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		abstinence, end of treatment, and reduce frequency of drug intake longest FU (low certainty), probably increase longest period of abstinence (moderate certainty); We are uncertain whether slightly increases continuous abstinence , longest FU (very low certainty) • , **contingency management** may reduce dropouts (low certainty), probably increases Continuous abstinence, end of treatment and longest period of abstinence, probably decreases frequency of drug intake (moderate certainty) • **Motivational interview** probably reduces frequency of drug intake (moderate certainty) • **Psychodynamic therapy** probably reduces the dropout (moderate certainty) • **Individual counselling** probably increases point abstinence end pf treatment • **Positive affect** probably reduces frequency of drug intake longest FU (moderate certainty) **No effect:** • **Any psychosocial intervention** makes little to no difference to point abstinence end of treatment (high certainty), may make little to no difference to Point abstinence and continuous abstinence longest FU (low certainty) • **CBT** probably makes little to no	(very low certainty) • **CBT versus Acceptance Commitment Therapy (ACT)** We are uncertain whether CBT makes little or no difference compared to ACT in dropout from study, point abstinence and of treatment and longest FU (very low certainty) • **CBT versus CM** We are uncertain whether CBT makes little or no difference compared to CM in frequency of drug intake, point abstinence and of treatment and longest FU (very low certainty) • **CBT versus Individual Counselling** CBT probably reduces dropout from study and point abstinence end of treatment compared to Individual counselling (moderate certainty) CBT probably makes little to no difference in point abstinence longest FU compared to individual counselling • **CBT versus interpersonal**

CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		difference to the dropout from study and point abstinence end of s of treatment (moderate certainty) ; makes little to no difference to Point abstinence, longest FU (very low certainty) • **CM** may make little to no difference to Point abstinence, end of treatment (low certainty), probably reduces Point abstinence, longest FU, We are uncertain whether CM have little to no effect on continuous abstinence , longest (very low certainty) • **motivational interviewing** may make little to no difference to dropout and point abstinence longest FU (low certainty) We are uncertain whether has little to no effect on continuous abstinence, longest FU (very low certainty) • **12 steps** . We are uncertain whether 12 step have little to no effect on dropout and point abstinence end of treatment (very low certainty) • **psychodynamic therapy** probably makes little to no difference to Point abstinence and continuous abstinence longest FU (moderate certainty) • **Individual counselling** probably makes little to no difference to Point abstinence longest FU (moderate certainty) **Compare to TAU:** **Effect:** • **any psychosocial intervention**	**therapy** We are uncertain whether CBT makes little to no difference in dropout from study, point abstinence and continuous abstinence end of treatment compared to interpersonal therapy (very low certainty). CBT probably make no difference in point abstinence longest FU (moderate certainty) • **Interpersonal therapy versus individual counselling** Interpersonal therapy probably makes little or no difference in dropout from study, point abstinence end of treatment and longest FU (moderate certainty) • **CM versus no contingency reinforcement management (no CM)** We are uncertain whether CM makes little to no difference in dropout from study, compared to no CM (very low certainty). CM probably reduces point abstinence longest FU but increases continuous abstinence end of treatment

CRITERIA, QUESTIONS		JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
			probably decreases dropouts from treatment (moderate certainty)M we are uncertain whether increases point abstinence at the end of treatment or longest follow up (very low certainty) • **CBT** may decrease the dropout and increase point abstinence longest FU (low certainty); We are uncertain whether increases point abstinence end of treatment (very low certainty) • **contingency management** We are uncertain whether reduces the dropout, point abstinence end of treatment, continuous abstinence longest FU (very low certainty) rate **No effect:** • **Any psychosocial** may make little to no difference to Continuous abstinence, end of treatment (low certainty) ; We are uncertain whether Psychosocial may make little to no difference to continuous abstinence , longest FU and longest period of abstinence (very low certainty) • **CBT** We are uncertain whether has little to no effect on Continuous abstinence, end of treatment and longest FU and on longest period of abstinence (very low certainty) • **Interpersonal therapy** We are uncertain whether has little to no effect on frequency of drug intake (very low certainty)	compared to no CM (moderate certainty) CM probably makes little to no difference in frequency of drug intake compared to no CM (moderate certainty)

	CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
			• **Motivational interview**: may make little to no difference to frequency of drug intake, end of treatment (low certainty); We are uncertain whether has little to no effect on Dropout (very low certainty) • **MI+CBT** probably makes little to no difference to frequency of drug intake, end of treatment (moderate certainty)	
Undesirable Effects	How substantial are the undesirable anticipated effects? The greater the harm, the less likely it is that an option should be recommended.			
	• Judgements for each outcome for which there is an undesirable effect • How substantial (large) are the undesirable anticipated effects (including harms to health and other harms) of the option (taking into account the severity or importance of the adverse effects and the number of people affected)?	☐ Large ☐ Moderate ☐ Small ☒ **Trivial** ☐ Varies ☐ Don't know	**Compared to no treatment** • **Any psychosocial:** adverse vent not assessed. We are uncertain whether has little to no effect on depression (very low certainty) • **CBT:** We are uncertain whether has little to no effect on depression (very low certainty) • **CM:** We are uncertain whether has little to no effect on depression (very low certainty • **Motivational interview, 12 steps, psychodynamic therapy, individual counselling, positive affect:** depression not assessed **Compared to TAU:** • **Any psychosocial:** We are uncertain whether has little to no effect on N subjects with AEs and depression (very low certainty) • **CBT:** We are uncertain whether has little to no effect on N subjects with AEs (very low certainty). Depression not assessed	

	CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
			• **MI**: Depression not assessed; No adverse event reported • **Contingency management, interpersonal therapy, MI+CBT:** adverse events and depression not assessed	
Certainty of evidence	What is the overall certainty of the evidence of effects? The less certain the evidence is for critical outcomes (those that are driving a recommendation), the less likely that an option should be recommended (or the more important it is likely to be to conduct a pilot study or impact evaluation, if it is recommended).			
	• What is the overall certainty of this evidence of effects, across all of the outcomes that are critical to making a decision? • See GRADE guidance regarding detailed judgements about the quality of evidence or certainty in estimates of effects	☐ Very low ☒ **Low** ☐ Moderate ☐ High ☐ No included studies	See above Low to moderate	
Values	Is there important uncertainty about or variability in how much people value the main outcomes? The more likely it is that differences in values would lead to different decisions, the less likely it is that there will be a consensus that an option is a priority (or the more important it is likely to be to obtain evidence of the values of those affected by the option). Values in this context refer to the relative importance of the outcomes of interest (how much people value each of those outcomes). These values are sometimes called "utility values".			
	• Is there important uncertainty about how much people value each of the main outcomes? • Is there important variability in how much people value each of the main outcomes?	☐ Important uncertainty or variability ☐ Possibly important uncertainty or variability ☒ **Probably no important uncertainty or variability** ☐ No important uncertainty or variability	•	

	CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Balance of effects	Does the balance between desirable and undesirable effects favour the intervention or the comparison? The larger the desirable effects in relation to the undesirable effects, taking into account the values of those affected (i.e. the relative value they attach to the desirable and undesirable outcomes) the more likely it is that an option should be recommended.			
	• Judgements regarding each of the four preceding criteria • To what extent do the following considerations influence the balance between the desirable and undesirable effects: - How much less people value outcomes that are in the future compared to outcomes that occur now (their discount rates)? - People's attitudes towards undesirable effects (how risk averse they are)? - People's attitudes towards desirable effects (how risk seeking they are)?	☐ Favours the comparison ☐ Probably favours the comparison ☐ Does not favour either the intervention or the comparison ☒ **Probably favours the intervention** ☐ Favours the intervention ☐ Varies ☐ Don't know	.	
Resources required	How large are the resource requirements (costs)? The greater the cost, the less likely it is that an option should be a priority. Conversely, the greater the savings, the more likely it is that an option should be a priority.			
	• How large is the difference in each item of resource use for which fewer resources are required? • How large is the difference in each item of resource use for which more resources are required? • How large an investment of resources would the option require or save?	☐ Large costs ☐ Moderate costs ☐ Negligible costs and savings ☐ Moderate savings ☐ Large savings ☐ Varies ☒ **Don't know**		

	CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Certainty of evidence of required resources	What is the certainty of the evidence of resource requirements (costs)?			
	• Have all-important items of resource use that may differ between the options being considered been identified? • How certain is the evidence of differences in resource use between the options being considered (see GRADE guidance regarding detailed judgements about the quality of evidence or certainty in estimates)? • How certain is the cost of the items of resource use that differ between the options being considered? • Is there important variability in the cost of the items of resource use that differ between the options being considered?	☐ Very low ☐ Low ☐ Moderate ☐ High ☒ **No included studies**		
Cost effectiveness	Does the cost-effectiveness of the intervention favour the intervention or the comparison? The greater the cost per unit of benefit, the less likely it is that an option should be a priority.			
	• Judgements regarding each of the six preceding criteria • Is the cost effectiveness ratio sensitive to one-way sensitivity analyses? • Is the cost effectiveness ratio sensitive to multivariable sensitivity analysis? • Is the economic evaluation on which the cost effectiveness estimate is based reliable? • Is the economic evaluation on which the cost effectiveness estimate is based applicable to the setting(s) of interest?	☐ Favours the comparison ☐ Probably favours the comparison ☐ Does not favour either the intervention or the comparison ☐ Probably favours the intervention ☐ Favours the intervention ☐ Varies ☒ **No included studies**	No reviews examining cost effectiveness identified	

	CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Health equity, equality and non-discrimination	What would be the impact on health equity, equality and non-discrimination? (WHO INTEGRATE) Health equity and equality reflect a concerted and sustained effort to improve health for individuals across all populations, and to reduce avoidable systematic differences in how health and its determinants are distributed. Equality is linked to the legal principle of non-discrimination, which is designed to ensure that individuals or population groups do not experience discrimination on the basis of their sex, age, ethnicity, culture or language, sexual orientation or gender identity, disability status, education, socioeconomic status, place of residence or any other characteristics. All recommendations should be in accordance with universal human rights standards and principles. The greater the likelihood that the intervention increases health equity and/or equality and that it reduces discrimination against any particular group, the greater the likelihood of a general recommendation in favour of this intervention.			
	• How are the condition and its determinants distributed across different population groups? Is the intervention likely to reduce or increase existing health inequalities and/or health inequities? Does the intervention prioritise and/or aid those furthest behind? • How are the benefits and harms of the intervention distributed across the population? Who carries the burden (e.g. all), who benefits (e.g. a very small sub-group)? • How affordable is the intervention for individuals, workplaces or communities? • How accessible - in terms of physical as well as informational access - is the intervention across different population groups? • Is there any suitable alternative to addressing the condition, does the intervention represent the only available option? Is this option proportionate to the need, and will it be subject to periodic review?	☐ Reduced ☐ Probably reduced ☐ Probably no impact ☒ **Probably increased** ☐ Increased ☐ Varies ☐ Don't know		
Feasibility	Is the intervention feasible to implement? The less feasible (capable of being accomplished or brought about) an option is, the less likely it is that it should be recommended (i.e. the more barriers there are that would be difficult to overcome).			
	• Can the option be accomplished or brought about? • Is the intervention or option sustainable? • Are there important barriers that are likely to limit the feasibility of implementing the intervention (option) or require consideration when implementing it?	☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☒**Varies** ☐ Don't know		

	CRITERIA, QUESTIONS	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Human rights and sociocultural acceptability	Is the intervention aligned with human rights principles and socioculturally acceptable? (WHO INTEGRATE) This criterion encompasses two distinct constructs: The first refers to an intervention's compliance with universal human rights standards and other considerations laid out in international human rights law beyond the right to health (as the right to health provides the basis of other criteria and sub-criteria in this framework). The second, sociocultural acceptability, is highly time-specific and context-specific and reflects the extent to which those implementing or benefiting from an intervention as well as other relevant stakeholder groups consider it to be appropriate, based on anticipated or experienced cognitive and emotional responses to the intervention. The greater the sociocultural acceptability of an intervention to all or most relevant stakeholders, the greater the likelihood of a general recommendation in favour of this intervention.			
	• Is the intervention in accordance with universal human rights standards and principles? • Is the intervention socioculturally acceptable to patients/beneficiaries as well as to those implementing it? To which extent do patients/beneficiaries value different non-health outcomes? • Is the intervention socioculturally acceptable to the public and other relevant stakeholder groups? Is the intervention sensitive to sex, age, ethnicity, culture or language, sexual orientation or gender identity, disability status, education, socioeconomic status, place of residence or any other relevant characteristics? • How does the intervention affect an individual's, population group's or organization's autonomy, i.e. their ability to make a competent, informed and voluntary decision? • How intrusive is the intervention, ranging from low intrusiveness (e.g. providing information) to intermediate intrusiveness (e.g. guiding choices) to high intrusiveness (e.g. restricting or eliminating choices)? Where applicable, are high intrusiveness and/or impacts on the privacy and dignity of concerned stakeholders justified?	☐ No ☐ Probably no ☒ **Probably yes** ☐ Yes ☐ Varies ☐ Don't know		

7.3. Summary of judgements

Table 5. Summary of judgements

Priority of the problem	- Don't know	- Varies		- No	- Probably No	- Probably Yes	✓ **Yes**
Desirable effects	- Don't know	✓ **Varies**		- Trivial	- Small	- Moderate	- Large
Undesirable effects	- Don't know	- Varies		- Large	- Moderate	- Small	✓**T rivial**
Certainty of the evidence	- No included studies			- Very low	✓ **Low**	- Moderate	- High
Values				- Important uncertainty or variability	- Possibly important uncertainty or variability	✓ **Probably no important uncertainty or variability**	- No important uncertainty or variability
Balance of effects	- Don't know	- Varies	- Favours comparison	- Probably favours comparison	- Does not favour either	✓ **Probably favours intervention**	- Favours intervention
Resources required	✓ **Don't know**	- Varies	- Large costs	- Moderate costs	- Negligible costs or savings	- Moderate savings	- Large savings
Certainty of the evidence on required resources	✓ **No included studies**			- Very low	- Low	- Moderate	- High
Cost–effectiveness	✓ **No included studies**	- Varies	- Favours comparison	- Probably favours comparison	- Does not favour either	- Probably favours intervention	- Favours intervention
Equity, equality and non-discrimination	- No included studies	- Varies	- Reduced	Probably reduced	- Probably no impact	✓ **Probably increased**	- Increased
Feasibility	- Don't know	✓ **Varies**		- No	- Probably No	- Probably Yes	- Yes
Human rights and sociocultural acceptability	- Don't know	- Varies		- No	- Probably No	✓ **Probably Yes**	- Yes

✓Indicates category selected, -Indicates category not selected

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Appendix I: mhGAP process note

mhGAP Guideline Update: Notes on process for identifying level of evidence review required v2_0 (13/12/2021)

This document is intended to provide guidance to focal points on the level of evidence review required as part of the evidence retrieval process for the mhGAP guideline update process. As a general rule, the update process should be informed by existing high quality systematic reviews.

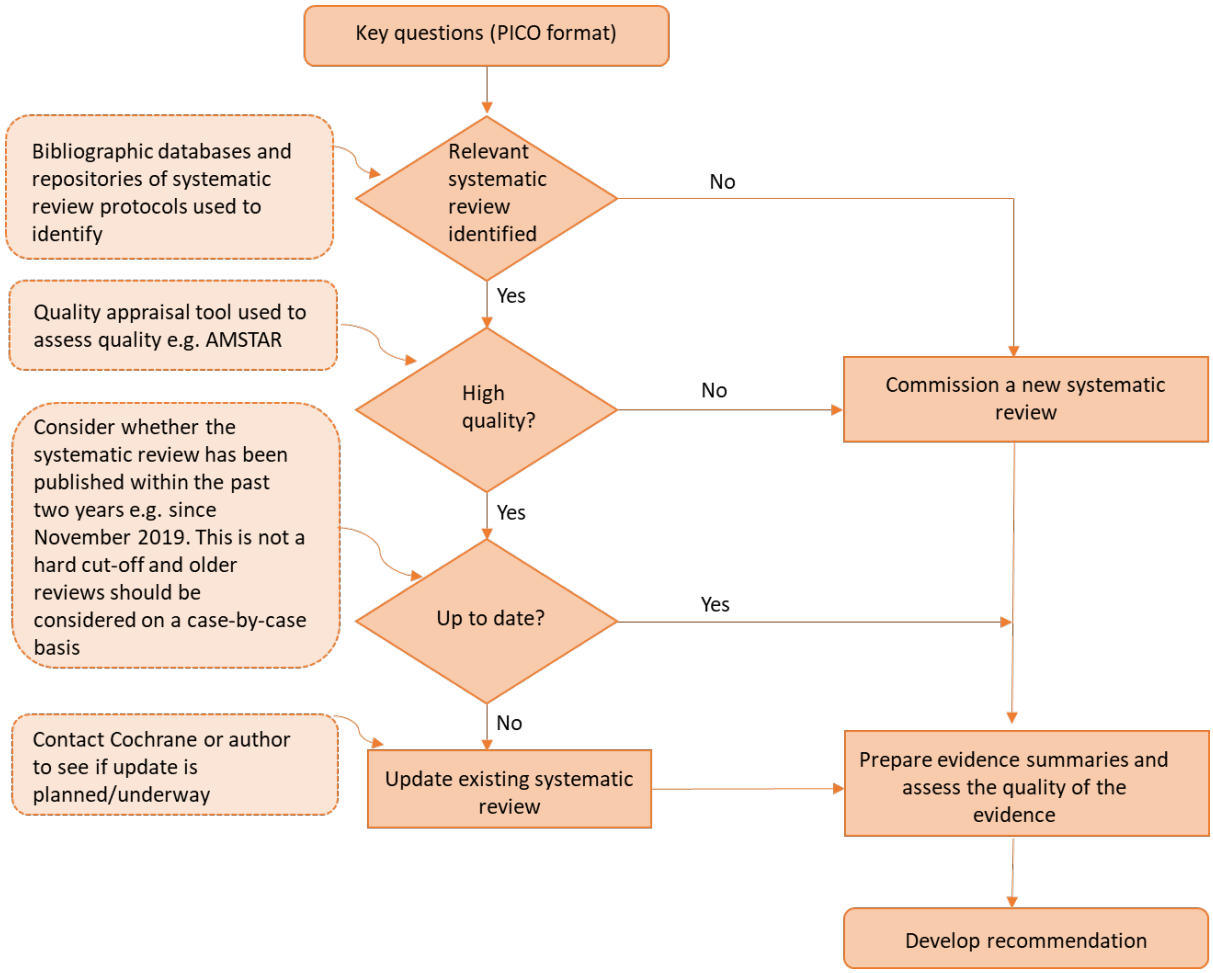
The process for evidence retrieval and synthesis is fully outlined in chapter 8 of the WHO handbook for guideline development https://apps.who.int/iris/handle/10665/145714.

Three main categories of evidence review are proposed in this document:

1) Existing relevant, up to date, high quality systematic review(s) provide the evidence required. **An existing systematic review is sufficient to prepare the evidence summaries**. It may be possible to include more than one systematic review for the same PICO, as different reviews may match different outcomes of a PICO. However, if more than one systematic review is available for the same PICO outcome, one review should be selected, based on quality, relevance, search comprehensiveness and date of last update. The selection process should be transparently reported, with justification of choices.
2) Existing high quality systematic reviews are either out of date or do not fully address the PICO, though it is considered that the review can be updated to meet these requirements. **An update of an existing systematic review is required before the evidence summaries can be prepared**. The update process may require addition of new studies published after the review, or inclusion of outcomes not covered by the existing reviews.
3) Existing systematic reviews are either not of sufficiently high quality or cannot be updated to fully address the PICO. **A new systematic review is required before the evidence summaries can be prepared**

Figure 1 below details the process to identify which level of evidence review is required to support the evidence retrieval process for a PICO.

Fig. 1. Is a new systematic review needed



All key questions are currently in PICO format as presented in the Appendix of the planning proposal PICOs. Subsequent steps include the following:

1. **Identify and evaluate existing systematic reviews**: Identify one or more systematic review(s) to address each PICO question. Existing systematic reviews will inform the guideline development process, whether or not a new systematic review or an update of an existing review is required, and the evidence review team will detail existing systematic reviews in each case. The method for identifying existing systematic reviews should be fully detailed in the evidence summary and include the following sources:
    a. Search of bibliographic databases, such as PubMed/MEDLINE, Embase, PsycInfo, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHIL, Scopus, African Index Medicus, Index Medicus for the Eastern Mediterranean Region, Index Medicus for the South-East Asian Region, Latin American and Caribbean Health Sciences Literature, and Western Pacific Region Index Medicus.
    b. Search of repositories of systematic reviews protocols, including PROSPERO, Open Science Framework (OSF), and Cochrane.
2. **Assess if systematic review is up to date:** It is preferred that identified systematic reviews have been published within the past two years e.g. since November 2019.

This is not a hard cut-off and older reviews should be considered on a case-by-case basis, particularly those covering the time period since the last update of the mhGAP guideline in 2015. It is acknowledged that COVID has led to a pausing of many mental health research activities over the past two years, and this may also impact the availability of systematic reviews within the preferred two year period. For any reviews that fall outside the two year period, the guideline methodologist will advise on suitability.

3. **Appraise quality of systematic review:** Use the AMSTAR-2 quality appraisal tool to assess the quality of the identified systematic review(s) https://amstar.ca/docs/AMSTAR-2.pdf . This includes consideration of the extent to which the PICO is fully addressed by the systematic review(s) identified.

By following the process outlined in figure 1, and steps 1-3 above, the FP and evidence review team will have sufficient evidence to assess which of the three main categories of evidence review apply to each PICO under consideration:

1) Existing systematic reviews are sufficient to prepare the evidence summaries
2) An update of an existing systematic review is required before the evidence summaries can be prepared
3) A new systematic review is required before the evidence summaries can be prepared

Appendix II a: Search terms used to identify systematic reviews

Database: Cochrane Library issue 1, 2022

#1 ((stimulant* or psychostimulant* or psycho-stimulant*) near/5 (abstain* or abstinence or abstinent or abuse* or addict* or chronic* or detox* or disorder* or depend* or habitual* or misuse* or overuse or reduce* or reducing or reduction or retain* or retention or users or withdrawal)):ti,ab

#2 (psychotherap* or psychosocial or voucher or reinforcement or motivation* or contingent* or biofeedback or community or stimulation or education* or counsel*):ti,ab

#3 #1 AND #2 in Cochrane Reviews

Database: Ovid MEDLINE(R) ALL <2015 to 12 January 2022>

1 ((stimulant* or psychostimulant* or psycho-stimulant*) adj5 (abstain* or abstinence or abstinent or abuse* or addict* or chronic* or detox* or disorder* or depend* or habitual* or misuse* or overuse or reduce* or reducing or reduction or retain* or retention or users or withdrawal)).tw,hw,id.

2 Cocaine-Related Disorders/ or ((cocaine* or crack-cocaine*) adj5 (abuse* or addict* or chronic* or disorder* or depend* or habitual* or misuse* or overuse or users)).tw,kf.

3 Amphetamine-Related Disorders/ or (methamphetamine* adj5 (abuse* or addict* or chronic* or disorder* or depend* or habitual* or misuse* or overuse or users)).tw,kf.

4 1 or 2 or 3

5 ((drug or polydrug* or substance or stimulant* or psychostimulant* or psycho-stimulant*) and (abuse* or addict* or disorder* or depend* or misuse* or overuse or users)).tw,kf.

6 substance-related disorders/ or drug overdose/ or substance abuse, intravenous/ or substance withdrawal syndrome/

7 5 or 6

8 Amphetamine/ or Diethylpropion/ or Methylphenidate/ or Pemoline/ or Phenmetrazine/ or Phenylpropanolamine/ or Ephedrine/ or Cocaine/ or Crack Cocaine/ or (amphetamine* or diethylpropion*or methylphenidate or methilphenidate or pemoline or phenmetrazine or phendimetrazine or phenilpropanolamine or phenylpropanolamine or ephedrine or cocaine or crack).tw.

9 7 and 8

10 4 or 9

11 exp Psychotherapy/

12 (psychotherap* or psychosocial or voucher or reinforcement or motivation* or contingent* or biofeedback or community or stimulation or education* or counsel*).tw.

13 (social adj2 skill*).tw.

14 (coping adj2 skill).tw.

15 exp Counseling/

16 (behavi* adj2 therap*).tw.

17 exp Reinforcement, Psychology/

18 ((brief or minimal or early or motivat$) adj3 (intervention$ or therap$ or interview$ or advice)).tw.

19 (cognitive adj3 therapy).tw.

20 (family adj2 therapy).tw.

21 stress management training.tw.

22 supportive expressive therapy.tw.

23 exp Social Support/

24 exp Case Management/

25 self control training.tw.

26 (behavio* adj2 (change or modification)).tw.

27 CBT.tw.
28 psychodynamic*.tw.
29 talking therap*.tw.
30 ((self adj2 help adj2 group$) or (twelve adj2 step) or 12-step).ti,ab.
31 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32 meta-analysis/ or systematic review/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/ (284030)
33 ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf,kw.
34 ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf,kw.
35 ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf,kw.
36 (data synthes* or data extraction* or data abstraction*).ti,ab,kf,kw.
37 (handsearch* or hand search*).ti,ab,kf,kw.
38 (handsearch* or hand search*).ti,ab,kf,kw.
39 (meta regression* or metaregression*).ti,ab,kf,kw.
40 (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.
41 (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw.
42 (cochrane or (health adj2 technology assessment) or evidence report).jw.
43 (comparative adj3 (efficacy or effectiveness)).ti,ab,kf,kw.
44 (outcomes research or relative effectiveness).ti,ab,kf,kw.
45 ((indirect or indirect treatment or mixed-treatment) adj comparison*).ti,ab,kf,kw.
46 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45
47 10 and 31
48 46 and 47
49 limit 48 to yr="2015 -Current"

Database: Embase <2015 to 13 January 2022>
1 ((stimulant* or psychostimulant* or psycho-stimulant*) adj5 (abstain* or abstinence or abstinent or abuse* or addict* or chronic* or detox* or disorder* or depend* or habitual* or misuse* or overuse or reduce* or reducing or reduction or retain* or retention or users or withdrawal)).tw,kf.
2 cocaine dependence/ or ((cocaine* or crack-cocaine*) adj5 (abuse* or addict* or chronic* or disorder* or depend* or habitual* or misuse* or overuse or users)).tw,kf.
3 amphetamine dependence/ or (methamphetamine* adj5 (abuse* or addict* or chronic* or disorder* or depend* or habitual* or misuse* or overuse or users)).tw,kf.
4 1 or 2 or 3
5 ((drug or polydrug* or substance or stimulant* or psychostimulant* or psycho-stimulant*) and (abuse* or addict* or disorder* or depend* or misuse* or overuse or users)).tw,kf.
6 drug dependence/ or amphetamine dependence/ or cocaine dependence/ or drug abuse pattern/ or drug craving/ or drug misuse/ or drug seeking behavior/ or methamphetamine dependence/ or multiple drug abuse/
7 5 or 6
8 Amphetamine/ or Diethylpropion/ or Methylphenidate/ or Pemoline/ or Phenmetrazine/ or Phenylpropanolamine/ or Ephedrine/ or Cocaine/ or Crack Cocaine/ or (amphetamine* or diethylpropion*or methylphenidate or methilphenidate or pemoline or phenmetrazine or phendimetrazine or phenilpropanolamine or phenylpropanolamine or ephedrine or cocaine or crack).tw.
9 7 and 8
10 4 or 9

11 exp psychotherapy/
12 (psychotherap* or psychosocial or voucher or reinforcement or motivation* or contingent* or biofeedback or community or stimulation or education* or counsel*).tw.
13 (social adj2 skill*).tw.
14 (coping adj2 skill).tw.
15 exp counseling/
16 (behavi* adj2 therap*).tw.
17 exp "reinforcement (psychology)"/
18 ((brief or minimal or early or motivat$) adj3 (intervention$ or therap$ or interview$ or advice)).tw.
19 (cognitive adj3 therapy).tw.
20 (family adj2 therapy).tw.
21 stress management training.tw.
22 supportive expressive therapy.tw.
23 exp social support/
24 exp case management/
25 self control training.tw.
26 (behavio* adj2 (change or modification)).tw.
27 CBT.tw.
28 psychodynamic*.tw.
29 talking therap*.tw.
30 ((self adj2 help adj2 group$) or (twelve adj2 step) or 12-step).ti,ab.
31 contingency management.mp.
32 financial incentives.mp.
33 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
34 10 and 33
35 "systematic review"/ or meta analysis/
36 "meta analysis (topic)"/
37 "systematic review (topic)"/
38 biomedical technology assessment/
39 ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab.
40 ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab.
41 ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab.
43 (data synthes* or data extraction* or data abstraction*).ti,ab.
44 (handsearch* or hand search*).ti,ab.
45 (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab.
45 (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab.
46 (meta regression* or metaregression*).ti,ab.
47 (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.
48 (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab.
49 (cochrane or (health adj2 technology assessment) or evidence report).jw.
50 (comparative adj3 (efficacy or effectiveness)).ti,ab.
51 (outcomes research or relative effectiveness).ti,ab.
52 ((indirect or indirect treatment or mixed-treatment) adj comparison*).ti,ab.

53 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 5
54 34 and 53
55 limit 54 to yr="2015 -Current"

Database: APA PsycInfo <2015 to January Week 1 2022>
1 ((stimulant* or psychostimulant* or psycho-stimulant*) adj5 (abstain* or abstinence or abstinent or abuse* or addict* or chronic* or detox* or disorder* or depend* or habitual* or misuse* or overuse or reduce* or reducing or reduction or retain* or retention or users or withdrawal)).mp.
2 ((cocaine* or crack-cocaine*) adj5 (abuse* or addict* or chronic* or disorder* or depend* or habitual* or misuse* or overuse or users)).mp.
3 (methamphetamine* adj5 (abuse* or addict* or chronic* or disorder* or depend* or habitual* or misuse* or overuse or users)).mp.
4 1 or 2 or 3
5 ((drug or polydrug* or substance or stimulant* or psychostimulant* or psycho-stimulant*) and (abuse* or addict* or disorder* or depend* or misuse* or overuse or users)).tw.
6 exp "substance use disorder"/ or addiction treatment/ or craving/ or drug addiction/ or drug seeking/ or "substance use treatment"/
7 5 or 6
8 Amphetamine/ or Diethylpropion/ or Methylphenidate/ or Pemoline/ or Phenmetrazine/ or Phenylpropanolamine/ or Ephedrine/ or Cocaine/ or Crack Cocaine/ or (amphetamine* or diethylpropion*or methylphenidate or methilphenidate or pemoline or phenmetrazine or phendimetrazine or phenilpropanolamine or phenylpropanolamine or ephedrine or cocaine or crack).tw.
9 7 and 8
10 4 or 9
11 exp psychotherapy/
12 (psychotherap* or psychosocial or voucher or reinforcement or motivation* or contingent* or biofeedback or community or stimulation or education* or counsel*).tw.
13 (social adj2 skill*).tw.
14 (coping adj2 skill).tw.
15 exp counseling/
16 (behavi* adj2 therap*).tw.
17 exp Reinforcement/
18 (cognitive adj3 therapy).tw.
19 (family adj2 therapy).tw.
20 stress management training.tw.
21 supportive expressive therapy.tw.
22 exp Social Support/
23 exp Case Management/
24 self control training.tw.
25 (behavio* adj2 (change or modification)).tw.
26 CBT.tw.
27 psychodynamic*.tw.
28 talking therap*.tw.
29 ((self adj2 help adj2 group$) or (twelve adj2 step) or 12-step).ti,ab.
30 contingency management.mp.
31 financial incentives.mp.
32 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
33 10 and 33
34 "systematic review"/ or meta analysis/

35 ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab.
36 ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab.
37 ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab.
38 (data synthes* or data extraction* or data abstraction*).ti,ab.
39 (handsearch* or hand search*).ti,ab.
40 (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab.
41 (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab.
42 (meta regression* or metaregression*).ti,ab.
43 (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.
44 (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab.
45 (comparative adj3 (efficacy or effectiveness)).ti,ab.
46 (outcomes research or relative effectiveness).ti,ab.
47 ((indirect or indirect treatment or mixed-treatment) adj comparison*).ti,ab.
48 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47
49 33 and 48
50 limit 49 to yr="2015 -Current"

Web of Science Core Collection:

1. TS=(((stimulant* or psychostimulant* or psycho-stimulant* or amphetamine* or diethylpropion*or methylphenidate or methilphenidate or pemoline or phenmetrazine or phendimetrazine or phenilpropanolamine or phenylpropanolamine or ephedrine or cocaine or crack)) AND (abstain* or abstinence or abstinent or abuse* or addict* or chronic* or detox* or disorder* or depend* or habitual* or misuse* or overuse or reduce* or reducing or reduction or retain* or retention or users or withdrawal))
2. TS=("contingency management" OR "financial incentives" OR voucher OR reinforcement OR counsel* OR psychoeducat* OR (psychological NEAR/2 (therap* OR treatment*)) OR psychotherap* OR psychosocial* OR psychoanalytic OR ((social OR peer OR group) NEAR/2 support) OR (self NEXT help) OR (cognitive NEAR/2 (therap* OR behav*)) OR mindfulness OR relax* OR ((family OR couple) NEAR/2 therap*) OR (twelve NEAR/2 step) OR "12-step")
3. TS=((systematic* NEAR/3 (review* OR overview*)) OR "meta-analysis")
4. #3 AND #2 AND #1 and 2022 or 2021 or 2020 or 2019 or 2018 or 2017 or 2016 or 2015 (Publication Years)

Epistemonikos
Publication year: Last 5 years

Publication type: Systematic Review

(title:(title:(stimulant* OR psychostimulant* OR psycho-stimulant* OR amphetamine* OR diethylpropion*or methylphenidate OR methilphenidate OR pemoline OR phenmetrazine OR phendimetrazine OR phenilpropanolamine OR phenylpropanolamine OR ephedrine OR cocaine OR crack) AND title:(abstain* OR abstinence OR abstinent OR abuse* OR addict* OR chronic* OR detox* OR disorder* OR depend* OR habitual* OR misuse* OR overuse OR reduce* OR reducing OR reduction OR retain* OR retention OR users OR withdrawal)) OR abstract:(title:(stimulant* OR psychostimulant* OR psycho-stimulant* OR amphetamine* OR diethylpropion*or methylphenidate OR methilphenidate OR pemoline OR phenmetrazine OR phendimetrazine OR phenilpropanolamine

OR phenylpropanolamine OR ephedrine OR cocaine OR crack) AND title:(abstain* OR abstinence OR abstinent OR abuse* OR addict* OR chronic* OR detox* OR disorder* OR depend* OR habitual* OR misuse* OR overuse OR reduce* OR reducing OR reduction OR retain* OR retention OR users OR withdrawal)))

Appendix IIb

	AMSTAR checklist -items	author & publication year
		Minozzi 2018
1	Did the research questions and inclusion criteria for the review include the components of PICO?	y
2	Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	y
3	Did the review authors explain their selection of the study designs for inclusion in the review?	y
4	Did the review authors use a comprehensive literature search strategy?	y
5	Did the review authors perform study selection in duplicate?	y
6	Did the review authors perform data extraction in duplicate?	y
7	Did the review authors provide a list of excluded studies and justify the exclusions?	y
8	Did the review authors describe the included studies in adequate detail?	y
9	Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	y
10	Did the review authors report on the sources of funding for the studies included in the review?	y
11	If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?	y
12	If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	y
13	Did the review authors account for RoB in primary studies when interpreting/discussing the results of the review?	y
14	Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	y
15	If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	y
16	Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	y
	Overall Rating	**HIGH**

Appendix II c

References of excluded reviews

AshaRani PV, Hombali A, Seow E, Ong WJ, Tan JH, Subramaniam M. Non-pharmacological interventions for methamphetamine use disorder: a systematic review. Drug Alcohol Depend. 2020 Jul 1;212:108060. doi: 10.1016/j.drugalcdep.2020.108060. Epub 2020 May 13. PMID: 32445927.

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Appendix II d: Search terms used to identify randomized controlled trials

CDAG Specialized register (via CRSLive)
from 2015 to 28 April 2022 (43 hits)

1. (amphetamine* OR cocaine OR diethylpropion OR ephedrine OR methylphenidate OR pemoline OR phenmetrazine OR phendimetrazine OR phenylpropanolamine OR phenilpropanolamine OR psychostimulant*):ti,xdi AND INREGISTER
2. (counsel* OR psychoeducat* OR educat*):ti,ab,xin AND INREGISTER
3. (psychological NEAR2 (therap* OR treatment*)):ti,ab,xin AND INREGISTER
4. ((social OR peer OR group) NEAR2 support) OR (self NEXT help) OR (cognitive NEAR2 (therap* OR behav*)):ti,ab,xin AND INREGISTER
5. CBT:ti,xin AND INREGISTER
6. (mindfulness OR relax* OR (family OR couple) NEAR2 therap*):ti,ab,xin AND INREGISTER
7. "Contingency Management" AND INREGISTER
8. CM:ti,ab,xin AND INREGISTER
9. incentive* OR voucher OR psychotherap* OR psychosocial* OR reinforcement OR motivation* OR contingent* OR advice AND INREGISTER
10. #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9
11. #1 AND #10
12. 2015 TO 2022:YR AND INREGISTER
13. #11 AND #12

Ovid MEDLINE
From 2015 to 29 April 2022 (513 hits)

1. ((stimulant* or psychostimulant* or psycho-stimulant*) adj5 (abstain* or abstinence or abstinent or abuse* or addict* or chronic* or detox* or disorder* or depend* or habitual* or misuse* or overuse or reduce* or reducing or reduction or retain* or retention or users or withdrawal)).tw,hw,id.
2. Cocaine-Related Disorders/ or ((cocaine* or crack-cocaine*) adj5 (abuse* or addict* or chronic* or disorder* or depend* or habitual* or misuse* or overuse or users)).tw,kf.
3. Amphetamine-Related Disorders/ or (methamphetamine* adj5 (abuse* or addict* or chronic* or disorder* or depend* or habitual* or misuse* or overuse or users)).tw,kf.
4. 1 or 2 or 3
5. ((drug or polydrug* or substance or stimulant* or psychostimulant* or psycho-stimulant*) and (abuse* or addict* or disorder* or depend* or misuse* or overuse or users)).tw,kf.
6. substance-related disorders/ or drug overdose/ or substance abuse, intravenous/ or substance withdrawal syndrome/
7. 5 or 6
8. Amphetamine/ or Diethylpropion/ or Methylphenidate/ or Pemoline/ or Phenmetrazine/ or Phenylpropanolamine/ or Ephedrine/ or Cocaine/ or Crack Cocaine/ or (amphetamine* or diethylpropion*or methylphenidate or methilphenidate or pemoline or phenmetrazine or phendimetrazine or phenilpropanolamine or phenylpropanolamine or ephedrine or cocaine or crack).tw.
9. 7 and 8
10. 4 or 9
11. exp Psychotherapy/
12. (psychotherap* or psychosocial or voucher or reinforcement or motivation* or contingent* or biofeedback or community or stimulation or education* or counsel*).tw.
13. (social adj2 skill*).tw.
14. (coping adj2 skill).tw.
15. exp Counseling/

16. (behavi* adj2 therap*).tw.
17. exp Reinforcement, Psychology/
18. ((brief or minimal or early or motivat$) adj3 (intervention$ or therap$ or interview$ or advice)).tw.
19. (cognitive adj3 therapy).tw.
20. (family adj2 therapy).tw.
21. stress management training.tw.
22. supportive expressive therapy.tw.
23. exp Social Support/
24. exp Case Management/
25. self control training.tw.
26. (behavio* adj2 (change or modification)).tw.
27. CBT.tw.
28. psychodynamic*.tw.
29. talking therap*.tw.
30. ((self adj2 help adj2 group$) or (twelve adj2 step) or 12-step).ti,ab.
31. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32. 10 and 31
33. randomized controlled trial.pt.
34. controlled clinical trial.pt.
35. random*.ab.
36. placebo.ab.
37. clinical trials as topic.sh.
38. random allocation.sh.
39. trial.ti.
40. 33 or 34 or 35 or 36 or 37 or 38 or 39
41. exp animals/ not humans.sh.
42. 40 not 41
43. 32 and 42
44. limit 43 to yr="2015 -Current"

Ovid Embase

From 2015 to 29 April 2022 (946 hits)

1. ((stimulant* or psychostimulant* or psycho-stimulant*) adj5 (abstain* or abstinence or abstinent or abuse* or addict* or chronic* or detox* or disorder* or depend* or habitual* or misuse* or overuse or reduce* or reducing or reduction or retain* or retention or users or withdrawal)).tw,kf.
2. cocaine dependence/ or ((cocaine* or crack-cocaine*) adj5 (abuse* or addict* or chronic* or disorder* or depend* or habitual* or misuse* or overuse or users)).tw,kf.
3. amphetamine dependence/ or (methamphetamine* adj5 (abuse* or addict* or chronic* or disorder* or depend* or habitual* or misuse* or overuse or users)).tw,kf.
4. 1 or 2 or 3
5. ((drug or polydrug* or substance or stimulant* or psychostimulant* or psycho-stimulant*) and (abuse* or addict* or disorder* or depend* or misuse* or overuse or users)).tw,kf.
6. drug dependence/ or amphetamine dependence/ or cocaine dependence/ or drug abuse pattern/ or drug craving/ or drug misuse/ or drug seeking behavior/ or methamphetamine dependence/ or multiple drug abuse/
7. 5 or 6
8. Amphetamine/ or Diethylpropion/ or Methylphenidate/ or Pemoline/ or Phenmetrazine/ or Phenylpropanolamine/ or Ephedrine/ or Cocaine/ or Crack Cocaine/ or (amphetamine* or

diethylpropion*or methylphenidate or methilphenidate or pemoline or phenmetrazine or phendimetrazine or phenilpropanolamine or phenylpropanolamine or ephedrine or cocaine or crack).tw.

9. 7 and 8
10. 4 or 9
11. exp psychotherapy/
12. (psychotherap* or psychosocial or voucher or reinforcement or motivation* or contingent* or biofeedback or community or stimulation or education* or counsel*).tw.
13. (social adj2 skill*).tw.
14. (coping adj2 skill).tw.
15. exp counseling/
16. (behavi* adj2 therap*).tw.
17. exp "reinforcement (psychology)"/
18. ((brief or minimal or early or motivat$) adj3 (intervention$ or therap$ or interview$ or advice)).tw.
19. (cognitive adj3 therapy).tw.
20. (family adj2 therapy).tw.
21. stress management training.tw.
22. supportive expressive therapy.tw.
23. exp social support/
24. exp case management/
25. self control training.tw.
26. (behavio* adj2 (change or modification)).tw.
27. CBT.tw.
28. psychodynamic*.tw.
29. talking therap*.tw.
30. ((self adj2 help adj2 group$) or (twelve adj2 step) or 12-step).ti,ab.
31. contingency management.mp.
32. financial incentives.mp.
33. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
34. 10 and 33
35. Clinical-Trial/ or Randomized-Controlled-Trial/ or Randomization/ or Single-Blind-Procedure/ or Double-Blind-Procedure/ or Crossover-Procedure/ or Prospective-Study/ or Placebo/
36. (((clinical or control or controlled) adj (study or trial)) or ((single or double or triple) adj (blind$3 or mask$3)) or (random$ adj (assign$ or allocat$ or group or grouped or patients or study or trial or distribut$)) or (crossover adj (design or study or trial)) or placebo or placebos).ti,ab.
37. 35 or 36
38. 34 and 37
39. limit 38 to yr="2015 -Current"

APA PsycInfo
From 2015 to Week 4 2022 (356 hits)

1. ((stimulant* or psychostimulant* or psycho-stimulant*) adj5 (abstain* or abstinence or abstinent or abuse* or addict* or chronic* or detox* or disorder* or depend* or habitual* or misuse* or overuse or reduce* or reducing or reduction or retain* or retention or users or withdrawal)).mp.
2. ((cocaine* or crack-cocaine*) adj5 (abuse* or addict* or chronic* or disorder* or depend* or habitual* or misuse* or overuse or users)).mp.

3. (methamphetamine* adj5 (abuse* or addict* or chronic* or disorder* or depend* or habitual* or misuse* or overuse or users)).mp.
4. 1 or 2 or 3
5. ((drug or polydrug* or substance or stimulant* or psychostimulant* or psycho-stimulant*) and (abuse* or addict* or disorder* or depend* or misuse* or overuse or users)).tw.
6. exp "substance use disorder"/ or addiction treatment/ or craving/ or drug addiction/ or drug seeking/ or "substance use treatment"/
7. 5 or 6
8. Amphetamine/ or Diethylpropion/ or Methylphenidate/ or Pemoline/ or Phenmetrazine/ or Phenylpropanolamine/ or Ephedrine/ or Cocaine/ or Crack Cocaine/ or (amphetamine* or diethylpropion*or methylphenidate or methilphenidate or pemoline or phenmetrazine or phendimetrazine or phenilpropanolamine or phenylpropanolamine or ephedrine or cocaine or crack).tw.
9. 7 and 8
10. 4 or 9
11. exp psychotherapy/
12. (psychotherap* or psychosocial or voucher or reinforcement or motivation* or contingent* or biofeedback or community or stimulation or education* or counsel*).tw.
13. (social adj2 skill*).tw.
14. (coping adj2 skill).tw.
15. exp counseling/
16. (behavi* adj2 therap*).tw.
17. exp Reinforcement/
18. (cognitive adj3 therapy).tw.
19. (family adj2 therapy).tw.
20. stress management training.tw.
21. supportive expressive therapy.tw.
22. exp Social Support/
23. exp Case Management/
24. self control training.tw.
25. (behavio* adj2 (change or modification)).tw.
26. CBT.tw.
27. psychodynamic*.tw.
28. talking therap*.tw.
29. ((self adj2 help adj2 group$) or (twelve adj2 step) or 12-step).ti,ab.
30. contingency management.mp.
31. financial incentives.mp.
32. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
33. 10 and 32
34. exp Clinical Trials/
35. (random* or (clinical adj3 trial*) or (reserch adj3 design*) or (evaluat adj3 stud*) or (prospective* adj3 stud*)).tw.
36. ((singl* or doubl* or trebl* or tripl*) adj3 (blind* or mask*)).tw.
37. 34 or 35 or 36
38. 33 and 37
39. limit 38 to yr="2015 -Current"

CINAHL (via EBSCO HOST)
from 2015 to 29 April 2022 (309 hits)

1. (MH "Substance Use Disorders+")

2. TX(drug N3 addict*) or TX(drug N3 dependen*) or TX(drug N3 abuse*) or TX(drug N3 misus*)
3. TX(substance N3 addict*) or TX(substance N3 dependen*) or TX(substance N3 abuse*) or TX(substance N3 misus*)
4. TX(addict* OR overdos* OR intoxicat* OR abstin* OR abstain OR withdraw* OR abus* OR misus* OR disorder* OR dependen*)
5. TX(use* N2 drug) or TX(use* N2 disorder) or TX(use* N2 illicit)
6. S1 OR S2 OR S3 OR S4 OR S5
7. (MH "Amphetamines+")
8. TI amphetamine* OR AB amphetamine*
9. TI Diethylpropion OR AB Diethylpropion
10. (MH "Methylphenidate") OR TX methylphenidate OR TX methilphenidate
11. TX pemoline
12. TI Phenmetrazine OR AB Phenmetrazine
13. MH Phenylpropanolamine OR TI phenilpropanolamine OR AB phenilpropanolamine OR TI phenylpropanolamine OR AB phenylpropanolamine
14. TX Ephedrine
15. MH Cocaine OR TI Cocaine OR AB Cocaine
16. S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15
17. S6 AND S16
18. TX((psychostimulant*) N3 (abuse* OR dependence* OR disorder* OR addict*))
19. S17 OR S18
20. (MM "Counseling")
21. (MH "Motivational Interviewing")
22. (MH "Psychotherapy+")
23. TI incentive* OR voucher OR psychotherap* OR psychosocial* OR reinforcement OR motivation* OR contingent* OR advice
24. AB incentive* OR voucher OR psychotherap* OR psychosocial* OR reinforcement OR motivation* OR contingent* OR advice
25. TI (contingency N1 management) OR AB (contingency N1 management)
26. TI (behaviour* N2 therapy) OR AB (behaviour* N2 therapy)
27. (MH "Reinforcement (Psychology)+")
28. TI(CBT or CM)
29. S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28
30. MH "Clinical Trials+"
31. PT Clinical trial
32. TI clinic* N1 trial* or AB clinic* N1 trial*
33. TI (singl* or doubl* or trebl* or tripl*) and TI (blind* or mask*)
34. AB (singl* or doubl* or trebl* or tripl*) and AB (blind* or mask*)
35. TI randomi?ed control* trial* or AB randomi?ed control* trial*
36. MH "Random Assignment"
37. TI random* allocat* or AB random* allocat*
38. MH "Placebos"
39. TI placebo* or AB placebo*
40. MH "Quantitative Studies"
41. S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40
42. S19 AND S29 AND S41

WOS (via THOMSON REUTERS)
from 2015 to 29 April (252 hits)

((TS=(counsel* OR psychoeducat* OR educat* OR (psychological NEAR/2 (therap* OR treatment*)) OR psychotherap* OR psychosocial* OR psychoanalytic OR ((social OR peer OR group) NEAR/2 support) OR (self NEXT help) OR (cognitive NEAR/2 (therap* OR behav*)) OR mindfulness OR relax* OR ((family OR couple) NEAR/2 therap*))) AND TS=(((amphetamine* OR cocaine OR diethylpropion OR ephedrine OR methylphenidate OR pemoline OR phenmetrazine OR phenmetrazine OR phenylpropanolamine OR phenylpropanolamine OR psychostimulant*) NEAR/3 (abuse* OR depend* OR use* OR disorder* OR addict*)))) AND TS=(3. " clinical trial" OR "comparative study" OR "evaluation study" OR "controlled trial" OR "prospective stud" OR random* OR placebo* OR "single blind" OR "double blind") and 2022 or 2021 or 2020 or 2019 or 2018 or 2017 or 2016 or 2015 (Publication Years)