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Interventions for Unhealthy Drug Use—Supplemental Report: A Systematic Review for the U.S. Preventive Services Task Force

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The information in this report is intended to help health care decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information (i.e., in the context of available resources and circumstances presented by individual patients).

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Abstract

Background: A U.S. Preventive Services Task Force (USPSTF) report found no consistent evidence that counseling interventions are effective at reducing drug use or improving other health outcomes in populations whose drug use was identified through primary care-based screening with questions about drug use or drug-related risks (i.e., "screen-detected populations"). Evidence from studies of persons seeking or referred for treatment for substance use or with clinical signs or symptoms of substance use (i.e., "treatment-seeking populations") might also be useful for informing assessments regarding screening in primary care settings.

Purpose: This report updates a 2008 USPSTF report on screening for illicit drug use and supplements an updated USPSTF report on screening for any drug use, focusing on the benefits and harms of pharmacotherapy and psychosocial interventions for persons whose drug use was identified when seeking substance use treatment, when presenting with signs or symptoms of drug use, when screened for drug use in primary care or other settings with questions about drug use or drug-related risks, or other means.

Data Sources: The Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Ovid MEDLINE, Embase, and PsycINFO from inception to September 2018; surveillance for new literature was conducted through November 22, 2019.

Study Selection: We included trials of Food and Drug Administration (FDA)-approved pharmacotherapies for opioid use disorder (methadone, buprenorphine, and naltrexone) and trials of psychosocial interventions for persons engaging in opioid, stimulant, cannabis, and mixed drug or polysubstance use. We also included trials of preemptive prescribing of naloxone in primary care settings as a rescue medication for opioid-related overdose. Trials compared included interventions against placebo, a minimal intervention, waitlist control, or usual care, and evaluated outcomes at $\geq$3 months for drug use or other risky behaviors; health, social, and legal consequences of drug use; or harms of treatment.

Data Extraction: One investigator abstracted data and a second investigator checked data abstraction for accuracy. Two investigators independently assessed study quality using methods developed by the USPSTF.

Data Synthesis (Results): We included a total of 71 trials, with 19 trials of pharmacotherapies and 52 trials of psychosocial interventions. All trials of pharmacotherapies and 25 trials of psychosocial interventions were conducted in treatment-seeking populations. Psychosocial interventions commonly incorporated cognitive-behavioral or motivational interventions and ranged from brief interventions consisting of one or two sessions of no more than one hour to multiple treatment sessions over weeks or months. In most pharmacotherapy trials, drug use counseling was provided to all patients. No study evaluated benefits or harms of preemptive naloxone prescribed in primary care settings versus placebo or no naloxone as a rescue medication for opioid-related overdose.

In treatment-seeking populations with opioid use disorder, naltrexone (12 trials; relative risk [RR] 0.73, 95% confidence interval [CI] 0.62 to 0.85; number needed to treat [NNT] 5.3) and

opioid agonist therapy with methadone or buprenorphine (4 trials; RR 0.75, 95% CI 0.59 to 0.82; NNT 2.9) were associated with decreased risk of drug use relapse compared with placebo or no pharmacotherapy. Naltrexone and methadone/buprenorphine therapy were also associated with increased likelihood of retention in substance use treatment (9 trials; RR 1.71, 95% CI 1.13 to 2.49; NNT 6.7 and 7 trials; RR 2.58, 95% CI 1.78 to 4.59; NNT 2.6; respectively). Evidence on harms of pharmacotherapies was limited, but indicated no increased risk of serious adverse events.

Psychosocial interventions were associated with increased likelihood of abstinence from drug use versus control conditions at 3 to 4 months (15 trials, RR 1.60, 95% CI 1.24 to 2.13; NNT 11) and at 6 to 12 months (14 trials; RR 1.25, 95% CI 1.11 to 1.52; NNT 17), based on trials primarily conducted in treatment-seeking populations. Psychosocial interventions were also associated with a greater decrease versus control conditions in the number of drug use days (19 trials; mean difference -0.49 day in the last 7 days, 95% CI -0.85 to -0.13) and a small but statistically significant greater decrease in drug use severity (16 trials; standard mean difference -0.18, 95% CI -0.32 to -0.05) at 3- to 4-month followup. There was no difference between psychosocial interventions versus controls on drug use days or severity at longer (6 to 12 month) followup. Effects of psychosocial interventions were generally stronger in trials of treatment-seeking than screen-detected populations, trials that evaluated cannabis use than other types of drug use, and trials of more intensive than brief interventions. Few trials evaluated effects of psychosocial interventions for opioid or stimulant use, and estimates were imprecise.

Limitations: Limitations included restriction to English-language articles, statistical heterogeneity in pooled analyses, and little evidence on drug-related health, social, or legal outcomes; most trials had methodological limitations. Evidence was lacking on effectiveness of treatments for opioid use disorder related to prescription drug use or stimulant use and evidence was limited for adolescents or pregnant persons.

Conclusions: Pharmacotherapy and psychosocial interventions are effective at improving drug use outcomes, but evidence of effectiveness remains primarily derived from trials conducted in treatment-seeking populations. Although the applicability of data from such trials to persons whose drug use is identified through primary care-based screening is uncertain, intervention trials that enrolled patients based on screening identified a spectrum of drug use, ranging from mild drug use to more severe, untreated disease. The applicability of current evidence on drug use interventions to screening might be greater for the subset of patients screened in primary care settings with severe, untreated drug use who could utilize pharmacotherapies or more intensive psychosocial interventions.

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Chapter 1. Introduction

This report supplements a review for the U.S. Preventive Services Task Force (USPSTF) on screening for drug use in primary care in adolescents and adults, including pregnant women,[1] focusing on evidence examining the benefits and harms of psychosocial interventions and pharmacotherapy for persons engaging in drug use. The USPSTF screening review updates a 2008 USPSTF review on screening for illicit drug use.[2] Like the 2008 USPSTF review, the screening review addresses the benefits and harms of screening through use of instruments with questions about drug use or drug-related risks, the accuracy of drug use screening instruments, and the benefits and harms of counseling interventions to reduce drug use detected through screening in primary care settings (referred to in this report as "screen-detected").[1] Such patients may have less severe drug use than persons seeking treatment for or referred for treatment of drug use or persons with clinical signs or symptoms of drug use (referred to in this report as "treatment-seeking"); however, symptom severity may overlap between screen-detected and treatment-seeking populations. Unlike the 2008 USPSTF review, the screening review does not address evidence on interventions among treatment-seeking persons,[2] because evidence from screen-detected populations is more directly applicable for guiding decisions about screening for drug use in primary care settings. A potential limitation of this approach is that it excludes some evidence on more intensive psychosocial interventions and evidence on the effectiveness of pharmacotherapies, which have been primarily studied in treatment-seeking populations.

This supplemental review focuses on the benefits and harms of counseling and other psychosocial interventions and pharmacotherapies for adolescents, adults, and pregnant women engaging in opioid, cannabis, stimulant, mixed drug, or polysubstance use, expanding the scope from screen-detected individuals to also address effectiveness of interventions in persons who were identified when seeking substance use treatment, when presenting with signs or symptoms of drug use, or through other means. Such evidence might further inform assessments regarding potential benefits and harms of drug use screening in primary care settings, given the variability in drug use severity among patients identified through screening. This supplemental review also differs from the 2008 USPSTF review in that it addresses the benefits and harms of preemptive naloxone prescribed in primary care settings as a rescue medication for treating acute overdose episodes in individuals with opioid use. A separate USPSTF update on drug use prevention in children, adolescents, and young adults through age 25 years is in progress.[3]

2008 USPSTF Review

The 2008 USPSTF review found fair- to good-evidence that pharmacologic therapy is effective at reducing short-term illicit drug use.[2] However, 16 of the 17 treatment trials included in the 2008 USPSTF review were conducted among treatment-seeking populations who had already developed health, social, and/or legal problems due to drug use. The exception was one trial which found a brief counseling intervention effective at decreasing opiate and cocaine use among 1,175 screen-detected primary care patients.[4] In addition, only two of the eight trials of pharmacotherapies included in the 2008 USPSTF review evaluated medications approved by the Food and Drug Administration (FDA) for treatment of substance use disorders.[5,6] The 2008

USPSTF review found limited and less consistent evidence of positive effects of pharmacotherapies or psychosocial interventions on social, legal, and health outcomes related to drug use. The 2008 USPSTF review also found limited evidence from observational studies conducted outside the United States for an association between stopping or reducing opioid (usually heroin) misuse and long-term improvement in mortality rates; none of the studies examining this association were conducted in screen-detected populations whose drug use was detected in primary care settings. Based on the 2008 review, the USPSTF concluded that the evidence was insufficient to determine the benefits and harms of screening for illicit drug use in primary care settings.[7]

USPSTF Screening Review

The USPSTF screening review included 27 trials on the effectiveness of psychosocial interventions for drug use in screen-detected populations.[1] Substance use eligibility criteria varied, frequently consisting of self-reported drug use within a specified time-frame (e.g., 30 days to 1 year), or requiring patients to meet a certain threshold score on a screening instruments (e.g., Alcohol, Smoking, and Substance Involvement Screening Test [ASSIST] score $\geq$4). No trial required patients to meet the Diagnostic and Statistical Manual of Mental Disorder (DSM)-IV criteria for abuse or dependence or DSM-5 criteria for substance use disorder. All but two trials evaluated brief counseling interventions (typically 1 or 2 sessions, less than an hour in duration), often incorporating motivational techniques. No trial evaluated pharmacotherapy.

The USPSTF screening review found no consistent evidence that psychosocial interventions were effective at reducing drug use at 3- to 12-month followup in screen-detected populations, or at improving health, social, or legal outcomes associated with drug use.[1] Evidence on harms was sparse, but indicated no serious harms associated with counseling interventions. Evidence on the effects of psychosocial interventions about drug use for adolescents, pregnant women, and postpartum women was very limited and also showed no clear benefits. Additional details on the benefits and harms of treatment for drug use in screen-detected populations are available in the full screening review.[1]

Interventions to Reduce Drug Use

This supplemental report to the USPSTF screening review addresses pharmacotherapy and psychosocial interventions to reduce drug use in persons engaging in opioid, cannabis, stimulant, or polysubstance use involving one or more of these drugs.

Currently, the only pharmacotherapies approved by the FDA for treatment of drug use disorders addressed in this report (opioids, cannabis, or stimulants) are opioid agonists, partial agonists, and antagonists for treatment of opioid use disorder. Lofexidine was recently approved by the FDA to mitigate symptoms of abrupt opioid withdrawal. As it is not a treatment for opioid use disorder, it is not addressed in this report. A recent guideline from the Department of Veterans Affairs/Department of Defense (VA/DoD) found insufficient evidence to recommend for or against pharmacotherapy for cannabis use or stimulant use disorder.[8] Several FDA-approved

medications are considered first-line therapy for treatment of opioid use disorder;[8-10] they are methadone (an opioid agonist), buprenorphine (a partial opioid agonist) with or without naloxone (available in combination with naloxone or as a mono-product, and in sublingual or buccal administration or extended-release implantable or injectable formulations), and naltrexone (an opioid antagonist, available as an oral or extended-release injectable formulation). In the United States, methadone for treatment of opioid use disorder must be dispensed through a licensed opioid treatment program.[11] Buprenorphine and naltrexone can be prescribed in office-based settings as well as dispensed in an opioid treatment program, though additional training and a waiver from the Drug Enforcement Agency (DEA) is required for office-based prescribing of buprenorphine. The purpose of medications for opioid use disorder is to block the euphoric and sedating effects of opioids, reduce cravings for opioids, and/or to mitigate symptoms of opioid withdrawal. Medications are used in combination with psychosocial interventions to prevent relapse to opioid use.[10] Use of medications for treatment of opioid use disorder is traditionally referred to as "medication assisted treatment" (MAT). However, experts have suggested that the term "medication assisted" is misleading because it implies that medications play an adjunctive role in treatment for opioid use disorder.[12,13] Rather, evidence indicates that medications are the main driver of therapeutic effectiveness, with several studies finding no clear differences in the effectiveness between more versus less intensive psychosocial interventions in persons receiving medications for opioid use disorder.[14,15] A potential alternative to the term "medication assisted treatment" that retains the MAT acronym and does not suggest that medications are a secondary component is "medications for addiction treatment." We used the term "pharmacotherapy" in this report to refer to methadone, buprenorphine, or naltrexone and "opioid agonist therapy" to refer to methadone and buprenorphine.

Psychosocial interventions are used for treatment of various drug use disorders. A recent guideline from the VA/DoD recommends psychosocial interventions for treatment of cannabis use and stimulant disorder.[8,16] In addition, medications for opioid use disorder are administered in conjunction with psychosocial interventions. Commonly used psychosocial techniques include cognitive-behavioral therapy (CBT), motivational interventions, 12-step facilitation therapy, contingency management, and family interventions. Psychosocial techniques can be combined in a variety of ways. CBT helps individuals to positively address unhealthy drug use behaviors by identifying and correcting maladaptive thought patterns, goal setting, and learning and applying coping strategies. Motivational intervention techniques, such as motivational interviewing (MI) and Motivational Enhancement Therapy (MET), seek to positively impact unhealthy behaviors by eliciting and enhancing motivations to change. Contingency management is based on operant conditioning principles, utilizing an incentive-based approach that rewards behaviors that meet desired outcomes.[16] Twelve-step facilitation therapy focuses on actively engaging individuals in a mutual support group guided based on twelve-step principles. Family interventions actively engage the family and address contributing factors to drug use, such as family communication and conflict, school and work issues, and peer networks. Family interventions are often used for treatment of adolescent substance misuse.[17]

Psychosocial interventions range in intensity, from brief interventions (e.g., 1 or 2 to sessions, each lasting less than 1 hour) to more intensive, ongoing treatments (e.g., once or twice weekly sessions for 1 to 2 hours). Brief interventions are usually designed for persons with unhealthy drug use but who do not have more serious substance use (e.g., do not meet DSM-5 criteria for

substance use disorder), though these interventions can be a bridge to more intensive therapy in persons who require it.[18] Brief interventions are often designed so that they can be delivered opportunistically in most settings, including primary care, with minimal training. More intensive psychosocial interventions often require additional training or expertise to deliver.

Naloxone for Risk Mitigation in Persons With Opioid Use Disorder or Misuse

Naloxone is an opioid antagonist that rapidly counteracts the central nervous system and respiratory depressant effects of opioids potentially preventing fatal overdose and mitigating overdose-related harms.[19] Unlike the pharmacotherapies described above, naloxone is preemptively prescribed as a rescue medication for acute overdose events administered by persons witnessing the overdose, not as a treatment for opioid use disorder or misuse. Therefore, it may help mitigate the risks of ongoing opioid use. The American Society of Addiction Medicine recommends, based on consensus opinion, that patients being treated for opioid use disorder and their family members/significant others be given prescriptions for naloxone.[9] Naloxone can be administered in a number of ways by witnesses to overdose events, including the intravenous, intramuscular, subcutaneous, and intranasal routes. The FDA recently approved new naloxone devices: a handheld intramuscular or subcutaneous auto-injector and a new intranasal formulation and delivery device. Both devices administer a consistent preset dose and are designed for use by individuals regardless of level of health care training. Improvised use of injectable naloxone administered intranasally using an atomizer is also used for cost or other reasons, but the naloxone is less concentrated compared to the FDA approved intranasal formulation. Data on the effectiveness of naloxone used in this way is uncertain, particularly for overdose related to high potency synthetic opioids (fentanyl and fentanyl analogues).[20] Naloxone has been shown to be effective for reversal of opioid overdose, but has mainly been evaluated in the context of non-randomized evaluations of community opioid overdose prevention and naloxone distribution programs.[21,22] The effectiveness of naloxone that is preemptively prescribed in clinical settings for mitigating overdose risk in individuals with opioid use is less certain.

Chapter 2. Methods

Key Questions and Analytic Framework

Using the methods developed by the USPSTF,[23] the USPSTF and the Agency for Healthcare Research and Quality (AHRQ) determined the scope and key questions for the full screening review, including an analytic framework (**Figure 1**) with the Key Questions and the patient populations, interventions, and outcomes reviewed.[1] This supplemental report addresses the following Key Questions included within the full analytic framework on screening, focusing on the benefits and harms of drug use treatments in screen-detected as well as treatment-seeking populations, and naloxone prescribed in clinical settings as a rescue medication for acute opioid overdose for purposes of risk mitigation:

- Do interventions to reduce drug use* reduce drug use or improve other risky behaviors? (Key Question 4a in the original screening analytic framework[1])
- Do interventions to reduce drug use* reduce morbidity or mortality or improve other health, social, or legal outcomes? (Key Question 4b in the original screening analytic framework[1])
- What are the harms of interventions to reduce drug use*? (Key Question 5 in the original screening analytic framework[1])
- Does naloxone reduce morbidity or mortality, or improve other health outcomes in persons with opioid use disorder or misuse? (New Key Question 6 in the analytic framework for supplemental review)
- What are the harms of naloxone in persons with opioid use disorder or misuse? (New Key Question 7 in the analytic framework for supplemental review)

*Drug use refers to substance use disorders or misuse related to opioids, stimulants, or cannabis, or polysubstance use related to one or more of these drugs.

Key Questions 1-3 in the analytic framework are addressed in a separate screening review.[1]

Search Strategies

We searched the Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Ovid MEDLINE, Embase, and PsycINFO for relevant studies and systematic reviews. Databases were searched from inception to September 2018. After September 2018, we conducted surveillance through article alerts and targeted searches of high-impact journals to identify major studies that may affect conclusions. The last surveillance was conducted on November 22, 2019. One new pilot trial[24] of a psychosocial intervention among adolescents identified through screening was identified in the surveillance scan; however, this study does not substantively change the findings or conclusions of this review and was not added to the final report. Search strategies are available in **Appendix A1**. We also reviewed reference lists of relevant articles.

Study Selection

At least two reviewers independently evaluated each study to determine inclusion eligibility. We selected studies on the basis of inclusion and exclusion criteria developed for the Key Questions addressed in this supplemental report (**Appendix A2**). We included randomized trials of pharmacotherapy and psychosocial interventions conducted in populations engaging in drug use regardless of whether their drug use was identified through primary care-based screening, including persons seeking substance use treatment or with signs and symptoms of drug use, and whether or not they met criteria for a substance use disorder. We incorporated all trials of drug use treatment from the USPSTF screening review[1] that enrolled screen-detected populations, along with additional trials of treatment-seeking populations. In addition, we included trials on the benefits and harms of naloxone in persons with opioid use disorder or misuse; this topic was not addressed in the 2008 review or the screening update.

We included trials of adolescents (defined as persons 12 to <18 years of age) and adults engaging in use of opioids, stimulants (e.g., cocaine, methamphetamines, and ecstasy), and cannabis. We also included trials of patients engaged in mixed drug use (defined as studies that evaluated more than one type of drug use, but individuals did not necessarily use more than one drug) or polysubstance use (defined as studies in which an individual used more than one drug), as long as one of the three drug classes was the predominant drug of use. We did not restrict inclusion to persons meeting formal criteria (e.g., DSM-IV criteria for abuse or dependence or DSM-5 criteria) for substance use disorder. Rather, we included trials in which patients reported any nonmedical drug use, including those meeting formal DSM-IV or DSM-5 criteria. We included studies of pregnant and postpartum women. We included trials of pharmacotherapies in which treatment was initiated in inpatient settings, as long as subsequent therapy was administered in outpatient settings. Trials in which all therapy was administered in inpatient settings were excluded. We excluded trials of incarcerated patients and trials in which patients were selected on the basis of having a concurrent medical (e.g., HIV or hepatitis C virus [HCV] infection) or psychiatric (e.g., depression or schizophrenia) condition; trials of individuals using prescribed opioids without signs or symptoms of misuse or addiction; and trials in which patients were selected based on use of alcohol, nicotine, or another substance other than opioids, stimulants, and cannabis.

For pharmacotherapies, we focused on medications that are FDA-approved for substance use disorder as of September 2018. These are buprenorphine (sublingual or extended-release injection or implant), buprenorphine/naloxone, methadone, and naltrexone (oral or extended-release injection) for treatment of opioid use disorder. We included two trials of extended-release naltrexone formulations, including implantable naltrexone[25] (formulation not FDA-approved as of 2019) and injectable naltrexone[26] (formulation FDA-approved in 2010). Analyses of naltrexone were stratified according to route of administration (oral versus implant/injectable). No pharmacotherapies are currently FDA-approved for treatment of cannabis or stimulant use disorder. We excluded trials of methadone or buprenorphine for detoxification (withdrawal management), as maintenance therapy with these medications is generally recommended due to a high risk of relapse.[10] We also included studies of preemptive naloxone prescribed in clinical settings as a rescue medication for acute overdose events, for mitigation of opioid-related harms. For psychosocial interventions, we included interventions that utilized one or more of the

following techniques: CBT, motivational interventions, contingency management, twelve-step facilitation therapy, family interventions, and adaptations or combinations of these methods.[8] We did not restrict inclusion of trials of psychosocial interventions based on the number or length of intervention sessions. However, we categorized interventions as brief (defined for this report as 1 or 2 sessions, each less than 1 hour in duration) or intensive (not meeting definition for brief). Psychosocial interventions could be delivered face-to-face or using other modalities (e.g., telephone, Internet, or computer). Interventions could be delivered in office-based settings or in opioid treatment programs. We excluded trials of school-based or community level interventions.

We included trials in which included interventions were compared against placebo, a minimal intervention (including attention control), or waitlist control. Minimal interventions and attention controls were similar in intensity (e.g., duration) to the intervention, but were designed to have minimal or no specific effect. Minimal interventions and attention controls commonly consisting of brief educational interventions without a psychosocial component. We only included trials that compared an included intervention against usual care if the usual care intervention did not represent active treatment for drug use disorders. In some trials, usual care could include referral to pharmacotherapy or psychosocial intervention, though we excluded trials in which patients were routinely referred for drug treatment. For trials of pharmacotherapy, we included trials in which all patients received psychosocial interventions, consistent with how pharmacotherapy for opioid use disorder is delivered in clinical practice and the standard of care.[10] Otherwise, we excluded head-to-head trials comparing one active intervention versus another, trials of combination versus single modality pharmacotherapy, and trials comparing different intensities or duration of pharmacologic therapy or psychosocial interventions.

We included trials that evaluated outcomes at 3 months or longer following the initiation of the interventions. Outcomes were drug use (i.e., abstinence, frequency and/or quantity of drug use, severity of drug use disorder, polysubstance use other risky behaviors), clinical outcomes (i.e., all-cause mortality, drug-related mortality, drug-related morbidity, obstetrical/perinatal/neonatal outcomes, quality of life), other drug-related problems (i.e., legal problems, social and family relations, employment, school/educational outcomes), and harms, including serious adverse events such as death and adverse events resulting in hospitalizations or study withdrawal. For trials of pharmacotherapy for opioid use disorder, we also included retention in substance use treatment as an outcome, because of the ongoing nature of treatment, the chronic relapsing nature of opioid use disorder, and the association between retention in treatment (implying ongoing engagement in care) with reductions in substance use and criminal behavior, and improvements in functioning and quality of life.[27-29] Because most measures of drug use severity (e.g., Severity of Dependence Scale [SDS], ASSIST, Marijuana Problem Scale [MPS], number of DSM-IV dependence symptoms met) include social, legal, and other consequences of drug use, we considered them measures of drug-related problems.

Additional details on study eligibility for inclusion are available in **Appendix A2**. The literature flow diagram (**Appendix A3**) summarizes the results of the literature search. **Appendix A4** lists the included studies, and **Appendix A5** lists excluded studies with reasons for exclusion.

Data Abstraction and Quality Rating

We abstracted details about the study design, inclusion criteria, patient population (including measures of drug use severity), recruitment and treatment setting, interventions, analysis, followup, and results (**Appendix B**). For trials of screen-detected populations, we utilized the quality ratings as reported in the USPSTF screening review.[1] For all other trials, investigators independently applied criteria developed by the USPSTF[23] (**Appendix A6**) to rate the quality of each study as good, fair, or poor. Discrepancies were resolved through a consensus process. In accordance with the USPSTF Procedure Manual, we excluded studies rated poor quality due to important methodological shortcomings that severely undermine their reliability.[23] **Appendix C1** shows all outcomes measures mentioned in the report.

Data Synthesis

We supplemented a random effects meta-analysis reported in the USPSTF screening review on effects of psychosocial interventions on differences in change from baseline in the number of drug use days in screen-detected populations with additional trials conducted in treatment-seeking populations. Drug use days were standardized to the number of days of drug use in the past 7 days and the analysis was stratified according to whether patients were screen-detected. Results were analyzed separately for outcomes assessed at 3 or 4 months and outcomes assessed at 6 to 12 months. The meta-analysis used the random effects profile likelihood model; additional details regarding statistical methods are available in the USPSTF screening review.[1]

We performed a new (not in the USPSTF screening review) random effects meta-analysis using the profile likelihood model on the dichotomous outcomes abstinence, retention in treatment (for trials of medications for opioid use disorder), and harms (serious adverse events, study withdrawal due to adverse events, nausea, diaphoresis, and constipation). We pooled data separately for the opioid antagonist naltrexone, the opioid agonists methadone and buprenorphine, and psychosocial interventions. The analysis for methadone and buprenorphine was stratified by drug. To explore heterogeneity, we also performed additional stratified analyses. For all interventions, we stratified analyses according to whether the population was screen-detected or treatment seeking, the main type of drug use measured by the study (cannabis, stimulant, opioid, or mixed drugs), age group (adolescent [12 to 17 years of age], young adult [18 to 25 years of age], or adult [>25 years of age]), study quality, and pregnancy or postpartum status. For pharmacotherapies, we also stratified by route of administration, naltrexone dose, timing of outcome assessment, and intensity of the interventions; and for psychosocial interventions, we stratified according to intervention intensity (brief versus intensive as defined above) and mode of delivery (face-to-face, or other).

For trials of psychosocial interventions, we also performed a new random effects meta-analysis using the profile likelihood method on the continuous outcome of drug use severity. Outcomes related to drug use severity were reported in too few trials of pharmacotherapies (which focused on abstinence/relapse and retention in treatment) to permit pooling. Because trials used different scales to measure drug use severity, we calculated the standardized mean difference as the effect measure. The followup scores were used in the primary analysis and sensitivity analyses were

conducted based on change score from baseline (results were similar and results based on change scores are not reported separately). Data were separately analyzed for 3 to 4 month and 6 to 12 month outcomes. The primary analysis was stratified according to the predominant type of drug use; we performed additional stratified analyses based on the intensity of psychosocial interventions, study population (age, whether or not screen detected), mode of delivery, and study quality. Heterogeneity between studies was evaluated by the χ^2 test and I^2 statistics. All analyses were conducted using Stata/IC 13.1 (StataCorp LP, College Station, TX). Analyses were repeated using the Dersimonian and Laird model; results were similar to results using the profile likelihood method and are not reported separately.

We assessed the aggregate internal validity (quality) of the body of evidence for each key question ("good", "fair", "poor") using methods developed by the USPSTF, based on the number, quality and size of studies, consistency of results between studies, and directness of evidence in the Summary of Evidence table.[23]

Expert Review and Public Comment

A draft version of this supplemental report was reviewed by content experts (**Appendix A7**), representatives of Federal partners, USPSTF members, and AHRQ Medical Officers. Reviewer comments were presented to the USPSTF during its deliberations and subsequently addressed in revisions of this report. Clarifications were made to the report in response to comments, including abstraction of additional details regarding the persons delivering interventions evaluated in the trials.

In addition, a draft of the full report was posted on the USPSTF Web site from August 13, 2019 through September 9, 2019. In response, a footnote was added to the Analytic Framework (**Figure 1**) to clarify that "screening" refers to screening methods that pose questions about drug use or drug-related risks, not laboratory testing of biologic samples for the presence of drugs, and the conclusion was clarified to state that although the applicability of data from such trials to persons whose drug use is identified through primary care-based screening is uncertain, intervention trials that enrolled patients based on screening identified a spectrum of drug use, ranging from mild drug use to more severe, untreated disease.

Chapter 3. Results

The literature flow diagram (**Appendix A3**) summarizes the results of the literature search, including the number of studies identified at the abstract and title stage, studies reviewed at the full-text stage, the number of studies included by Key Question and intervention, and the number of studies excluded. For this supplemental report, we reviewed 10,091 abstracts, of which 1,125 were reviewed as full text articles. We included a total of 71 trials (reported in 87 publications) of interventions for drug use. From the 2008 USPSTF review,[2] we carried forward seven trials, which are included in the results below.[4-6,30-33] One trial from the 2008 USPSTF review evaluated naltrexone,[5] one trial evaluated methadone,[6] and five trials evaluated psychosocial interventions. Only one trial from the 2008 USPSTF review evaluated a treatment (brief psychosocial intervention) for drug use in a screen-detected population.[4] We excluded 10 other trials of treatments included in the 2008 USPSTF report. Six trials evaluated a medication not approved by the FDA for treatment of substance use disorders (desipramine, baclofen, fluoxetine, nefazodone, or disulfiram),[34-39] two trials evaluated non-included interventions (acupuncture[40] or an intervention that involved provision of housing),[41] and two trials had duration of followup less than 3 months.[42,43]

The USPSTF screening review included 27 trials on the effectiveness of psychosocial interventions for treatment of drug use in screen-detected populations, all of which are included in this supplemental report.[4,44-69] It identified no trials of pharmacotherapy for drug use in screen-detected populations.

We identified 17 additional trials of FDA-approved pharmacotherapies for treatment of opioid use disorder (12 evaluated naltrexone, one evaluated methadone, and five evaluated buprenorphine; one trial evaluated both naltrexone and buprenorphine)[70] and 22 additional trials of psychosocial therapies for treatment of drug use in treatment-seeking (non-screen-detected) settings that were not included in the 2008 USPSTF report[2] or screening review.[1] The total numbers of studies included in this supplement are 19 trials of pharmacotherapies and 52 trials of psychosocial interventions (27 in screen-detected populations, 25 in treatment-seeking populations).

Key Questions 4a And 4b. Do Interventions to Reduce Drug Use Reduce Drug Use or Improve Other Risky Behaviors? Do Interventions to Reduce Drug Use Reduce Morbidity or Mortality or Improve Other Health, Social, or Legal Outcomes?

Summary

- In treatment-seeking populations with opioid use disorder due to heroin use, naltrexone was associated with decreased risk of drug use relapse (12 trials; relative risk [RR] 0.73, 95% confidence interval [CI] 0.62 to 0.85, I^2=78%; absolute risk difference [ARD] -18%,

95% CI -26% to -10%) and increased likelihood of retention in treatment (9 trials, RR 1.71, 95% CI 1.13 to 2.49, I^2=67%; ARD 15%, 95% CI 5% to 22%) versus placebo or no naltrexone (**Figures 2 and 3**); the duration of treatment was 6 months in 10 of 13 trials.

- In treatment-seeking populations with opioid use disorder primarily due to heroin use, opioid agonist therapy with methadone or buprenorphine was associated with decreased risk of relapse while on treatment (4 trials; RR 0.75, 95% CI 0.59 to 0.82; I^2=75%; ARD -35%, 95% CI -67% to -3%) and increased likelihood of retention in treatment (7 trials; RR 2.58, 95% CI 1.78 to 4.59, I^2=71%; ARD 39%, 95% CI 23% to 54%) versus placebo or no opioid agonist treatment (**Figures 4 and 5**); the duration of treatment ranged from 3 to 12 months (6 months in 4 of 7 trials).
    - In stratified analyses, effects on risk of relapse and retention in treatment were similar for methadone and buprenorphine.
- Psychosocial interventions were associated with increased likelihood of abstinence from drug use versus control conditions (waitlist, minimal intervention, or usual care) at 3 to 4 months (15 trials; RR 1.60, 95% CI 1.24 to 2.13, I^2=61%; ARD 9%, 95% CI 5% to 15%) and at 6 to 12 months (14 trials; RR 1.25, 95% CI 1.11 to 1.52, I^2=38%; ARD 6%, 95% CI 2% to 10%) (**Figures 6 and 7**).
    - In a stratified analysis, effects were statistically significant for abstinence at 3 to 4 months from cannabis use (7 trials; RR 2.08, 95% CI 1.51 to 3.07, I^2=28%) (**Figure 6**), but were weaker and not statistically significant for abstinence from mixed drug use (7 trials; RR 1.24, 95% CI 0.92 to 1.80, I^2=60%).
    - Effects on abstinence were greater at 3 to 4 months in trials of treatment-seeking populations (7 trials; RR 2.08, 95% CI 1.51 to 3.07, I^2=28%) than in trials of screen-detected populations (8 trials; RR 1.28, 95% CI 0.97 to 1.84, I^2=57%; p for interaction=0.05) (**Figure 8**).
    - Effects on abstinence were greater at in trials of face-to-face interventions than in trials with other (web, computer, telephone) interventions and effects were smaller in trials of brief than intensive interventions, but the differences were not statistically significant.
- Psychosocial interventions were associated with decreased number of drug use days (standardized to use in the last 7 days) versus controls at 3 to 4 months (19 trials, mean difference -0.49 day, 95% CI -0.85 to -0.13, I^2=89%) but not at 6 to 12 months (15 trials, mean difference -0.08, 95% CI -0.30 to 0.11, I^2=45%) (**Figures 9 and 10**).
    - Beneficial effects of psychosocial interventions on drug use days at 3 to 4 months were present in trials of treatment-seeking populations (10 trials, mean difference -0.91 day, 95% CI -1.52 to -0.31, I^2=86%) but not in trials of screen-detected populations (9 trials, mean difference -0.10 day, 95% CI -0.31 to 0.12, I^2=46%) (**Figure 11**).
- Psychosocial interventions were associated with a small but statistically significant decrease in drug use severity versus controls at 3 to 4 months (17 trials, standardized mean difference [SMD] -0.18, 95% CI -0.32 to -0.05, I^2=73%) but not at 6 to 12 months (13 trials, SMD -0.10, 95% CI -0.24 to 0.02, I^2=65%) (**Figures 12 and 13**).
- Evidence on the effects of pharmacotherapies and psychosocial interventions on other health, social, and legal outcomes was limited and inconsistent.

Evidence

Naltrexone for Opioid Use Disorder

The 2008 USPSTF review included one trial of naltrexone for treatment of opioid use disorder.[5] Including this trial, we identified thirteen trials (in 14 publications) on the effects of naltrexone versus placebo or no naltrexone for opioid use disorder in persons receiving drug use counseling (**Table 1**, **Appendixes B1, B2, and B3**).[5,25,26,70-80] Sample sizes ranged from 31 to 306 (total N=1,718). In these trials, the diagnosis of opioid use disorder was generally based on meeting DSM-II-R, DSM-III, or DSM-IV criteria. Drug use counseling was usually described as individual (most common) or group counseling with a frequency ranging from 3 times/week to biweekly; however, details regarding counseling methods were limited. Twelve trials assessed oral naltrexone, one trial[26] injectable naltrexone (300 mg every 4 weeks), and one trial[25] implantable (not FDA-approved) naltrexone (1000 mg twice a month). Among trials of oral naltrexone, the dose was 50 mg daily in seven trials;[5,25,73-75,79,80] up to 150 mg daily in two trials,[70,72] and 100 or 150 mg two or three times weekly in three trials.[71,77,78] Two trials evaluated naltrexone and placebo with or without a second medication (fluoxetine or guanfacine); the second medication did not appear to affect findings so we combined the naltrexone and non-naltrexone arms in analyses. The duration of treatment was 6 months in 10 trials. In the other three trials, the duration of treatment was 2,[77] 3,[79] or 9 months.[72] Outcomes were assessed at the end of treatment in all trials except for two, which evaluated outcomes at 6 or 10 months following the completion of treatment.[77,78] Five trials were conducted in Russia,[25,26,73-75] two in Israel,[77,79] two in the United States[71,72], two in Europe,[78,80] one in Malaysia,[70] and one in China.[5] Patients were recruited from inpatient settings, drug treatment settings, or from the criminal justice system (e.g., parolees); no study reported recruitment of patients from primary care settings, or identification of drug use through screening in primary care settings. Naltrexone treatment was administered in outpatient settings.

In all trials that reported the opioid of use, heroin was the primary opioid of use in all or nearly all patients. Study participants were predominantly men (proportion female ranged from 0 to 31 percent); no trial reported outcomes stratified by patient sex. The mean age ranged from 21 to 29 years, with no studies conducted in adolescents. In studies that reported the duration of drug use, the mean ranged from 2 to over 16 years.[5,25,26,70,73-79] Information to characterize the severity of drug use was otherwise limited. All trials required patients to be withdrawn from opioids prior to initiation of naltrexone. Four trials[25,26,70,78] described inpatient or residential withdrawal from opioids; details about withdrawal methods and setting were otherwise not reported well.

Three studies were rated good quality[25,26,75] and the remainder were rated fair quality (**Appendix B4**). Methodological shortcomings in the fair-quality trials included unclear randomization or allocation concealment methods and unclear or high attrition. All trials were blinded.

Detailed Results: Drug Use and Other Risky Behaviors

Thirteen trials reported effects of naltrexone versus placebo or no naltrexone on risk of drug use relapse.[5,25,26,70-80] Definitions for relapse varied and were based on findings on urine drug tests, self-report, and/or presence of signs or symptoms of withdrawal; in two trials[5,80] relapse was not defined (**Table 1**). Among the non-naltrexone arms, the proportion of patients with relapse

ranged from 41 to 93 percent. Naltrexone was associated with decreased risk of relapse versus placebo or no naltrexone (12 trials; RR 0.73, 95% CI 0.62 to 0.85; **Figure 2**; ARD -18%, 95% CI -26% to -10%).[5,25,26,70,72-80] Treatment with naltrexone was for 2 to 9 months (6 months in 9 trials) and outcomes were assessed at 3 to 12 months after the start of treatment. Although statistical heterogeneity was high (I^2=78%), the RR estimate favored naltrexone in all but two trials,[70,78] which both reported point estimates close to one. Estimates were similar for naltrexone administered orally (11 trials; RR 0.76, 95% CI 0.65 to 0.88; I^2=70%)[5,25,70,72-80] or by injection/implant (2 trials; RR 0.41, 95% CI 0.06 to 2.40; I^2=98%) (**Table 2**).[25,26] Excluding two trials[77,78] that evaluated risk of relapse 6 or 10 months after discontinuation of naltrexone had little impact on the pooled estimate (10 trials; RR 0.71, 95% CI 0.59 to 0.84; I^2=82%). Restricting the analysis to trials of oral naltrexone at a dose of 50 mg/day (7 trials; RR 0.69, 95% CI 0.58 to 0.81; I^2=47%)[5,25,73-75,79,80] or to good-quality trials (3 trials; RR 0.67, 95% CI 0.48 to 0.94; I^2=84%)[25,26,75] also resulted in similar pooled estimates. One trial that did not provide poolable relapse data reported results consistent with the pooled findings.[71]

Nine trials reported effects of naltrexone versus placebo or no naltrexone on the likelihood of retention in treatment.[25,26,70,71,73-75,78,79] In some trials, relapse was included in the definition of non-retention. Among the arms not receiving naltrexone, rates of retention ranged from 9 to 56 percent. Naltrexone was associated with increased likelihood of treatment retention (9 trials; RR 1.71, 95% CI 1.13 to 2.49; I^2=67%; **Figure 3;** ARD 15%, 95% CI 5% to 22%). There was no interaction between route of naltrexone administration and likelihood of treatment retention (oral: 8 trials; RR 1.59, 95% CI 1.00 to 2.38; I^2=61%; injection/implant: 2 trials; RR 2.48, 95% CI 0.58 to 11.75; I^2=94%; p for interaction=0.37) (**Table 2**). Results were similar when analyses were restricted to trials of oral naltrexone at a dose of 50 mg/day (6 trials; RR 1.84, 95% CI 1.22 to 2.71; I^2=49%)[25,73-75,79] or to good quality trials (3 trials; RR 2.10, 95% CI 1.21 to 4.13; I^2=78%).[25,26,75]

Effects on other outcomes related to other drug use and/or risk behaviors were reported less consistently (**Appendix B3**). Five trials reported no difference between naltrexone versus placebo or no naltrexone in risk of alcohol, marijuana, or other (non-opiate) drug use.[72-74,78,79] There were no clear differences between naltrexone versus placebo or versus no naltrexone in measures of addiction severity (2 trials)[73,74] or severity of drug use or risky sexual behaviors (4 trials).[26,70,73,74]

Detailed Results: Health, Social and Legal Outcomes

Mortality was rare in the naltrexone trials, with a total of three deaths (2 naltrexone and 1 placebo) in five trials.[26,70,73,74,78]

Evidence on the effects of naltrexone versus placebo or no naltrexone on health outcomes such as global function, quality of life, depression, and anxiety was limited. One trial found no difference between naltrexone versus placebo in the Global Assessment of Function (GAF).[75] Another trial found naltrexone associated with improved quality of life, as measured by the mean change in Euro-Qol-5 score (14.1 versus 2.7; p=0.0005), the proportion of patients with improvement in Clinical Global Impressions scale (86% versus 58%; p=0.0002), and mean difference in Short Form Health Survey (SF)-36 mental component score (5.09, 95% CI 2.09 to

8.09; p=0.004)[26] Five trials reported effects of naltrexone on psychiatric measures. Four trials found no differences between naltrexone versus placebo in risk of anxiety[80]or depression,[75,79] or in scores on the Brief Psychiatric Rating Scale (BPRS).[73] One other trial found naltrexone associated with more severe depression, based on the Minnesota Multifactorial Personality Inventory (MMPI) depression scores (mean 73.7 versus 65.5; p<0.02).[78] Two other trials reported results that appeared to favor naltrexone based on scales measuring depression (Beck Depression Inventory [BDI]) and anxiety (Spielberger State-Anxiety Inventory [SSAI], State-Trait Anxiety Inventory [STAI]) severity, but the statistical significance of between group comparisons was not reported.[73,76]

Three trials reported legal outcomes.[71,72,77] One trial of persons on parole or probation found those taking naltrexone had lower rates of reincarceration than those taking no medication (26% versus 56%; RR 0.45, 95% CI 0.23 to 0.89).[71] Two other trials reported no difference between naltrexone versus placebo in the likelihood of contact with law enforcement.[72,77] One trial reported no difference between naltrexone versus placebo in likelihood of employment.[78]

Opioid Agonist Therapy (Buprenorphine or Methadone) for Opioid Use Disorder

The 2008 USPSTF report included one trial of methadone for treatment of opioid use disorder.[6] Including this trial, we identified seven trials (reported in 9 publications) on the effects of opioid agonist therapy with buprenorphine or methadone versus placebo or no medication (waitlist or usual care) for opioid use disorder (**Table 1**, **Appendixes B5, B6, and B7**).[6,70,81-87] Sample sizes ranged from 40 to 319 (total N=1,109). Two trials[6,81,86,87] evaluated oral methadone. The dose of methadone was up to 90 mg/day in one trial[81] and averaged 78 mg/day in the other trial.[6,86,87] Five trials[70,82-85] evaluated buprenorphine. Buprenorphine was taken sublingually in four trials[70,82,83,85] (dose ranged from 8 to 24 mg/day) and administered by implant in two trials[84,85] (4 implants, with a total dose of 320 mg). One trial[85] evaluated both oral and implanted buprenorphine. The duration of treatment ranged from three to twelve months (6 months in 4 trials[70,81,84,85] and 3,[83] 4,[86] or 12[82] months in 1 trial each). The buprenorphine implant trials required that patients successfully undergo induction with sublingual buprenorphine prior to randomization. Oral methadone and sublingual buprenorphine were administered daily under direct observation, though some trials allowed take-home doses for weekends and holidays. In five trials, all patients received some individual and/or group drug use counseling.[70,81,82,84,85] The intensity of counseling ranged from "minimal" (not described) to "standard" counseling for 45 to 60 minutes on a weekly or twice weekly basis. Two trials did not include a counseling intervention;[6,83,86,87] both were designed to evaluate bridging therapy with methadone or buprenorphine while awaiting entry into more comprehensive care.

The main type of opioid used was heroin in all of the trials. In two trials, prescription opioids were the main opioid of use in about one-third of patients.[84,85] Prescription opioid use was not described in the other trials. In five trials, the diagnosis of opioid use disorder was based on DSM-IV criteria.[6,70,81,84-87] Criteria for the diagnosis of opioid use disorder were not specified in the other two trials.[81,83] Four trials were conducted in the United States,[6,81,84-87] two trials in Europe,[82,83] and one trial in Malaysia.[70] Patients were recruited from inpatient settings in one trial,[82] from the community in one trial,[70] and from outpatient addiction treatment settings in the

other five trials. In one trial, treatment was initiated on an inpatient basis.[82] Otherwise, treatment was administered in outpatient addiction treatment settings.

Study participants were predominantly male (proportion female ranged from 25% to 43%) and mean age ranged from 29 to 43 years; no study was conducted in adolescents. No trial stratified outcomes by patient sex. In studies that reported the duration of drug use, the mean ranged from 5 to 20 years.[70,81-83] Three studies reported that the mean number of days of heroin use in the last 30 days ranged from 19 to 30.[6,70,81,86,87]

Two studies were rated good-quality[6,85-87] and the remainder were rated fair quality (**Appendix B8**). Methodological shortcomings in the fair-quality trials included unclear randomization or allocation concealment methods and unclear or high attrition. Both methadone trials utilized an unblinded design; one trial[81] compared methadone versus usual care and the other trial[6,86,87] compared methadone versus waitlist control.

Detailed Results: Drug Use and Other Risky Behaviors

Four trials reported effects of opioid agonist therapy with buprenorphine or methadone versus placebo or no medication on risk of drug use (**Table 1**).[6,70,82,85-87] Drug use outcomes were informed by urine drug test findings, though specific criteria varied (**Table 1**). Among the control arms, the proportion of patients with relapse ranged from 79 to 100 percent. Opioid agonist therapy was associated with decreased risk of relapse versus controls after 4 to 12 months of treatment (4 trials; RR 0.75, 95% CI 0.59 to 0.82; I^2=75%; **Figure 4**; ARD -35%, 95% CI -67% to -13%).[6,70,82,85-87] Although statistical heterogeneity was high, all four trials found opioid agonist therapy to be effective, with relative risk estimates ranging from 0.22 to 0.81. Estimates were similar in one trial of methadone (RR 0.71, 95% CI 0.61 to 0.84)[6,86,87] and three trials of buprenorphine (RR 0.59, 95% CI 0.21 to 1.31; I^2=84%);[70,82,85] stratification by drug did not reduce statistical heterogeneity and there was no statistically significant interaction (p=0.78). The methadone trial did not include counseling. Stratification of the buprenorphine trials according to whether administration was sublingual (2 trials, RR 0.46, 95% CI 0.08 to 2.19, I^2=93%)[70,82] or by implant (1 trial, RR 0.77, 95% CI 0.68 to 0.88)[85] also did not reduce statistical heterogeneity, with no statistically significant interaction (p=0.70). Restricting the analysis to two good quality trials resulted in a pooled estimate (RR 0.75, 95% CI 0.65 to 0.85, I^2=0%) very similar to the overall estimate (**Table 3**).[6,85-87]

Three trials reported effects of opioid agonist therapy with buprenorphine or methadone on drug use outcomes that could not be pooled.[81,83,84] Results also indicated positive effects of opioid agonist therapy on drug use (**Table 1**). One trial found methadone with minimal or standard counseling associated with fewer self-reported days of heroin use versus usual care (4.2 to 5.9 vs. 18.4); counseling intensity had no clear effect.[81] One trial found sublingual buprenorphine without counseling associated with greater decrease in self-reported heroin use versus placebo (-3.2 vs. 0.52 on a 0 to 10 Visual Analog Scale [VAS], p<0.001).[83] A third trial found sublingual buprenorphine associated with a higher proportion of negative urine drug tests versus placebo (37% vs. 22%, p=0.01).[84]

Seven trials reported effects of opioid agonist therapy versus placebo or versus no medication on likelihood of retention in treatment.[6,70,81-87] In some trials, relapse was included in the definition of non-retention (**Appendixes B5, B6, and B7**). Among patients who did not receive opioid agonists, rates of retention ranged from 0 to 38 percent. Opioid agonist therapy was associated with increased likelihood of treatment retention (7 trials; RR 2.58, 95% CI 1.78 to 4.59; I^2=71%; **Figure 5;** ARD 39%, 95% CI 23% to 54%). Statistical heterogeneity was present, but all trials reported estimates in favor of buprenorphine or methadone; relative risk estimates ranged from 1.30 to 31.00. Pooled estimates were similar for five trials[70,82-85] of buprenorphine (RR 2.52, 95% CI 1.89 to 4.74, I^2=51%) and two trials[6,81,86,87] of methadone (RR 2.22, 95% CI 0.63 to 7.56, I^2=92%), with no statistically significant interaction (p=0.54) (**Table 3**). Among trials of buprenorphine, there was no statistically significant interaction between sublingual administration (4 trials; RR 2.95, 95% CI 1.97 to 12.06, I^2=57%)[70,82,83,85] or administration as an implant (2 trials; RR 2.27, 95% CI 1.58 to 3.31, I^2=0%)[84,85] and retention in treatment (p for interaction=0.46). Restricting the analysis to two good quality trials (RR 3.15, 95% CI 1.90 to 4.81; I^2=42%) resulted in a pooled estimate similar to the overall estimate (**Table 3**).[6,85] Pooled estimates were also similar for trials with minimal or no counseling (3 trials; RR 2.78, 95% CI 0.93 to 13.74; I^2=86%)[6,81,83,86,87] and trials with standard counseling (5 trials; RR 2.09, 95% CI 1.54 to 3.33; I^2=56%; p for interaction=0.79).[70,81,82,84,85]

Effects on other outcomes related to other drug use and/or risk behaviors were reported less consistently (**Appendix B7**). Two trials reported inconsistent effects of methadone versus placebo on cocaine use,[6,81,86,87] one trial found methadone associated with decreased alcohol use,[81] and one trial found no effects of methadone on the Addiction Severity Index (ASI).[81] One trial found sublingual buprenorphine associated with decreased non-opioid drug use versus placebo.[83] Another trial found sublingual buprenorphine associated with more days in treatment without heroin relapse versus placebo (79 vs. 39, p=0.007) and no difference in HIV risk behaviors based on the AIDS Risk Inventory score.[70]

Detailed Results: Health, Social, and Legal Outcomes

Evidence on health outcomes associated with opioid agonist therapy versus placebo or versus no opioid agonist therapy was very limited. Mortality was reported in two trials of buprenorphine. There were a total of four deaths, all in patients randomized to placebo.[70,82] Two trials found implanted buprenorphine associated with greater likelihood of reporting a "very much" or "much" improved Clinical Global Impressions (CGI) (RR 1.36, 95% CI 1.06 to 1.74; I^2=43%).[84,85] One trial found no difference between sublingual buprenorphine versus placebo in anxiety and depression (based on the Symptom Checklist [SCL]-5 scale), but buprenorphine was associated with greater wellbeing (mean change from baseline -2.00 vs. -0.43 on a 0 to 10 VAS, p<0.001) and life satisfaction (mean change -0.65 vs. -0.24 on the 0 to 10 Temporal Satisfaction with Life Scale [TSLS], p<0.05).[83] No trial reported the effects of opioid agonist therapy on social or legal outcomes.

Psychosocial Interventions

Fifty-two trials (reported in 65 publications) evaluated psychosocial interventions for unhealthy drug use or drug use disorders (**Table 4, Appendixes B9, B10, and B11**).[4,30-33,44-69,88-121]

Twenty-seven trials enrolled patients who were not seeking treatment for substance use, but were identified through screening for unhealthy drug use (additional details available in the USPSTF screening review[1]; also see **Appendixes B9, B10, and B11**).[4,44-69] One of these trials[4] was included in the 2008 USPSTF review.[2] None of the trials of screen-detected populations required patients to meet DSM criteria for substance dependence, abuse, or use disorder at baseline, but used thresholds to define unhealthy drug use (e.g. use of drugs within a specific time frame, ASSIST score ≥4, or Drug Abuse Screening Test [DAST]-10 score ≥3; **Appendixes B9 and B10**).

Twenty-five trials (in 30 publications) were conducted in persons engaging in drug use who were not identified through screening in primary care settings (**Table 4, Appendixes B9, B10, and B11**).[30-33,88-90,92-113,121] Three of these trials[31-33] were included in the 2008 USPSTF review.[2] In these trials, patients were seeking substance use treatment or recruited based on known substance use ("treatment-seeking"). In 17 trials, patients were primarily recruited through advertisements for study participation. In the other nine trials, patients were directly recruited in target settings; referred by peers, clinician, family members, or social workers/counselors; or recruited from callers to a cannabis help line. Of the 25 trials, five required patients to meet DSM-IV criteria for substance abuse or dependence.[30,100-103] The severity of substance use at baseline varied. For example, among trials of persons using cannabis, mean scores on the SDS (range 0 to 15; higher scores indicate higher level of dependence) ranged from 4.1[107] to 9.8[31] and mean scores on the MPS (range 0 to 38; higher scores indicate higher level of dependence) ranged from 3.7[59] to 9.5.[30]

Across all trials, sample sizes ranged from 34 to 1,175 (total N=15,659.) The duration of followup was 3 to 4 months after the start of interventions in 18 trials,[30,33,44l,48-51,56,60,64,68,93,94,99,103,104,106,109,110] 6 to 9 months in 21 trials,[4,31,52,54,55,57-59,62,63,66,88,90,96,100,102,105,107,111,113] and ≥12 months in 13 trials.[32,44-46,61,65,67,69,95,98,101,112,115] Thirty-five trials[4,30,33,44,46,48-50,52-59,61-68,95,100-104,111,112,115] were conducted in the United States, seven trials in Europe,[69,94,96,105,107,108,110] and 10 trials in other countries.[31,51,60,88,90,97,99,106,109,113]

The primary substance used was cannabis in 29 trials,[30,31,33,44-46,53,55,59,63-65,93-96,98,99,101-104,106-110,112] stimulants in six trials,[4,88,90,105,111,113] opioids in two trials,[67,100] and mixed or multiple drugs in 15 trials.[48-51,54,56-58,60-62,66,68,69,115] Among the trials reporting mixed or multiple drug use at baseline, the proportion of patients that reported opioid use ranged from 5 to 26 percent. Five trials evaluated adolescents,[44,55,65,95,96,106] eight trials evaluated young adults (18 to 25 years of age),[52,59,60,63,93,94,98,113] and six trials evaluated mixed populations of adolescents or young adults.[32,45,53,105,107,108] Thirty-two trials evaluated adults or mixed populations of adults and adolescents,[4,30,31,33,46-50,54,56-58,61,62,64,66-69,88,90,99-104,109-112] including three trials of postpartum females[56-58] and two trials[64,68] of pregnant females. All trials of postpartum and pregnant females were conducted in screen-detected populations; they are discussed in more detail in the USPSTF screening report and not presented separately in this report.[1] Among the psychosocial intervention trials that did not focus on pregnant or postpartum females, three only enrolled females;[54,63,93] in the other trials the proportion of females ranged from 13 to 71 percent (median 34%).

Thirty-seven trials evaluated brief psychosocial interventions, defined here as one or two sessions, each ≤60 minutes in duration.[4,30,44-65,67,69,88,90,93,95,97,103,105-108,112] The most commonly used techniques in the brief intervention trials utilized motivational interventions (e.g., MET or MI) or CBT. Nineteen trials evaluated more intensive (non-brief) psychosocial interventions; in these, the number of sessions ranged from two to 14, aside from one trial[100] that utilized 57 sessions.[30,31,33,66,68,88,90,94,96,99-104,109-111,113] The most commonly used techniques in the intensive psychosocial interventions trials were motivational interventions and CBT; some trials used contingency management.

The mode of delivery for psychosocial interventions was face-to-face in 37 trials[4,30,31,33,44,45,48,49,51,53,55,60-63,66,67,69,88,90,93-96,98,100-108,111,112,115] and by computer, Internet, or telephone in 12 trials;[50,53,56-59,64,68,99,109,110,113] three trials used multiple modes of delivery.[46,54,65] The intervention was delivered by someone with graduate level education in 65 percent of the studies; 15 percent of studies utilized research staff without graduate level education or mixed educational levels, one study was delivered by substance treatment outreach workers who were in recovery,[4] and 17 percent of studies were solely computer-based. The control intervention consisted of a minimal intervention in 30 trials,[4,44,48,49,52,53,55-64,68,69,88,90,93,94,98,105,107-109,111,112,115] waitlist in 11 trials,[30,31,33,50,51,99,103,104,106,110,113] and usual care in 11 trials.[45,46,54,65-67,95,96,100-102] Minimal intervention controls typically consisted of brief education without a defined psychological intervention. In some trials, usual care could have included referral to drug treatment, though trials in which patients assigned to usual care were routinely referred for drug treatment were excluded (see Methods).

Eight trials[30,46,54,61,62,94,105,112] were rated good quality and the remainder were rated fair quality (**Appendix B12**). Methodological limitations in the fair quality trials included high attrition, failure to blind or unclear blinding of outcome assessors, and unclear randomization methods. Attrition was generally high; at three to four months attrition ranged from two to 67 percent and at six to 12 months attrition ranged from two to 46 percent. Blinding of patients and care providers to receipt of psychosocial interventions was not feasible given the nature of the interventions. Commonly reported drug use outcomes were changes in days of drug use (in the last 90 days, 30 days, or week), various measures of drug use severity (e.g., the ASSIST score, the SDS, the MPS, the Rutgers Alcohol Problems Index [RAPI; adapted for cannabis use], and others), and rates of drug use abstinence (based on self-report, urine testing, and/or hair sample testing). All studies assessed drug use frequency based on patient self-report using standardized questionnaires. Nineteen studies reported use of timeline followback methods (a method which uses a calendar and memory aids to prompt recall)[122] and one study[33] reported use of collaterals (family members, friends) to verify self-report. Thirteen studies reported use of urine testing to detect drug use in all or a sample of patients, three studies reported use of hair samples,[57,58,62] and one study reported use of saliva testing.[105]

Detailed Results: Drug Use and Other Risky Behaviors

Abstinence. Psychosocial interventions were associated with increased likelihood of abstinence from drug use at 3 to 4 months (15 trials; RR 1.60, 95% CI 1.24 to 2.13, I^2=61%; ARD 9%, 95% CI 5% to 15%; **Figure 6**)[30,33,47,49,56,58,64,68,69,99,107-110] and at 6 to 12 months (14 trials; RR 1.25, 95% CI 1.11 to 1.52, I^2=38%; ARD 6%, 95% CI 2% to 10%; **Figure 7**)[4,31,45,47,57,58,62,69,88-90,92,105,

[107,108,113] versus controls (waitlist, minimal intervention, or usual care). Stratified according to the primary type of drug of use, estimates favored psychosocial interventions for abstinence from cannabis use (7 trials; RR 2.08, 95% CI 1.51 to 3.07 at 3 to 4 months; I^2=28%[30,33,99,107-110] and 4 trials, RR 1.58, 95% CI 1.17 to 3.06 at 6 to 12 months, I^2=36%).[31,45,107,108] Effects on stimulant use (4 trials, RR 1.45, 95% CI 0.86 to 2.56 at 6 to 12 months, I^2=65%),[88-90,105,113] and mixed drug use (7 trials, RR 1.24, 95% CI 0.92 to 1.80 at 3 to 4 months, I^2=60%[47,49,56-58,64,68] and 5 trials, RR 1.12, 95% CI 0.92 to 1.36 at 6 to 12 months, I^2=0%) were not statistically significant. There was a statistically significant interaction between type of drug use and effects of psychosocial interventions on abstinence at 3 to 4 months (p for interaction=0.10) but not at 6 to 12 months (p for interaction=0.43) (**Table 5**). Only one trial evaluated effects of a psychosocial intervention on prescription drug use (type of prescription drug use not specified); estimates were imprecise (RR 2.08, 95% CI 0.81 to 5.38 at 3 to 4 months, and RR 1.25, 95% CI 0.65 to 2.40 at 12 months).[69] One trial of patients with opioid (heroin) use (n=126) found contingency management associated with increased likelihood of opioid abstinence versus usual care (OR 2.15, 95% CI 1.16 to 4.00), but could not be pooled because the number of patients evaluated in each group for this outcome was not reported.[100] In all of the trials of cannabis and stimulant use, abstinence was based on self-report. All trials of mixed drug use utilized hair or urine testing to assess abstinence, except for one trial that evaluated 6 sessions of MET plus CBT in pregnant women (RR 0.95, 95% CI 0.59 to 1.55).[68]

Effects of psychosocial interventions on likelihood of drug use abstinence at 3 to 4 months were stronger in trials of treatment-seeking populations (7 trials, RR 2.08, 95% CI 1.51 to 3.07, I^2=28%)[30,33,99,107-110] than trials of screen-detected populations (8 trials, RR 1.28, 95% CI 0.97 to 1.84, I^2=57%; p for interaction=0.05) (**Figure 8**).[47,49,56-58,64,68,69] Of the screen-detected trials, all except for one[69] enrolled persons with mixed drug use and five trials[56-58,64,68] enrolled pregnant or postpartum women. At 6 to 12 months, effects on likelihood of abstinence were weaker in trials of screen-detected (7 trials, RR 1.17, 95% CI 0.99 to 1.41, I^2=2%)[4,45,47,57,58,62,69] compared with treatment-seeking (7 trials, RR 1.51, 95% CI 1.14 to 2.37, I^2=57%)[31,88-90,92,105,107,108,113] populations (**Figure 14**), but the interaction was not statistically significant (p for interaction=0.26). None of the trials of screen-detected populations at 6 to 12 months evaluated pregnant women and two enrolled postpartum women;[57,58] five of the seven trials enrolled persons with mixed drug use.

Effects of psychosocial interventions on abstinence were somewhat stronger in trials of intensive compared with brief interventions and in trials that used face-to-face versus other (web, computer, or telephone) delivery methods, but the differences were not statistically significant (**Table 5**). No trial reporting abstinence enrolled only adolescents and there were no statistically significant differences between trials that enrolled adults >25 years of age and those that enrolled adolescents and young adults (up to 25 years of age) (**Table 5**).

At 3 to 4 months, five trials reporting effects of psychosocial interventions on drug use abstinence enrolled pregnant or postpartum females (RR 1.24, 95% CI 0.99 to 1.89, I^2=41%)[56-58, 64,68] and at 6 to 12 months two trials enrolled postpartum females (RR 1.07, 95% CI 0.76 to 1.71, I^2=0%).[57,58] Restricting the analysis to trials of adults who were not pregnant or postpartum resulted in pooled estimates for drug use abstinence that were similar to the overall estimates at 3 to 4 months (8 trials, RR 1.77, 95% CI 1.17 to 2.80, I^2=71%) and at 6 to 12 months (7 trials, RR

1.41, 95% CI 1.04 to 2.16, I^2=57%). No trial that enrolled men and women reported effects on abstinence stratified by sex. There was no statistically significant interaction between study quality and effects of psychosocial interventions on drug use abstinence, but only three trials were rated good quality, limiting the usefulness of this stratified analysis (**Table 5**).[30,62,105]

Drug Use Days. Twenty trials reported effects of psychosocial interventions on frequency of drug use based on the number of drug use days. Standardized to drug use in the past 7 days, effects of psychosocial interventions versus controls at 3 to 4 months after the start of the intervention ranged from a decrease of -2.30 days to an increase of 0.26 day. When the data were pooled, psychosocial interventions were associated with decreased number of drug use days versus controls at 3 to 4 months (19 trials, mean difference -0.49 day, 95% CI -0.85 to -0.13), but statistical heterogeneity was high (I^2=89%) (**Figure 9**).[30,33,45-47,52-54,59,61,67,93,94,97-99,106,107,109,110]

In stratified analyses (**Table 6)**, effects of psychosocial interventions on drug use days at 3 to 4 months were present in trials of treatment-seeking populations (10 trials, mean difference -0.91 day, 95% CI -1.52 to -0.31, I^2=86%)[30,33,93,94,97-99,106,107,109,110] but not in trials of screen-detected populations (9 trials, mean difference -0.10 day, 95% CI -0.31 to 0.12, I^2=46%;[45-47,52-54,59,61,67] p for interaction=0.02) (**Figure 11**). Effects on drug use days were also present in trials of intensive interventions (10 trials, mean difference -0.88 day, 95% CI -1.50 to -0.28, I^2=91%)[30,33,45,47,61,67,93,94,99,106,109,110] but not in trials of brief interventions (9 trials, mean difference -0.13 day, 95% CI -0.36 to 0.12, I^2=42%;[46,52-54,59,97,98,107] p for interaction=0.03). Effects were also present in trials that evaluated cannabis use (14 trials, mean difference -0.68 day, 95% CI -1.14 to -0.23, I^2=89%)[30,33,45,52,53,59,67,93,94,97-99,106,107,109] but not in trials that evaluated "any drug use" (5 trials, mean difference -0.05 day, 95% CI -0.39 to 0.31, I^2=58%),[46,47,54,61,110] though the interaction between drug use type and effects on drug use days was not statistically significant (p=0.11) (**Figure 9**). All trials that reported any drug use except for one[110] were conducted in screen-detected populations. No trial evaluated effects of psychosocial interventions on opioid use days.

When trials were stratified according to age, effects of psychosocial interventions on drug use days were greater in trials of adults (10 trials, mean difference -0.63, 95% CI -1.22 to -0.03, I^2=93%)[30,33,46,47,54,61,67,99,109,110] than trials of young adults (8 trials, mean difference -0.15, 95% CI -0.37 to 0.03; I^2=0%).[45,52,53,59,93,94,97,98] One trial evaluated adolescents[106] and one of the young adult trials also enrolled adolescents,[107] each showing no statistically significant effect. There was no statistically significant interaction between age group and effects on drug use days (p=0.38). None of the trials that reported effects on drug use days enrolled pregnant or postpartum persons.

Effects of psychosocial interventions on drug use days at 6 to 12 months versus controls were smaller than at 3 to 4 months and not statistically significant (15 trials, mean difference -0.08, 95% CI -0.30 to 0.11, I^2=45%) (**Figure 10**).[45-47,52-54,59,61,62,67,97,98,105,107,111,112] Differences ranged from a decrease of -1.37 days to an increase of 0.51 days. There were also no statistically significant effects on drug use days at 6 months in subgroup analyses based on whether the population was screen-detected (**Figure 15**), type of drug use (cannabis, stimulants, or any drug), age group, whether the intervention was brief, or whether the intervention included a face-to-face

component. Estimates were similar for good and fair quality trials at 3 to 4 months and at 6 to 12 months (**Table 6**).

Thirteen trials reported drug use outcomes that could not be pooled.[48,50,55,63,66,95,96,100-104,119] As in the pooled analyses on drug use outcomes, findings from these trials were inconsistent. Four trials that could not be pooled reported less drug use in the intervention group;[48,95,100,103] the remaining trials found no differences between groups. None of the trials reported effects of psychosocial interventions on drug use days enrolled pregnant or postpartum women and no trial stratified effects on drug use days by sex.

Detailed Results: Health, Social, and Legal Outcomes

Twenty-two trials reported effects of psychosocial interventions on severity or consequences of drug use, measured using a variety of drug use severity scales (e.g., MPS, DSM-IV Cannabis Problem Scale, the SDS, or the ASSIST scale).[30,31,33,44,51-53,58-62,65,67,92,94,99,106,107,109,110,112,113] At 3 to 4 months, the effects of psychosocial interventions versus controls (minimal intervention, waitlist, or usual care) on measures of drug use severity ranged from an improvement in the standardized mean difference of -1.00 to a worsening of 0.14. When data were pooled, psychosocial interventions were associated with a small but statistically significant effect on drug use severity (17 trials, SMD -0.18, 95% CI -0.32 to -0.05),[30,33,44,52,53,59,65,94,99,106,107,109,110] but statistical heterogeneity was high (I^2=73%) (**Figure 12)**. In stratified analyses, psychosocial interventions were associated with a statistically significant effect on drug use severity in persons primarily using cannabis (13 trials, SMD -0.21, 95% CI -0.39 to -0.04, I^2=78%)[44,94,99,107,109,110] but not in persons with mixed substance use (4 trials, SMD -0.05, 95% CI -0.20 to 0.05, I^2=1.3%);[51,58,60,67] however, there was no statistically significant interaction (p for interaction=0.45). Similarly, effects were somewhat stronger in trials of treatment-seeking populations (8 trials, SMD -0.30, 95% CI -0.57 to -0.03, I^2=82%)[30,33,94,99,106,107,109,110] than in trials of screen-detected populations (9 trials, SMD -0.05, 95% CI -0.15 to 0.05, I^2=17%),[44,51-53,58-60,65,67] but there was no statistically significant interaction (p for interaction=0.12) (**Figure 16**). Effects were also somewhat stronger in trials of intensive interventions (6 trials; SMD -0.32, 95% CI -0.70 to 0.06, I^2=89%)[30,33,94,99,109,110] than in trials of brief interventions (12 trials; SMD -0.09, 95% CI -0.20 to -0.002, I^2=36%; p for interaction=0.18)[30,44,51-53,58-60,65,67,106,107] and in trials that included adults (8 trials, SMD -0.31, 95% CI -0.57 to -0.07, I^2=82%)[30,33,51,58,67,99,109,110] than in trials of young adults with or without adolescents (6 trials, SMD -0.01, 95% CI -0.15 to 0.08, I^2=22%)[52,53,59,60,94,107] or trials of only adolescents (3 trials, SMD -0.08, 95% CI -0.26 to 0.10, I^2=0%; p for interaction=0.20).[44,65,106] Among the trials that included adults (including young adults), estimates were similar when one trial of postpartum women (SMD -0.29, 95% CI -0.67 to 0.10)[58] was excluded (13 trials, SMD -0.19, 95% CI -0.37 to -0.03, I^2=79%). There were no subgroup differences based on mode of delivery (face-to-face or non-face-to-face), or study quality (good or fair) (**Table 7**). In five trials that reported cannabis use severity using the SDS (scale 0 to 15; higher scores indicate higher level of dependence), the mean difference between psychosocial interventions versus control conditions was less than 1 point (-0.66, 95% CI -1.39 to 0.07, I^2=62%).

At 6 to 12 months, the effects of psychosocial interventions on measures of drug use severity versus control conditions ranged from an improvement in the SMD of -0.61 to a worsening of

0.11. When data were pooled, there was no difference between psychosocial interventions versus control conditions in drug use severity (13 trials, SMD -0.10, 95% CI -0.24 to 0.02, I^2=65%)[31,44,52,53,58,59,61,62,65,67,92,107,112,113] (**Figure 13)**. There were also no statistically significant differences when trials were stratified according to whether the main drug of use was amphetamines (1 trial, SMD 0.10, 95% CI -0.35 to 0.54),[113] cannabis (8 trials, SMD -0.16, 95% CI -0.37 to 0.03, I^2=72%),[31,44,52,53,59,65,92,107,112] or mixed drugs (4 trials, SMD -0.001, 95% CI -0.18 to 0.12, I^2=42%).[58,61,62,67]No study evaluated effects of psychosocial interventions on opioid drug use severity.

Psychological interventions also were not associated with statistically significant effects on drug use severity in subgroups defined by age group, intensity of interventions, or mode of delivery (**Table 7**). However, effects on drug use severity were absent in trials of brief interventions (10 trials, SMD -0.02, 95% CI -0.13 to 0.06, I^2=35%)[44,52,53,58,59,61,62,65,67,107] and favored psychosocial interventions in trials of intensive interventions (3 trials, SMD -0.36, 95% CI -0.80 to 0.14, I^2=70%; p for interaction=0.03).[31,92,112,113] Similarly, effects were absent in trials of screen-detected populations (9 trials, SMD -0.03, 95% CI -0.15 to 0.06, I^2=40%)[44,52,53,58,59,61,62,65,67] but favored psychosocial interventions in trials of treatment-seeking populations (4 trials, SMD -0.23, 95% CI -0.62 to 0.17, I^2=82%; p for interaction=0.27) (**Figure 17**).[31,92,107,112,113] No trial evaluated effects of psychosocial interventions on drug use severity stratified by patient sex.

Data on effects of psychosocial interventions on other health, social, and legal outcomes was limited. Mortality was reported in four trials. In these trials, there were few mortality events, resulting in imprecise estimates.[47,61,66,69] Two trials found no differences between psychosocial interventions versus control conditions in risk of emergency department visits or hospital admissions.[62,66] Six trials found no statistically significant effects of psychosocial interventions on measures related to mental health.[30,48,62,90,110,111] Two trials found no effect of psychosocial interventions on likelihood of driving after cannabis use[45,97,98] and four of five trials found no effect on risk of incarceration or involvement in criminal activity.[47,61,88-90] One trial[32,108] found a brief intervention associated with decreased likelihood of selling drugs to friends (15% vs. 40%, OR 0.42, p=0.008). Three trials reported inconsistent effects of psychosocial interventions on measures of employment,[30,100,111] with two trials showing no effects.[30,111] Six trials found no effects of psychosocial interventions versus control conditions on quality of life or function (measured by the SF-12 Physical Component Scale, EUROHIS, General Health Questionnaire [GHQ]-28, or a 0 to 100 Health-related Quality of Life [HRQOL] scale).[48,62,66,88,111,113]

Seven trials found no statistically significant differences between psychosocial interventions versus control conditions in injection drug or sexual risk behaviors.[57,61,62,64,88-91] One other trial found a brief therapist-initiated, computer guided behavioral intervention with a 3 month booster session associated with a reduction in scores on the sexual risk subscale of the HIV Risk Taking Behaviour Scale over 12 months compared with a minimal intervention, but brief interventions that were computer-delivered or did not include a booster session had no significant effects.[91]

Key Question 5. What Are the Harms of Interventions to Reduce Drug Use?

Summary

- There was no difference between naltrexone versus placebo or versus no naltrexone in risk of withdrawal due to adverse events (3 trials; RR 1.54; 95% CI 0.35 to 8.31; I^2=0%), but the estimate was imprecise; three other trials reported no study withdrawals in either naltrexone or control groups.
    - Naltrexone was not associated with increased risk of serious adverse events, but reporting of serious adverse events was suboptimal and few events were reported.
- There was no difference between buprenorphine versus placebo in risk of serious adverse events (2 trials; RR 0.32, 95% CI 0.09 to 1.12; I^2=0%); buprenorphine was associated with increased risk of constipation (2 trials; RR 2.36, 95% CI 1.16 to 4.92, I^2=0%; ARD 12%, 95% CI -5% to 41%).
- Harms were not reported in two trials of methadone.
- Most psychosocial trials did not report harms, though no serious adverse events were noted; four trials reported no harms.

Evidence

Naltrexone for Opioid Use Disorder

Eleven trials of naltrexone versus placebo or no medication reported harms of treatment (**Appendixes B1, B2, and B3**). Two studies described no or few adverse events during the study in either naltrexone or control groups,[71,75] but did not provide additional details or data about specific adverse events, and one study reported the number of adverse events but the denominator was not provided.[72] Among the other studies, three provided data on study withdrawals due to adverse events.[25,26,74] All reported few events in either group, with no difference between naltrexone and control when pooled, based on an imprecise estimate (RR 1.54; 95% CI 0.35 to 8.31; I^2=0%). Three other studies reported no study withdrawals due to adverse events in either group.[5,70,78] There were also no differences in risk of serious adverse events (3 studies[25,26,70]; RR 1.24, 95% CI 0.11 to 10.21; I^2=59%). One other study[5] reported no serious adverse events in either group. One study[73] reported on increase in risk of suicide attempts (4% [1/27] vs. 0% [0/25]; RR 2.39, 95% CI 0.12 to 65), and another study[26] reported no suicide events in either group. There was no difference between naltrexone versus placebo or no medication in risk of diarrhea (2 studies; RR 1.94, 95% CI 0.70 to 6.53; I^2=0%),[5,79] nausea or vomiting (1 study; RR 1.40, 95% CI 0.33 to 5.93),[5] or constipation (2 studies; RR 0.97, 95% CI 0.37 to 2.39; I^2=0%).[5,70]

Opioid Agonist Therapy (Buprenorphine or Methadone) for Opioid Use Disorder

Four trials of opioid agonist therapy versus placebo, each of which evaluated buprenorphine, reported harms (**Appendixes B5, B6, and B7**).[70,83-85] There was no difference between

buprenorphine versus placebo in risk of serious adverse events, which were uncommon (2 trials; RR 0.32, 95% CI 0.09 to 1.12; I^2=0%)[84,85]; one trial reported no hospitalizations due to serious medication-related adverse events.[70] One trial found no difference between buprenorphine versus placebo in risk of withdrawal due to adverse events (RR 0.89, 95% CI 0.06 to 13.7)[70] and one trial found no difference in risk of any adverse event (RR 1.14, 95% CI 0.90 to 1.43).[85] There were no differences between buprenorphine versus placebo in risk of diaphoresis (3 trials; RR 1.15, 95% CI 0.55 to 2.73; I^2=44%)[70,83,85] or nausea (2 trials; RR 1.13, 95% CI 0.41 to 6.07; I^2=30%).[83,85] Buprenorphine was associated with increased risk of constipation versus placebo, based on two trials (RR 2.36, 95% CI 1.16 to 4.92, I^2=0%; ARD 12%, 95% CI -5% to 41%).[70,84]

Psychosocial Interventions

Four trials of psychosocial interventions reported no adverse events in either intervention or control groups.[52,53,57,58] Harms were otherwise not reported in trials of psychosocial interventions, with no serious adverse events noted.[57]

Key Questions 6 and 7. Does Naloxone Reduce Morbidity or Mortality, or Improve Other Health Outcomes in Persons With Opioid Use Disorder or Misuse? What Are the Harms of Naloxone in Persons With Opioid Use Disorder or Misuse?

No study evaluated the benefits or harms of preemptive prescribing of naloxone versus placebo or versus no naloxone for mitigating overdose risk in persons with opioid use disorder or misuse in primary care settings. Although one nonrandomized intervention study found provision of naloxone in primary care settings associated with decreased likelihood of opioid-related emergency department visits after 6 months (incidence rate ratio 0.53, 95% CI 0.34 to 0.83) and 1 year (incidence rate ratio 0.37, 95% CI 0.22 to 0.64), the intervention consisted of training and support in naloxone prescribing to providers and clinic staff, and patients were prescribed long-term opioid therapy for pain and were not selected on the basis of drug misuse or abuse.[123] A trial from the United Kingdom of provision of naloxone upon release to incarcerated adults with heroin injection use was stopped early because two-thirds of naloxone administrations were to persons other than the ex-prisoner. At the time that the study ended, five drug-related deaths had occurred within 12 weeks post-release, among over 1,500 persons randomized.[124]

Chapter 4. Discussion

Summary of Review Findings

This report updates a 2008 USPSTF review on screening for drug use in adolescents and adults.[2] It also supplements a USPSTF screening review by including trials of interventions for drug use conducted in treatment-seeking populations.[1]

Table 8 summarizes the evidence reviewed for this update. Compared to the 2008 USPSTF review, substantially more evidence is available to support the effectiveness of FDA-approved pharmacotherapies for treatment of opioid use disorder on drug use outcomes (two trials included in the 2008 USPSTF review, compared with 19 trials in this report) and to support the effectiveness of psychological interventions for cannabis, stimulant, or mixed drug use outcomes (five trials included in the 2008 USPSTF review, compared with 52 trials in this report). Our findings supplement the USPSTF screening review,[1] which found no consistent evidence that psychosocial interventions are effective at improving drug use or health outcomes, based on 27 trials of persons with unhealthy drug use identified through screening. With the inclusion of 25 additional trials conducted in treatment-seeking populations, we found psychosocial interventions effective for improving drug use outcomes. Effects of psychosocial interventions were generally stronger in treatment-seeking populations than in screen-detected populations, for cannabis use than other drug use outcomes, for shorter-term (3 to 4 month) than longer-term (6 to 12 month) outcomes, and for more intensive interventions versus brief interventions. Few trials evaluated psychosocial interventions for stimulant or opioid use and estimates were imprecise; therefore, effects on these types of drug use are uncertain.

With regard to pharmacotherapies, evidence indicates that naltrexone (an opioid antagonist) and opioid agonists (methadone and the partial agonist buprenorphine) are effective at reducing the likelihood of drug use relapse and increasing the likelihood of retention in treatment. Although the 2008 USPSTF review[2] also found that pharmacotherapies are effective at improving drug use outcomes, five of the seven trials of pharmacotherapies in the 2008 USPSTF report evaluated medications that are not FDA-approved for treatment of drug use, and are not first-line or recommended treatments. For this report, which was restricted to pharmacological medications approved by FDA as of September 2018, trials were primarily conducted in persons using heroin and/or meeting DSM-IV criteria for opioid use disorder, and medications were typically administered in conjunction with drug use counseling, in accordance with recommended practice.[8,9] Based on pooled estimates, the number needed to treat to avoid one additional case of relapse was 5.3 for naltrexone and 2.9 for opioid agonists and the number needed to treat for one additional case of treatment retention was 6.7 for naltrexone and 2.6 for opioid agonists. Results were similar when analyses of opioid agonists were stratified according to whether the medication was methadone or buprenorphine. Definitions for relapse varied across trials, though most trials incorporated urine drug test findings. Although statistical heterogeneity was high in the naltrexone analyses, relative risk estimates for drug use abstinence favored naltrexone in 10 of 12 trials and results were consistent in stratified and sensitivity analyses based on the mode of administration, timing of outcome assessment, dose, and study quality. Most naltrexone trials evaluated oral naltrexone, some naltrexone trials recruited patients from the criminal justice

system, oral medications were administered daily under direct observation, and almost half of the naltrexone trials were conducted in Russia, where opioid agonist therapy with methadone or buprenorphine is not permitted. These factors could potentially reduce the applicability of findings to current U.S. primary care practice, where pharmacological alternatives to naltrexone are available and extended-release, injectable naltrexone was approved by the FDA in 2010.[125] Head-to-head trials, which were not included in this report, suggest that extended-release injectable naltrexone is similarly effective as sublingual buprenorphine/naloxone for improving drug use outcomes, though naltrexone can be more difficult to initiate.[126,127]

Like the 2008 USPSTF review, we found psychosocial interventions to be effective at improving some drug use outcomes when all trials of screen-detected or treatment-seeking populations were included in analyses. Effects were present at 3 to 4 months for increased likelihood of drug use abstinence, decreased number of drug use days, and decreased drug use severity, but at 6 to 12 months were only observed for drug use abstinence. Most trials of psychosocial interventions utilized CBT or motivational interventions, with contingency management evaluated in some trials, and ranged in intensity from one or two session brief interventions to ongoing treatment for months. The majority of trials of psychosocial interventions recruited patients with cannabis use or mixed drug use. Based on overall pooled estimates, psychosocial interventions were associated with a number needed to treat for one additional case of drug use abstinence compared with controls of 11 at 3 to 4 months and 17 through 6 to 12 months. A factor that complicates interpretation of abstinence findings is that trials varied with regard to how abstinence was assessed, with some trials relying on self-report and others incorporating laboratory measures (drug testing of urine or hair). Psychosocial interventions were also associated with an average reduction of 0.5 drug use days per week and a small but statistically significant decrease in drug use severity at 3 to 4 months (SMD -0.18). Effects on continuous outcomes such as drug use severity and drug use days could be harder to detect than effects on a dichotomous outcome such as drug use abstinence because of variability in baseline drug use severity, including trials that enrolled patients with infrequent drug use or mild drug use severity. Trials of psychosocial interventions were characterized by marked variability in patient populations, interventions, outcomes, recruitment and treatment settings, and other factors, likely contributing for the substantial statistical heterogeneity observed in pooled analyses. Effects of psychosocial interventions tended to be greater in trials of treatment-seeking than screen-detected individuals, trials evaluating cannabis use than those evaluating stimulant or mixed drug use, trials evaluating face-to-face than other modes of delivery, and trials evaluating more intensive rather than brief interventions. However, these findings should be interpreted with caution, as none of these factors fully accounted for statistical heterogeneity, the relatively small number of trials limited the usefulness of subgroup analyses, and most tests for interaction effects were not statistically significant.

Some considerations that might explain why psychosocial interventions appear to be more effective in trials of treatment-seeking than screen-detected populations are that the drug use thresholds for enrolling patients in screening trials (based on measures of drug use severity; frequency or duration or use; or type of drug use) were generally lower than trials of treatment-seeking individuals, and most trials of psychosocial interventions in screen-detected populations evaluated brief interventions, often consisting of a single session. One recent intervention trial conducted in a primary care safety net setting (practices that organize and deliver a significant

level of health care and other services to uninsured, Medicaid, and other vulnerable patients)[128] found that 8 percent of persons identified through screening who met the screening threshold for trial participation reported use of intravenous drugs in the past 30 days and 30 percent had a DAST-10 score of $\geq$6, indicating substantial or severe drug use.[61] Another intervention trial conducted in a primary care setting found that 18 percent of persons meeting the drug use screening threshold for trial participation had an ASSIST score $\geq$27,[62] indicating a high risk of dependence.[129] Neither trial excluded patients with a past history of drug use or current or past treatment for drug use, which could have increased the proportion of patients with more severe drug use. Nonetheless, these studies suggest that some persons with drug use identified on screening in primary care settings may have more severe drug use. The effectiveness of psychosocial interventions implemented in primary care settings might be enhanced by targeting interventions to those patients identified on screening as having more severe drug use and/or by offering more intensive (e.g., multisession) interventions.

As in the 2008 USPSTF report and the USPSTF screening review, we found limited and inconsistent evidence on the effects of pharmacotherapy and psychological interventions on other health outcomes. Trials were not designed or powered to assess outcomes such as mortality or overdose events, which were infrequently reported, though they appeared to be rare. No trial assessed effects of interventions for drug use on risk of HIV or other infectious diseases associated with injection drug use, though limited evidence from pharmacotherapy trials found no clear effects on HIV risk behaviors. A meta-analysis of observational studies that did not meet inclusion criteria found opioid agonist therapy associated with decreased risk of HIV infection in persons who inject drugs (rate ratio 0.60, 95% CI 0.42 to 0.85, I^2=23%, based on 6 studies reporting adjusted risk estimates).[130] We found limited evidence showing no clear effects of drug use interventions on legal outcomes such as incarceration, criminal activity, quality of life, or social outcomes. However, most trials did not assess these outcomes. The 2008 USPSTF review previously found fair evidence that stopping or reducing drug misuse is associated with reduced mortality and morbidity.[2] A subsequent meta-analysis of cohort studies found treatment with methadone and buprenorphine associated with decreased mortality risk; retention in treatment was also associated with decreased risk of overdose mortality.[131]

Assessment and reporting of harms in trials of pharmacotherapies was suboptimal, but indicated no increase in risk of serious adverse events or study withdrawal due to adverse events versus placebo or no pharmacotherapy. Buprenorphine was associated with an increased risk of constipation versus placebo (number needed to harm 8), though this finding was based on only two trials. Although reporting on harms in trials of methadone included in this review was very limited and inconsistent, observational studies indicate that methadone may be associated with higher risk of constipation relative to buprenorphine.[132,133] Trials of psychosocial interventions did not assess for harms, though serious harms are not anticipated with this type of intervention.

Evidence on the benefits and harms of preemptive naloxone prescribed in primary care settings for reducing overdose risk in persons with opioid use disorder or misuse is not available. Although one study found coprescription of naloxone to patients prescribed opioids for pain was associated with reduced risk of opioid-related emergency department visits, it was nonrandomized and enrolled patients who did not necessarily have opioid misuse or use

disorder.[123] To date, the effectiveness of naloxone has mainly been demonstrated in the context of evaluations of community opioid overdose prevention and naloxone distribution programs.[21,22]

Limitations

Our review methods has some limitations. We restricted inclusion to English language articles and did not search for studies published only as abstracts. There was substantial variability in populations, interventions, comparisons, and measurement of outcomes, with unexplained statistical heterogeneity that was only partially explained in stratified and sensitivity analyses based on these and other factors. Therefore, we performed random effects analyses, which result in wider confidence intervals than fixed effects models when statistical heterogeneity is present, reflecting the greater uncertainty in estimates. In addition, we performed analyses using the profile likelihood method, which may be more reliable when statistical heterogeneity is present,[134] though results using the profile likelihood and Dersimonian and Laird methods were very similar. The relatively small number of trials limited the usefulness of subgroup and sensitivity analyses; therefore, results of such analyses should be interpreted with caution. We restricted inclusion to trials with at least three months followup, which might have excluded relevant evidence from shorter-term trials. We also excluded head-to-head trials, which are useful for directly assessing the relative effects of different therapies. We did not evaluate the evidence on several therapies that are not considered first-line options for treatment of drug use, such as mindfulness interventions, acupuncture, and music therapy.

There were also limitations in the evidence. Most trials had methodological limitations, though we excluded poor-quality trials with serious flaws and findings were generally similar when we restricted analyses to good quality trials. Trials primarily focused on evaluation of effects of interventions on intermediate outcomes such as drug use or retention in treatment. There was little direct evidence on the effects of interventions on mortality or other clinical, social, and legal outcomes. However, as noted above, the 2008 USPSTF review and other analyses have found limited evidence from observational studies for an association between reduction in opioid (usually heroin) misuse and improved health outcomes.[2,131] Evidence was also limited on the effectiveness of treatments for opioid use disorder related to prescription drug use and stimulant use. Trials varied in how abstinence was assessed, with some trials relying on self-report and others incorporating results from drug testing of urine or hair. Similarly, drug use severity was assessed using a variety of scales that varied in terms of the extent to which they focused on frequency of use versus consequences of use. For trials of pharmacotherapies, the outcome of retention in treatment often incorporated drug use relapse; therefore, these two drug use outcomes are not independent. Evidence was not available for naloxone for mitigation of risks associated with opioid use disorder or misuse.

Emerging Issues/Next Steps

The FDA approved an injectable, once-monthly buprenorphine formulation for treatment of moderate to severe opioid use disorder in 2017.[135] The approval was based on two trials showing

effectiveness at improving drug use outcomes versus placebo. However, these trials have not yet been published.

A number of pharmacotherapies have been evaluated for treatment of drug use disorder that are not approved by the FDA for this indication, and are not currently recommended treatments. For cannabis use, off-label pharmacotherapies that have been studied include dronabinol, N-acetylcysteine, gabapentin, buspirone, divalproex, and cannabis replacement therapy. For stimulant use disorder, off-label pharmacotherapies that have been studied include modafinil, disulfiram, propanolol, methylphenidate, vigabatrin, topiramate, rivastigmine, naltrexone, and serotoninergic agents.[136,137]

Relevance for Priority Populations

Drug use is associated with adverse maternal and neonatal outcomes. The only trials of interventions to reduce drug use in pregnant or postpartum women were conducted in screen-detected populations and are discussed in more detail in the USPSTF screening review,[1] which found no clear evidence of benefits in these populations. In this review, no trial evaluated pharmacotherapy for opioid use disorder in pregnant women. The American College of Obstetricians and Gynecologists recommends screening for opioid use in pregnant women and opioid agonist therapy with methadone or buprenorphine in those with opioid use disorder.[138] Evidence to determine whether effects of interventions vary by sex was very limited. Trials did not report effects of pharmacotherapies or psychosocial interventions on drug use abstinence/relapse, retention in treatment, drug use severity, or drug use days stratified by patient sex; few trials evaluated the interaction between drug use interventions and sex on other outcomes, with most reporting no statistically significant interactions.[4,46,48,55,95,96,111]

Substance use in adolescents is associated with increased risk of adult substance use disorders, and can be associated with serious consequences. We found some evidence suggesting that psychosocial interventions may be less effective at reducing drug use days in adolescents or young adults (less than 25 years of age) compared with older adults. Although family-based approaches are a recommended psychosocial technique for treatment of adolescent drug use, no trial of a family-based approach met inclusion criteria.[17] We also did not include trials of school-based therapies or community-level therapies, which may be relevant for this population. Although no trial of pharmacotherapy for opioid use disorder in adolescents met inclusion criteria, the FDA approved the use of buprenorphine for patients 16 years and older in 2002.[139] Methadone can also be used in adolescents, but requires two documented failed treatments of opioid detoxification or drug-free treatment and parental or legal guardian consent.[140]

No trial was designed to assess effectiveness of interventions for drug use specifically in older adults or to determine how effectiveness of interventions varies according to race or ethnicity.

Future Research

Research is needed to determine effective interventions for drug use primarily related to

prescription opioids or stimulant use, and for drug use related to illicit opioids that does not meet criteria for an opioid use disorder. In screen-detected populations with unhealthy drug use, trials that target therapies to persons with more severe drug use or evaluate more intensive psychosocial interventions would be helpful for clarifying whether psychosocial interventions that have been shown to improve drug use outcomes in treatment-seeking populations can be effectively applied to screen-detected populations. In trials that identify patients through screening, stratification of results according to drug use severity and whether patients are newly diagnosed or have a history of past drug use would be helpful for understanding the effectiveness of interventions in these different populations. Ideally, future trials of interventions to reduce drug use should evaluate drug use outcomes using standardized measures as well as health outcomes, including measures of morbidity, quality of life, psychological outcomes, and function. Direct evidence is limited on the effects of drug use interventions on risk of acquisition of HIV and other infectious diseases related to injection drug use. Research is also needed to understand the extent to which the newly FDA-approved extended release injectable buprenorphine formulation impacts treatment uptake of or adherence to this therapy and retention in substance use treatment in the future. Studies are needed to understand optimal interventions in important populations with unique needs such as adolescents, pregnant or postpartum women, and older adults. Finally, research is needed to estimate the effects of naloxone for mitigating overdose risk associated with opioid use disorder or misuse.

Conclusions

Pharmacological and psychosocial interventions are effective at improving some drug use outcomes, but evidence of effectiveness remains primarily derived from trials conducted in treatment-seeking individuals. Although the applicability of data from such trials to persons whose drug use is identified through primary care-based screening is uncertain, intervention trials that enrolled patients based on screening identified a spectrum of drug use, ranging from mild drug use to more severe, untreated disease. The applicability of current evidence on drug use interventions to screening might be greater for the subset of patients screened in primary care settings with severe, untreated drug use who could utilize pharmacotherapies or more intensive psychosocial interventions.

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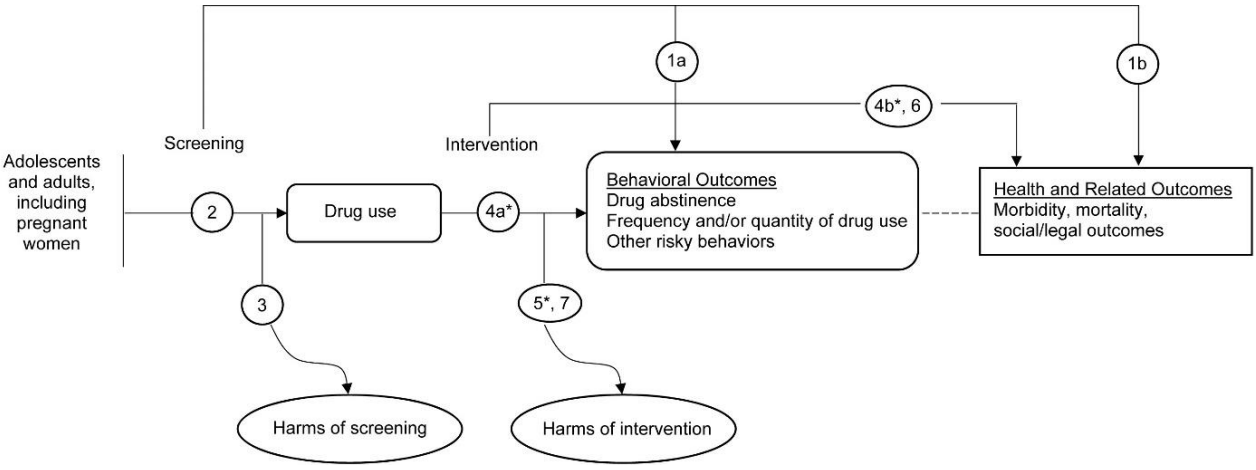
Figure 1. Analytic Framework and Key Questions



*Drug use refers to substance use disorders or misuse related to opioids, stimulants, or cannabis, or polysubstance use related to one or more of these drugs for Key Questions 4 and 5.
Note: Numbers on the figure refer to the numbers of the Key Questions.

Key Questions Addressed in a Separate Report[1]

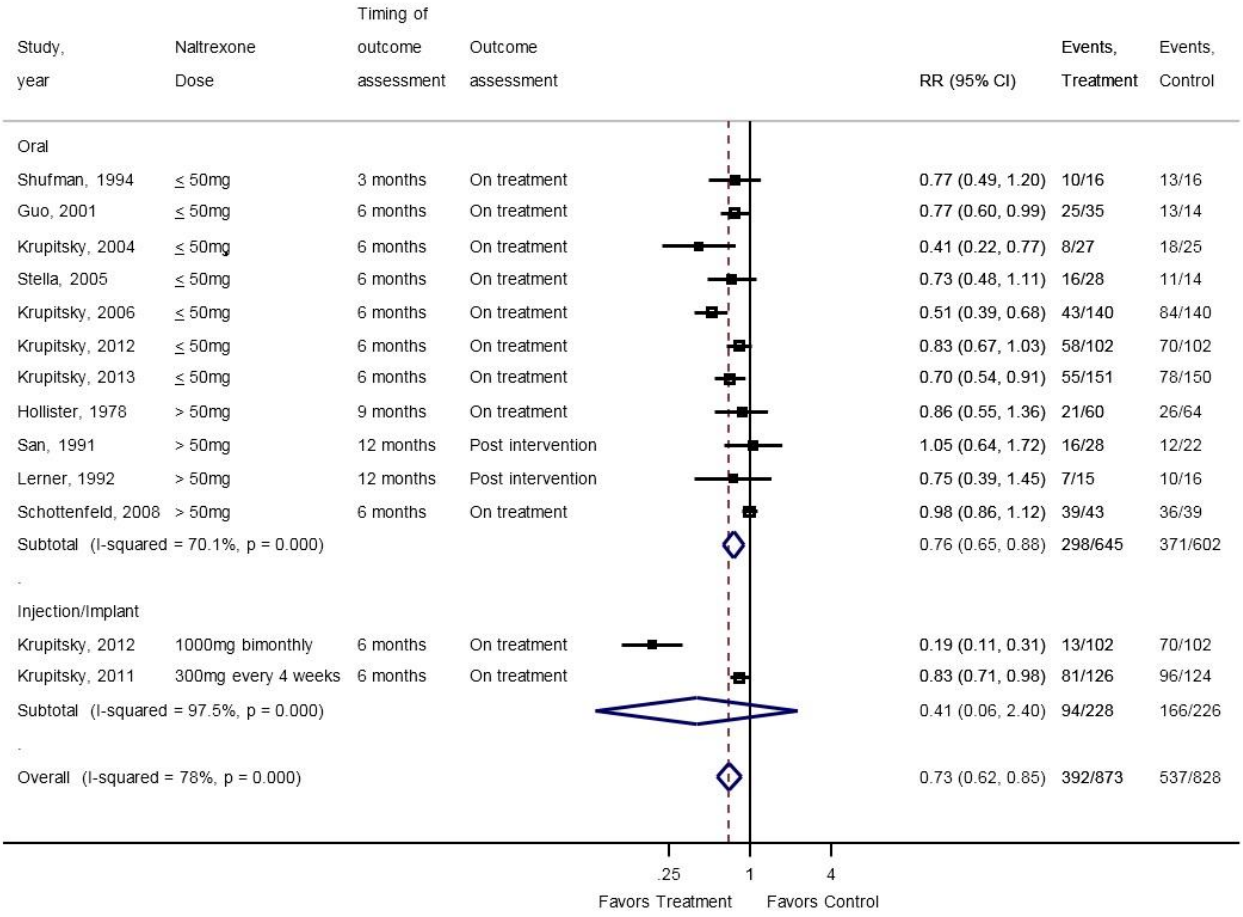
1. a. Does primary care screening for drug use* in adolescents and adults, including pregnant women, reduce drug use or improve other risky behaviors?
   b. Does primary care screening for drug use* in adolescents and adults, including pregnant women, reduce morbidity or mortality or improve other health, social, or legal outcomes?
2. What is the accuracy of drug use screening instruments?
3. What are the harms of primary care screening for drug use in adolescents and adults, including pregnant women?

Key Questions Addressed in this Report

4. a. Do interventions to reduce drug use† reduce drug use or improve other risky behaviors?
   b. Do interventions to reduce drug use† reduce morbidity or mortality or improve other health, social, or legal outcomes?
5. What are the harms of interventions to reduce drug use†?
6. Does naloxone reduce morbidity or mortality, or improve other health outcomes in persons with opioid use disorder or misuse?
7. What are the harms of naloxone in persons with opioid use disorder or misuse?

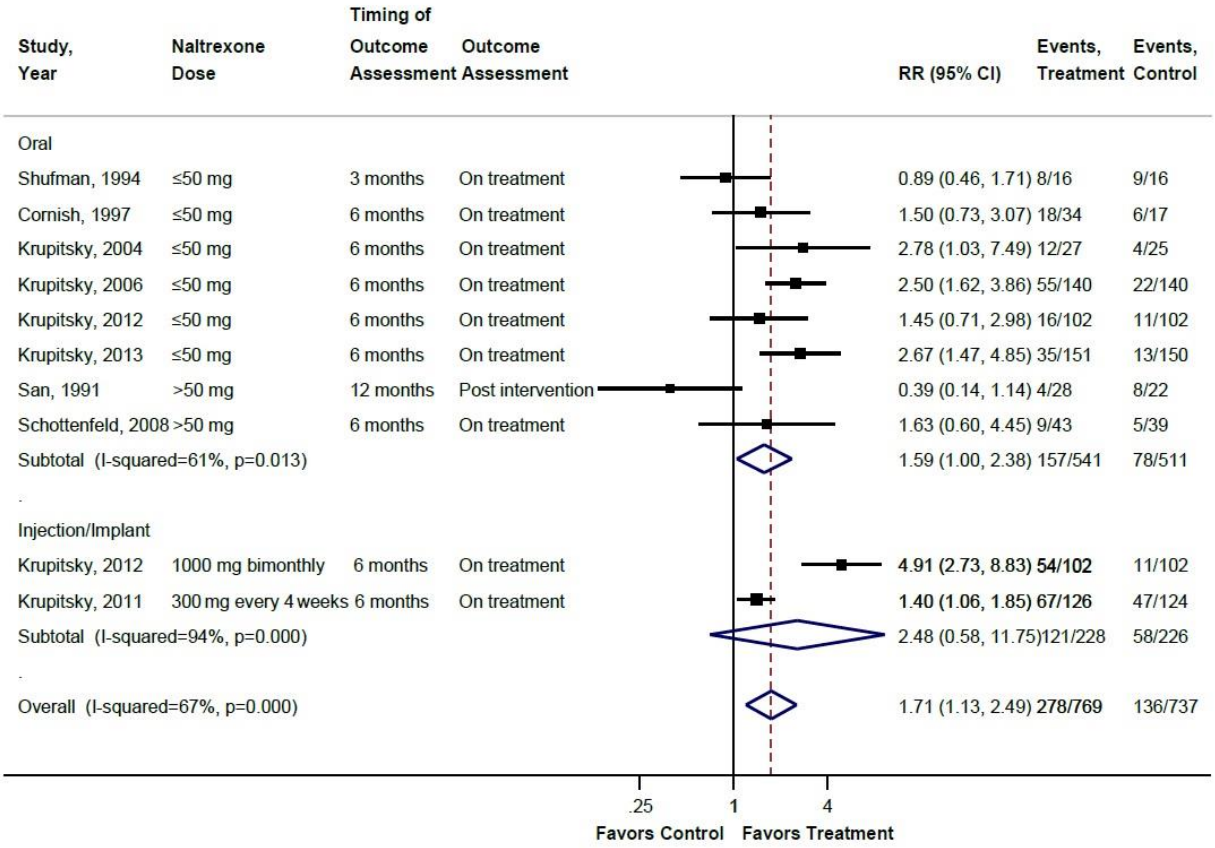
Note: "Screening" refers to screening methods that pose questions about drug use or drug-related risks, not laboratory testing of biologic samples for the presence of drugs.
*Includes illicit drug use and nonmedical pharmaceutical drug use.
†Drug use refers to substance use disorders or misuse related to opioids, stimulants, or cannabis, or polysubstance use related to one or more of these drugs for Key Questions 4 and 5.

Figure 2. Naltrexone vs. Placebo/No Medication—Relapse



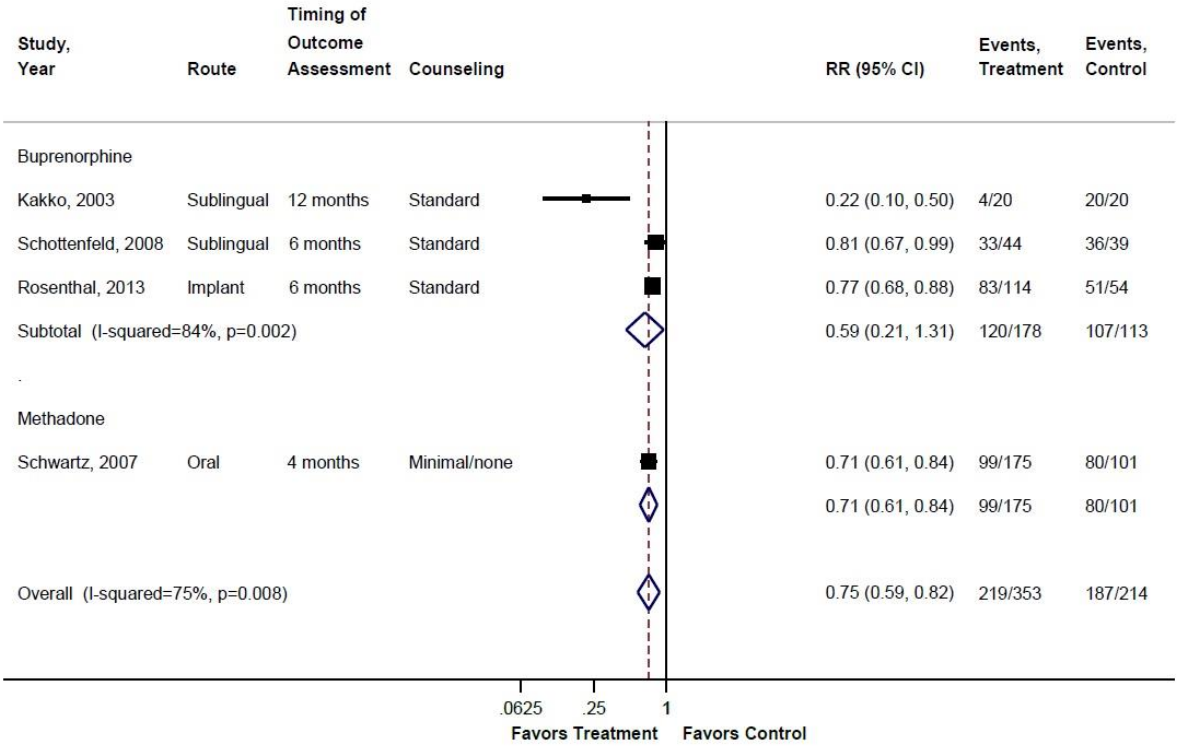
Abbreviations: CI = confidence interval; RR = relative risk.

Figure 3. Naltrexone vs. Placebo/No Medication—Retention in Treatment



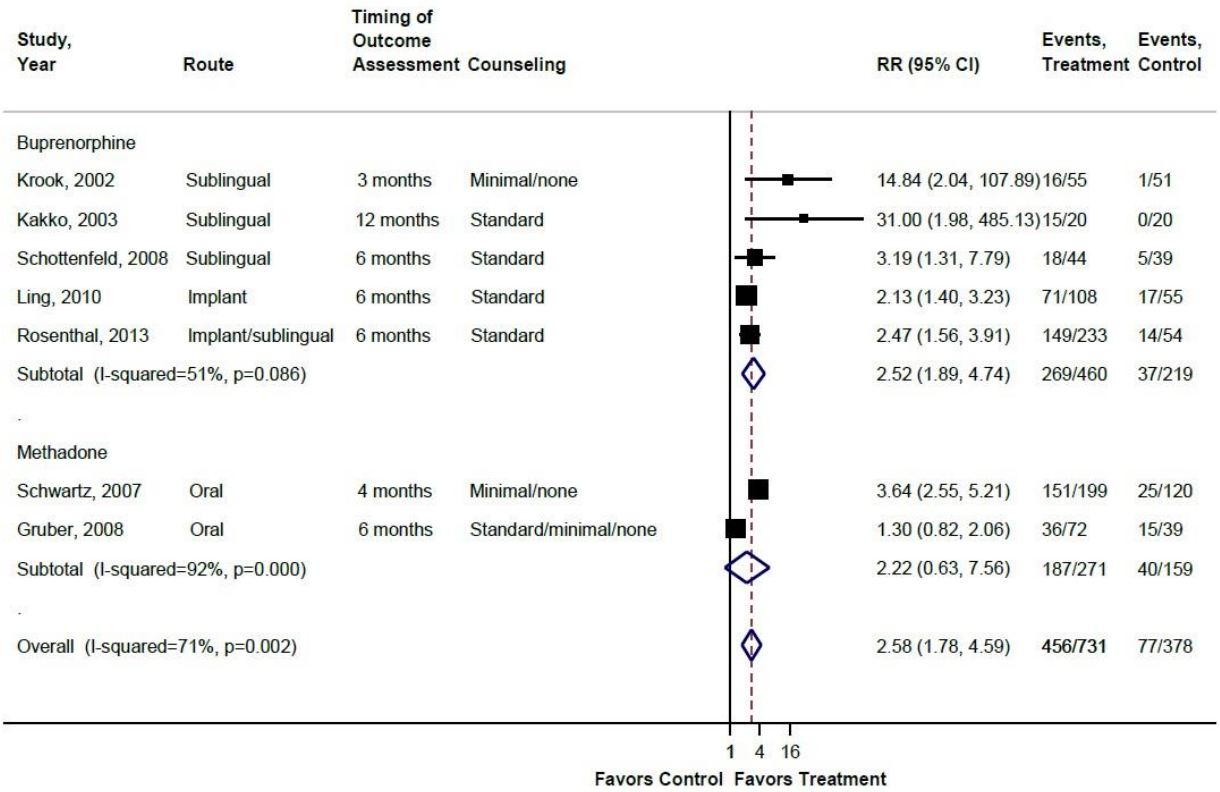
Abbreviations: CI = confidence interval; RR = relative risk.

Figure 4. Opioid Agonist Therapy vs. Placebo/No Medication—Relapse



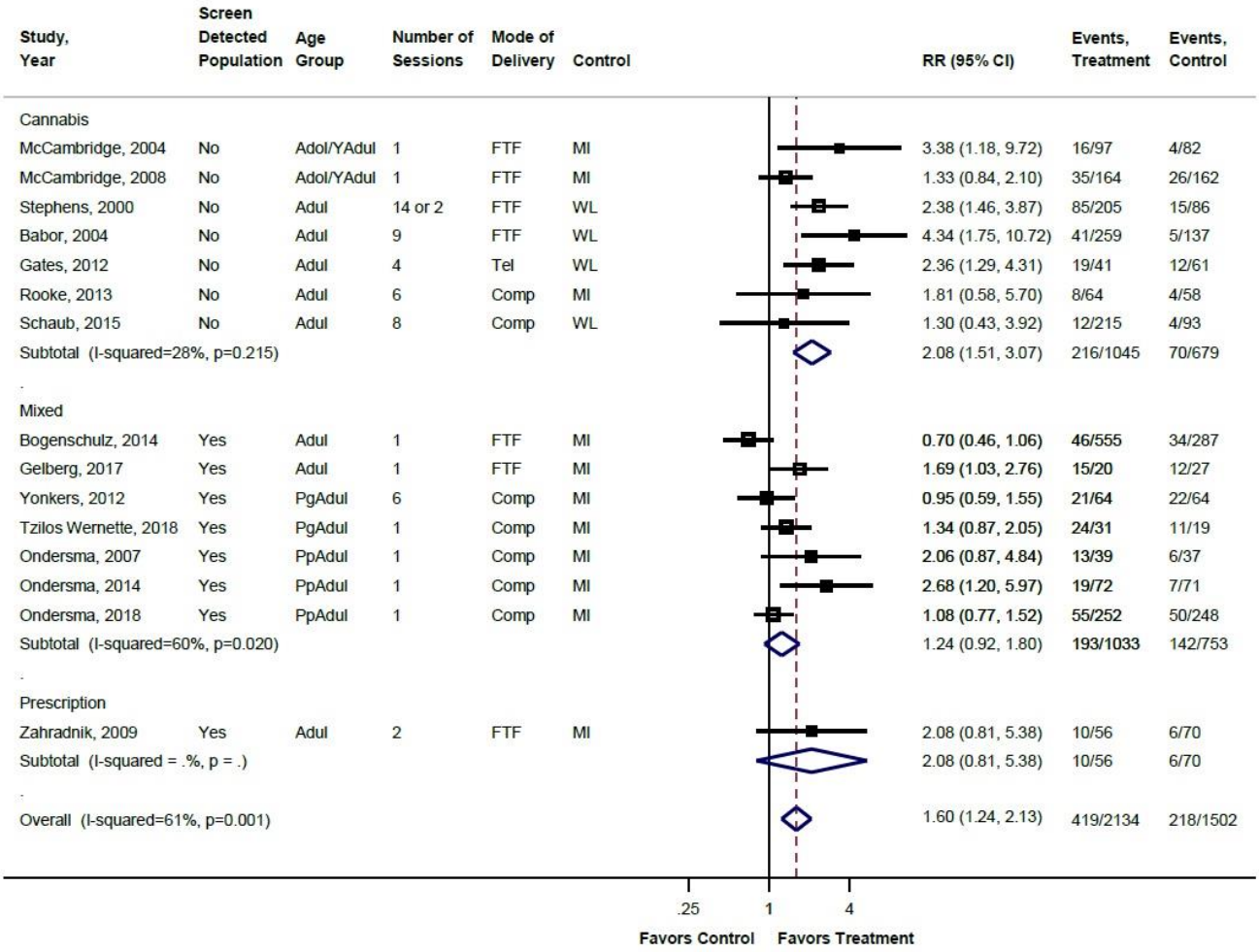
Abbreviations: CI = confidence interval; RR = relative risk.

Figure 5. Opioid Agonist Therapy vs. Placebo/No Medication—Retention in Treatment



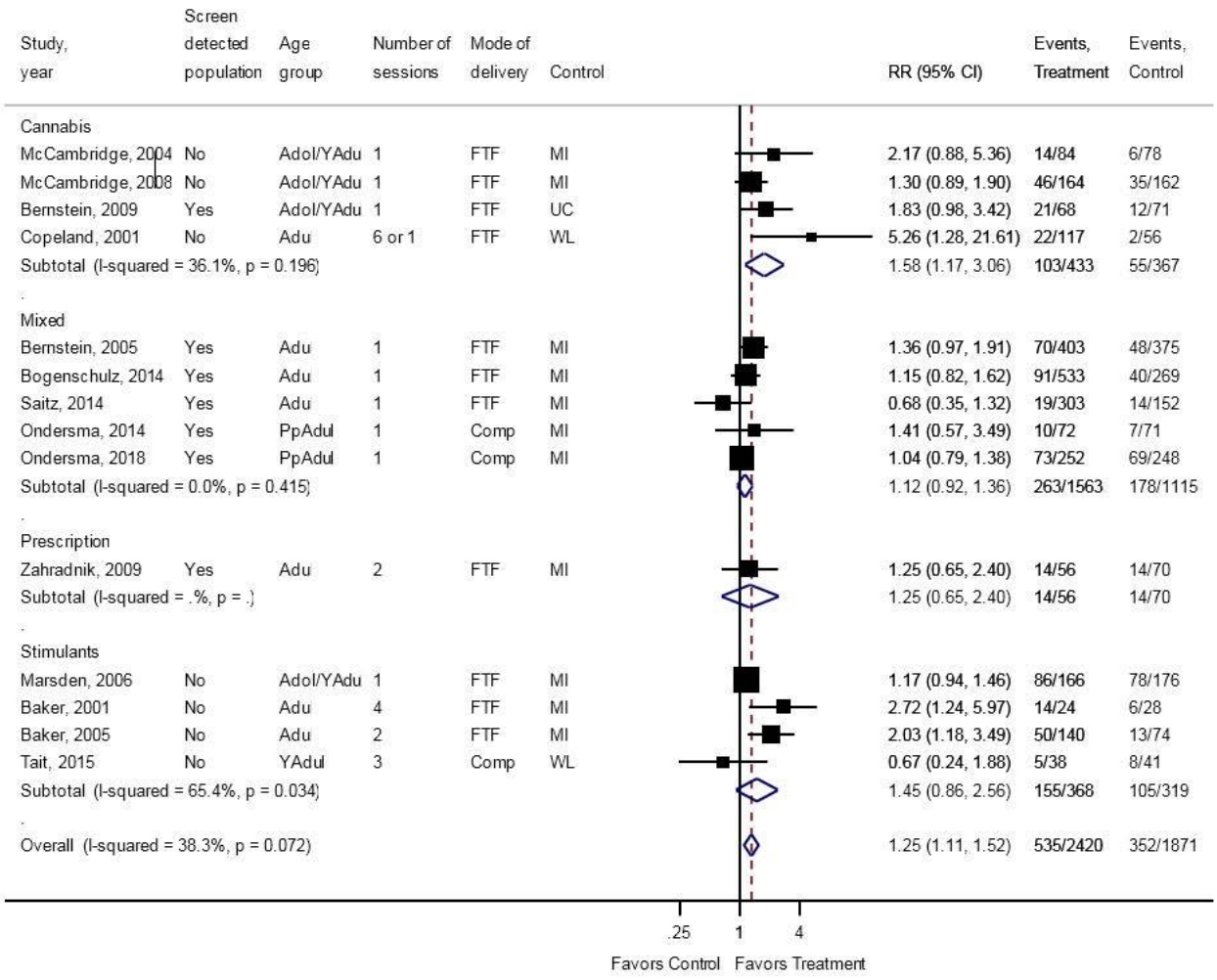
Abbreviations: CI = confidence interval; RR = relative risk.

Figure 6. Psychosocial Interventions vs. Control Conditions—Abstinence at 3- to 4-Month Followup, Stratified by Drug



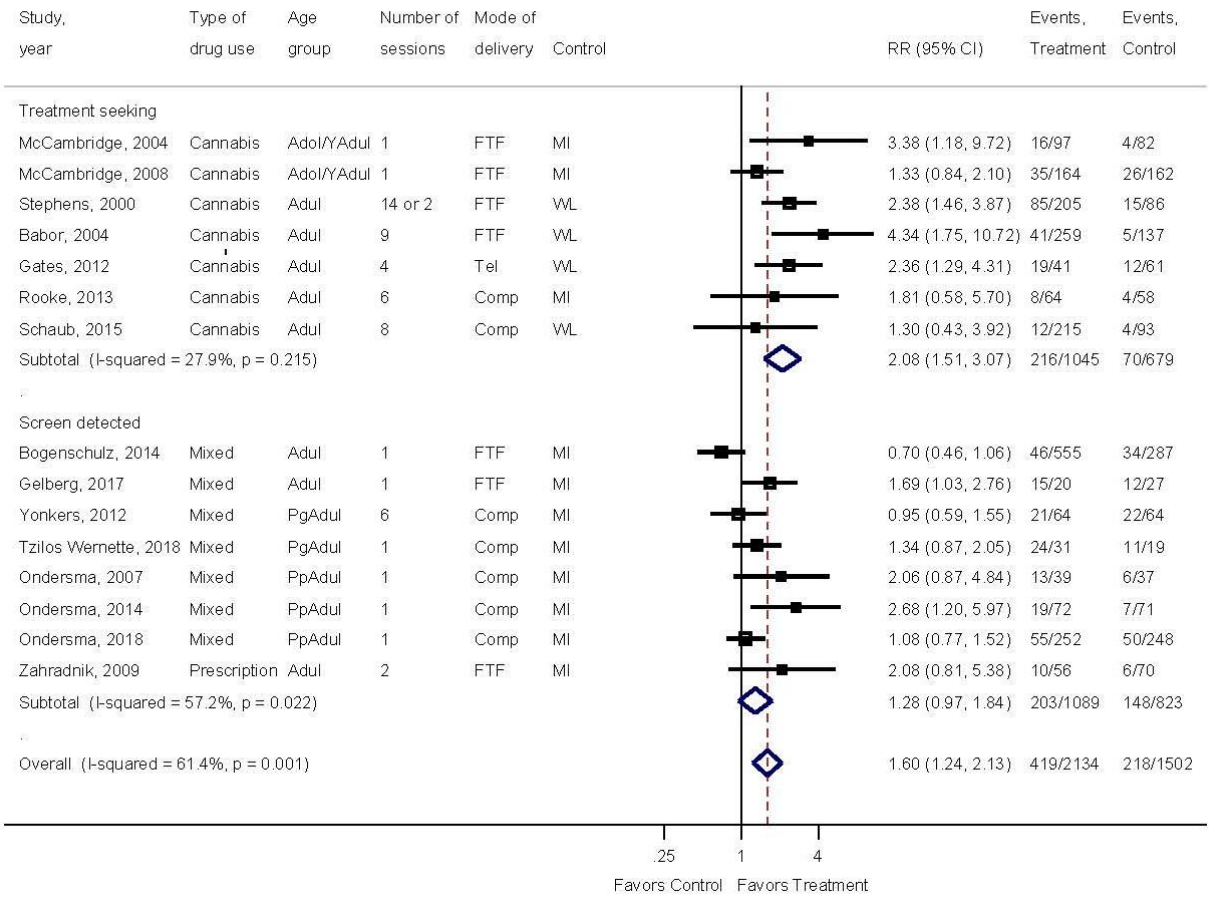
Abbreviations: Adol = adolescent; Adul = adult; CI = confidence interval; Comp = computer; FTF = face-to-face; MI = minimal intervention; Pg = pregnant; Pp = postpartum; RR = relative risk; Tel = telephone; WL = waitlist; Yadult = young adult.

Figure 7. Psychosocial Interventions vs. Control Conditions—Abstinence at 6- to 12-Month Followup, Stratified by Drug



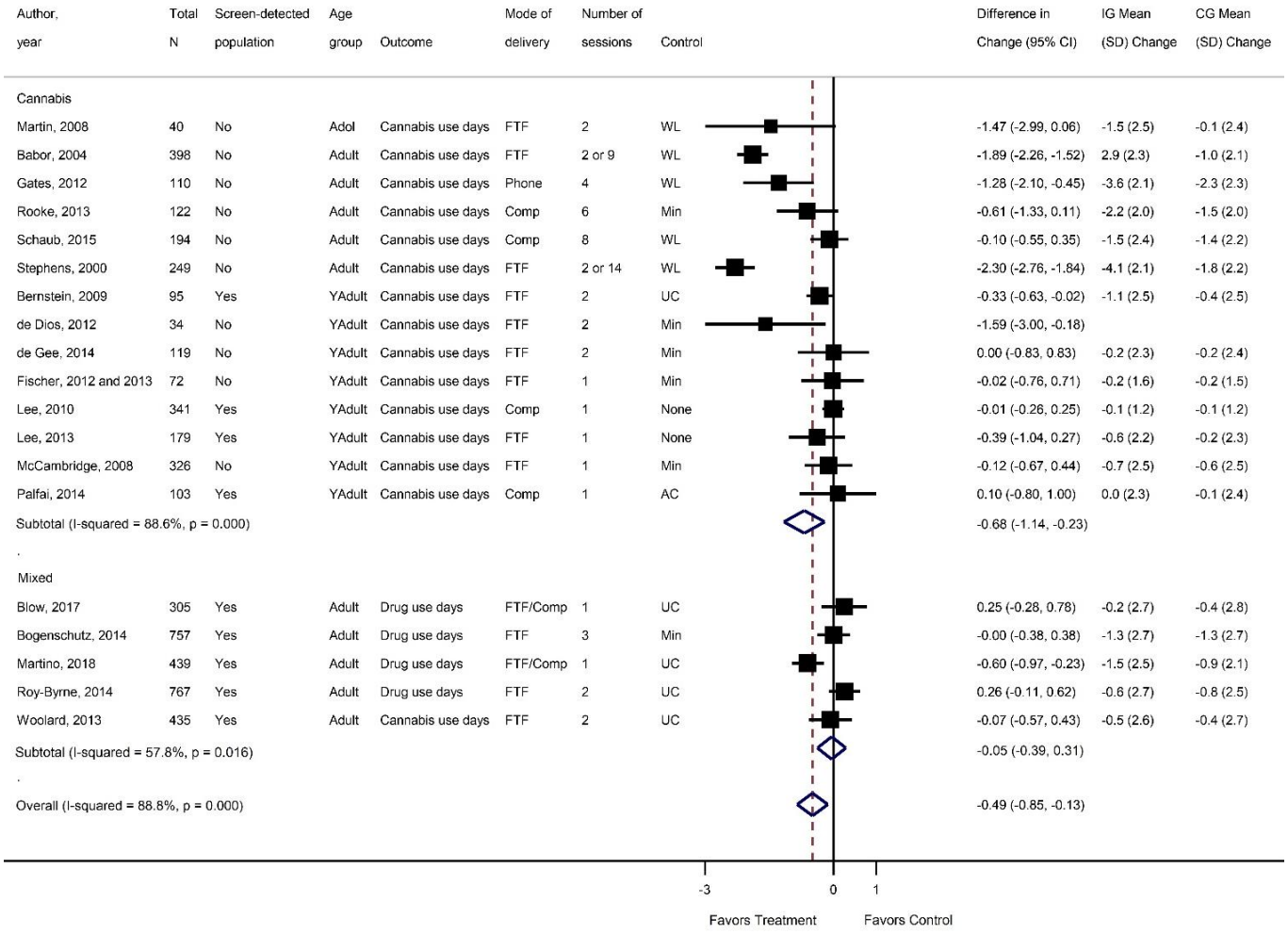
Abbreviations: Adol = adolescent; Adul = adult; CI = confidence interval; Comp = computer; FTF = face-to-face; MI = minimal intervention; Pg = pregnant; Pp = postpartum; RR = relative risk; Tel = telephone; UC = usual care; WL = waitlist; YAdult = young adult.

Figure 8. Psychosocial Interventions vs. Control Conditions—Abstinence at 3- to 4-Month Followup, Stratified by Population



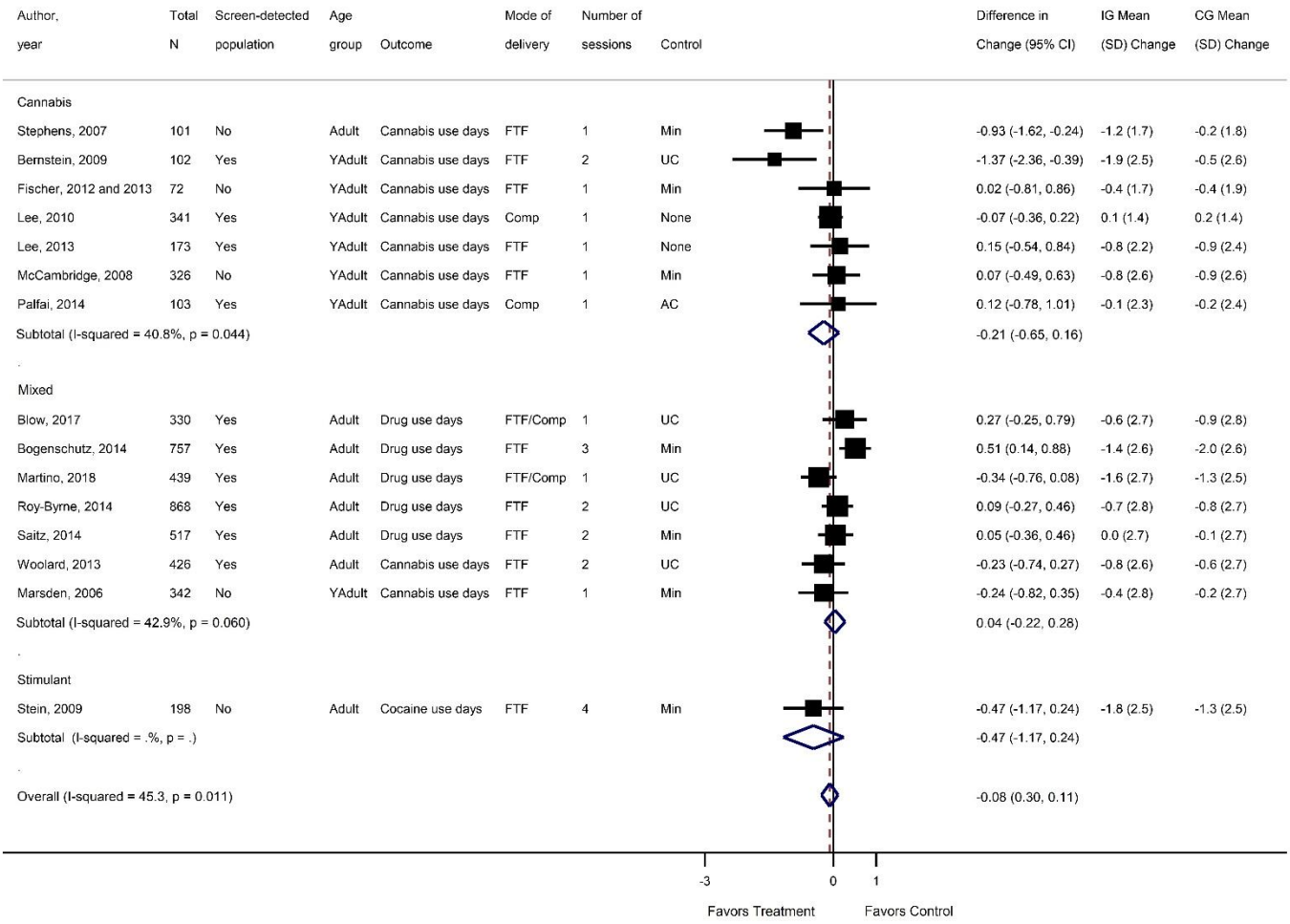
Abbreviations: Adol = adolescent; Adul = adult; CI = confidence interval; Comp = computer; FTF = face-to-face; MI = minimal intervention; Pg = pregnant; Pp = postpartum; RR = relative risk; Tel = telephone; WL = waitlist; Yadult = young adult.

Figure 9. Psychosocial Interventions vs. Control Conditions—Drug Use Days, Standardized to Drug Use in the Past 7 Days at 3- to 4-Month Followup, Stratified by Drug



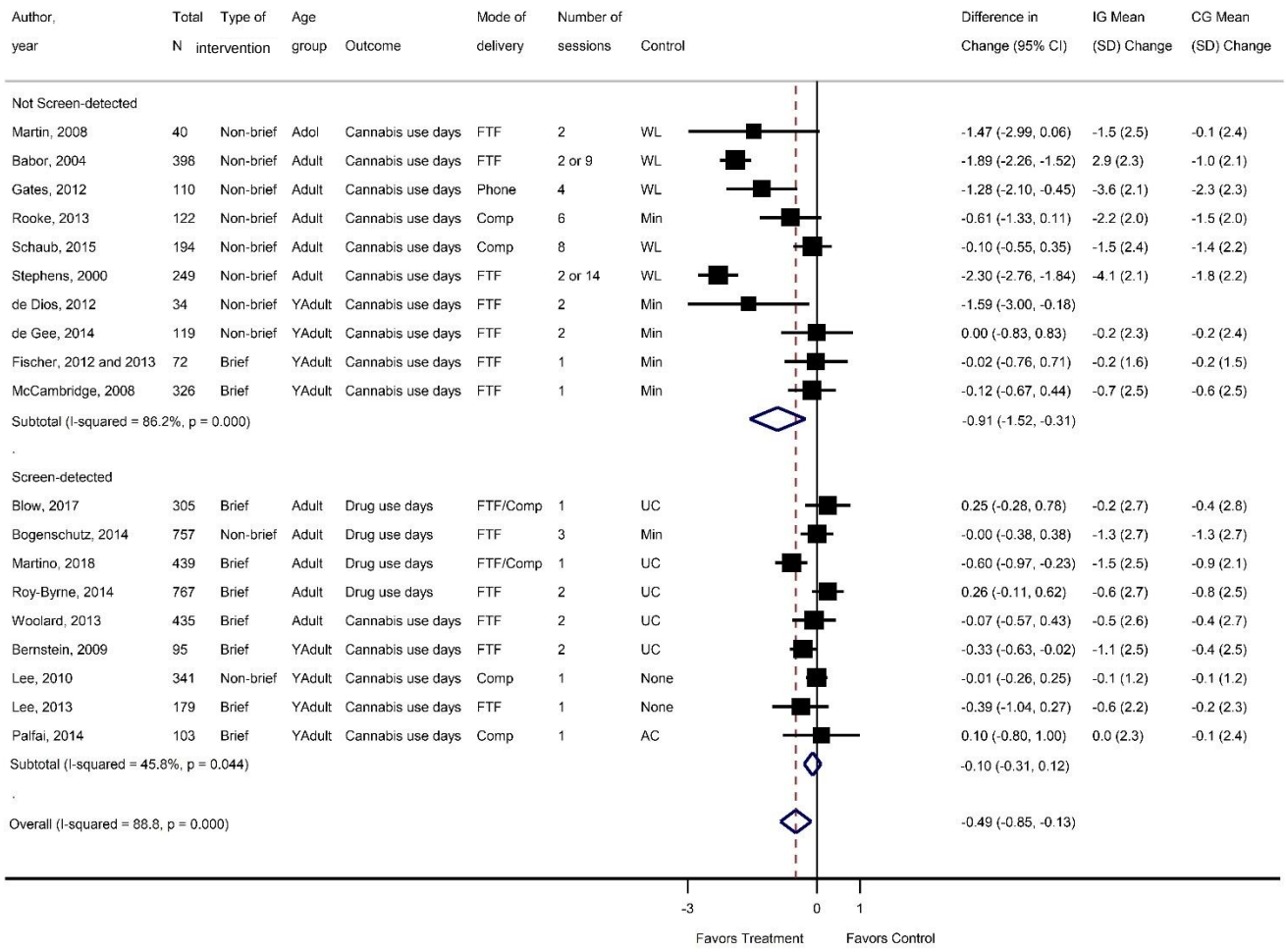
Abbreviations: AC = active control; Adol = adolescent; CG = control group; CI = confidence interval; Comp = computer; FTF = face-to-face; IG = intervention group; min = minimal intervention; SD = standard deviation; UC = usual care; WL = wait list; YAdult= young adult.

Figure 10. Psychosocial Interventions vs. Control Conditions—Drug Use Days, Standardized to Drug Use in the Past 7 Days, at 6- to 12-Month Followup, Stratified by Drug



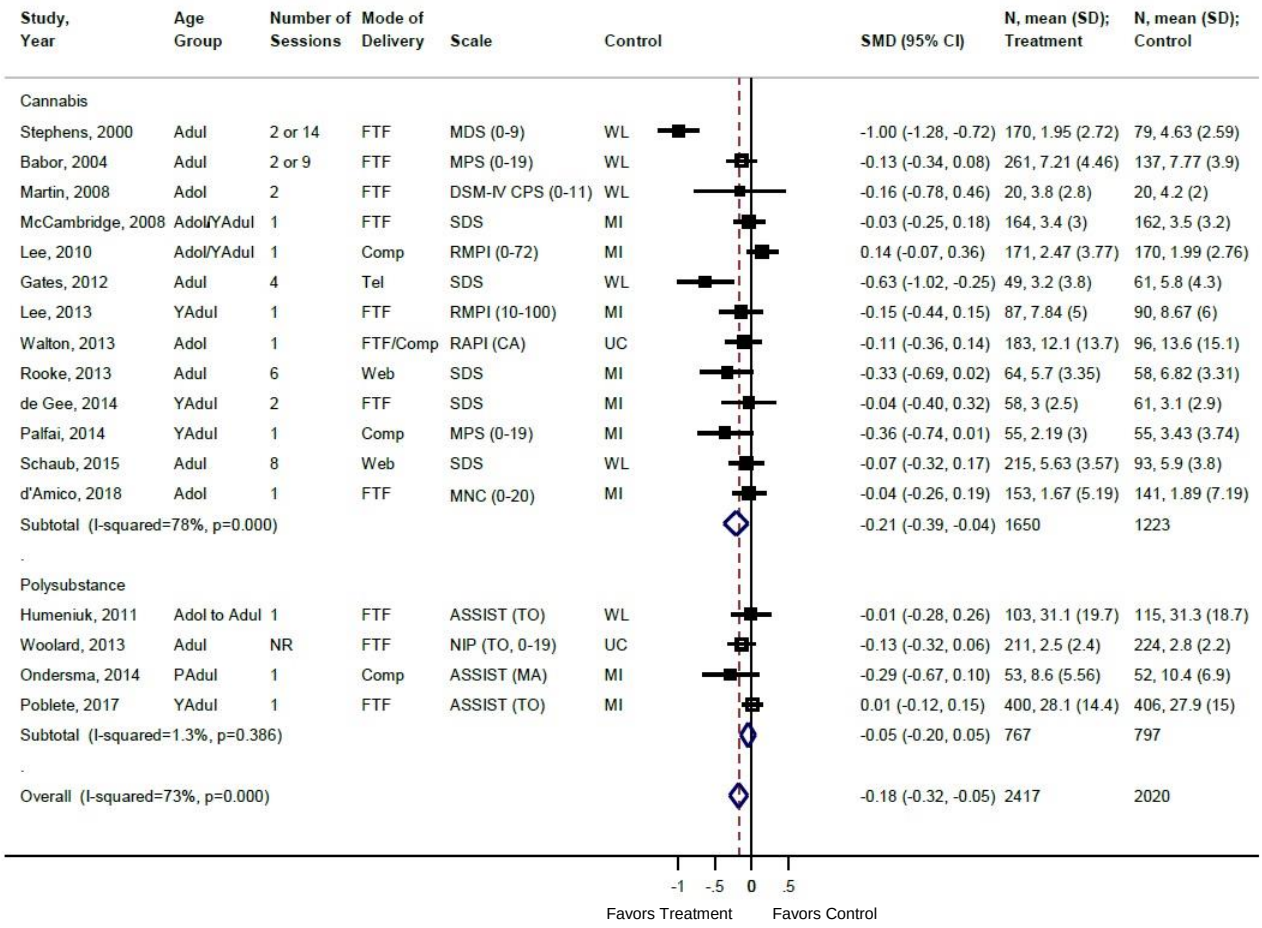
Abbreviations: AC = active control; CG = control group; CI = confidence interval; Comp = computer; FTF = face-to face; IG = intervention group; Min = minimal intervention; SD = standard deviation; UC = usual care; YAdult = young adult.

Figure 11. Psychosocial Interventions vs. Control Conditions—Drug Use Days, Standardized to Drug Use in the Past 7 Days at 3- to 4-Month Followup, Stratified by Population



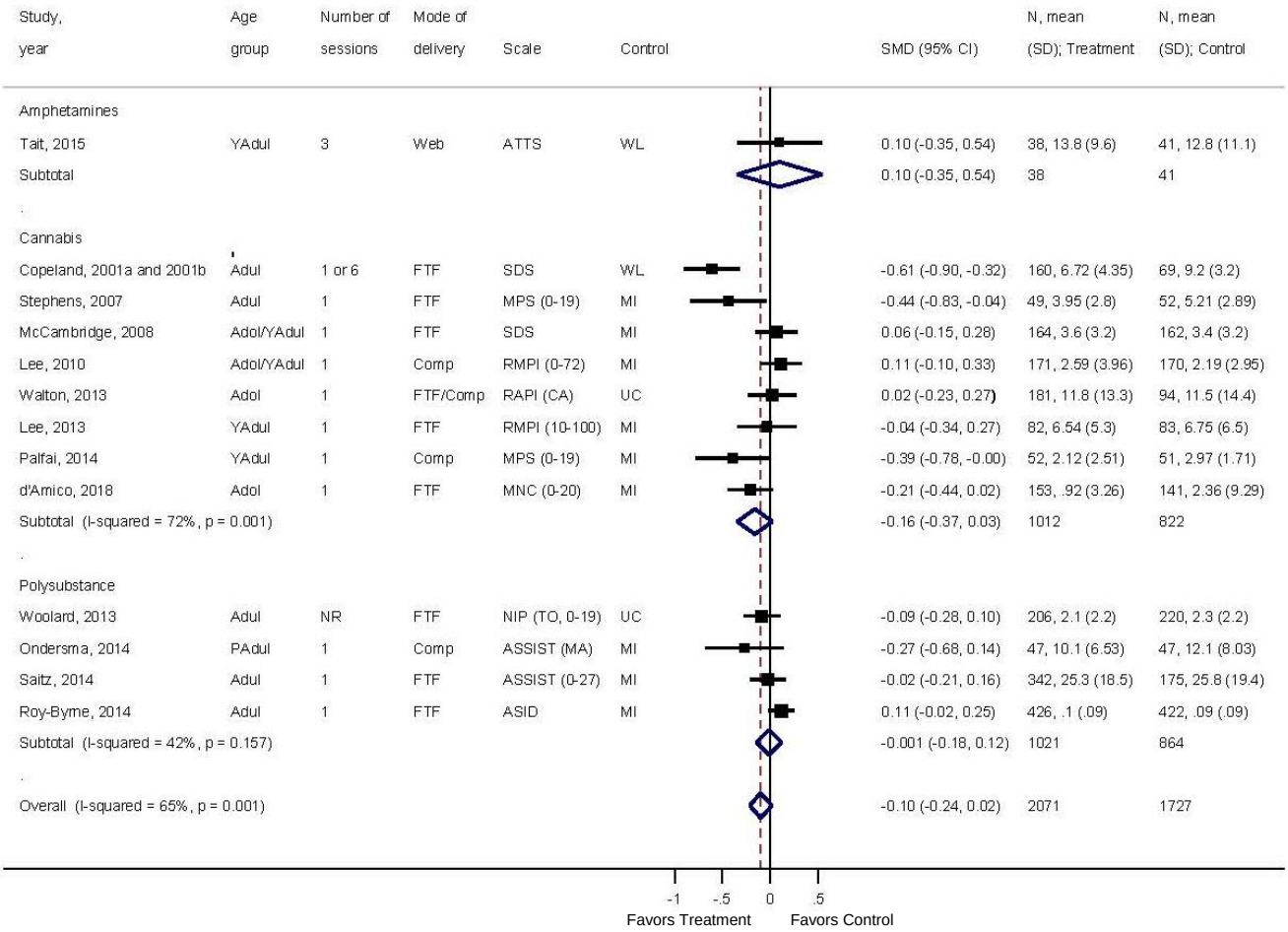
Abbreviations: AC = active control; Adol = adolescent; CG = control group; CI = confidence interval; Comp = computer; FTF = face-to-face; IG = intervention group; Min = minimal intervention; SD = standard deviation; UC = usual care; WL = wait list; YAdult= young adult.

Figure 12. Psychosocial Interventions vs. Control Conditions—Drug Use Severity at 3- to 4-Month Followup, Stratified by Drug



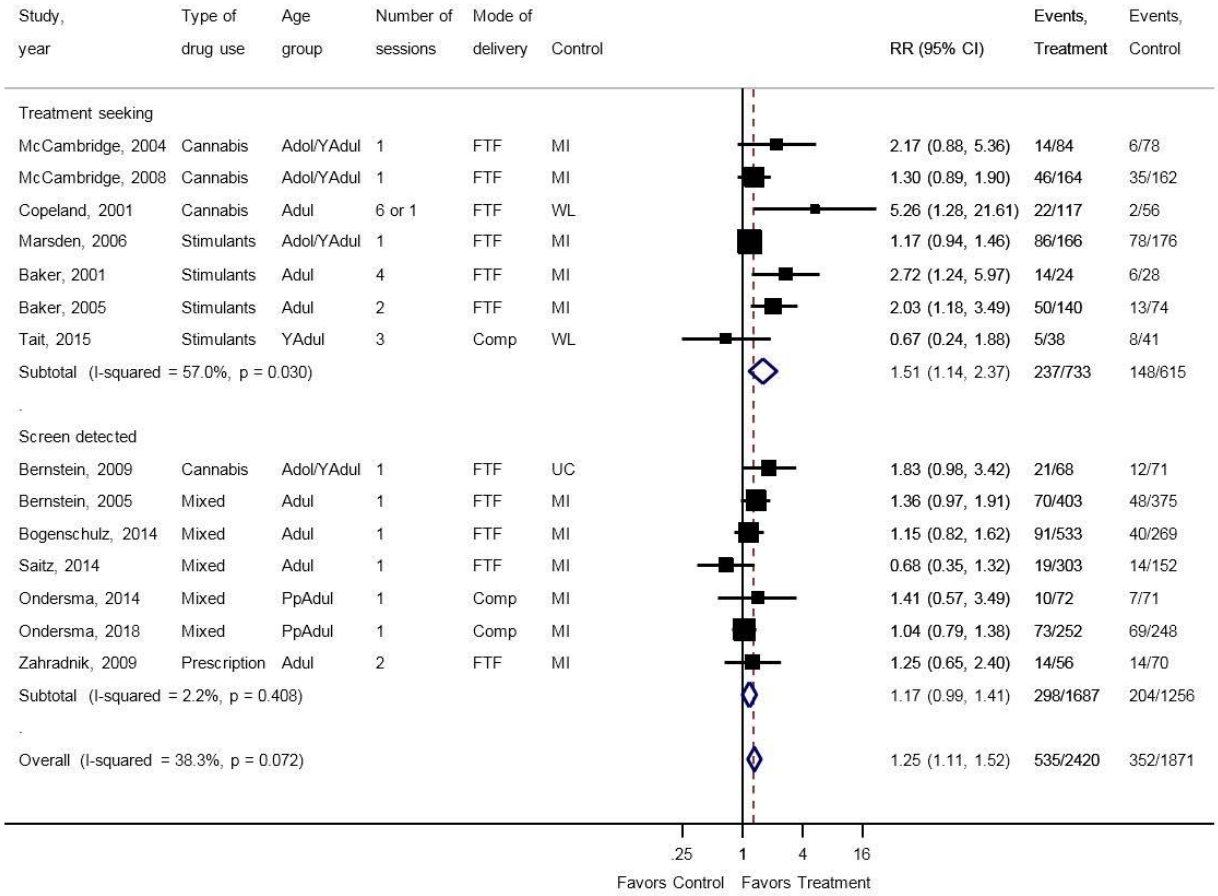
Abbreviations: Adul = adult; Adol = adolescent; ASSIST = Alcohol, Smoking, and Substance Involvement Screening Test; CI = confidence interval; Comp = computer; DSM-IV CPS = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Compendium of Pharmaceuticals and Specialties; FTF = face-to-face; MA = marijuana subscale; MI = minimal intervention; MDS = Marijuana Dependence Scale; MNC = marijuana negative consequences; MPS = Marijuana Problem Scale; NIP = Noteworthy Index of Problems; NR = not reported; PAdul = postpartum adult; RAPI = Rutgers Alcohol Problems Index; RMPI = Rutgers Marijuana Problem Index; SD = standard deviation; SDS = Severity of Dependence Scale; SMD = standardized mean difference; Tel = telephone; TO = total (scale); UC = usual care; WL = waitlist; YAdul = young adult.

Figure 13. Psychosocial Interventions vs. Control Conditions—Drug Use Severity at 6- to 12-Month Followup, Stratified by Drug



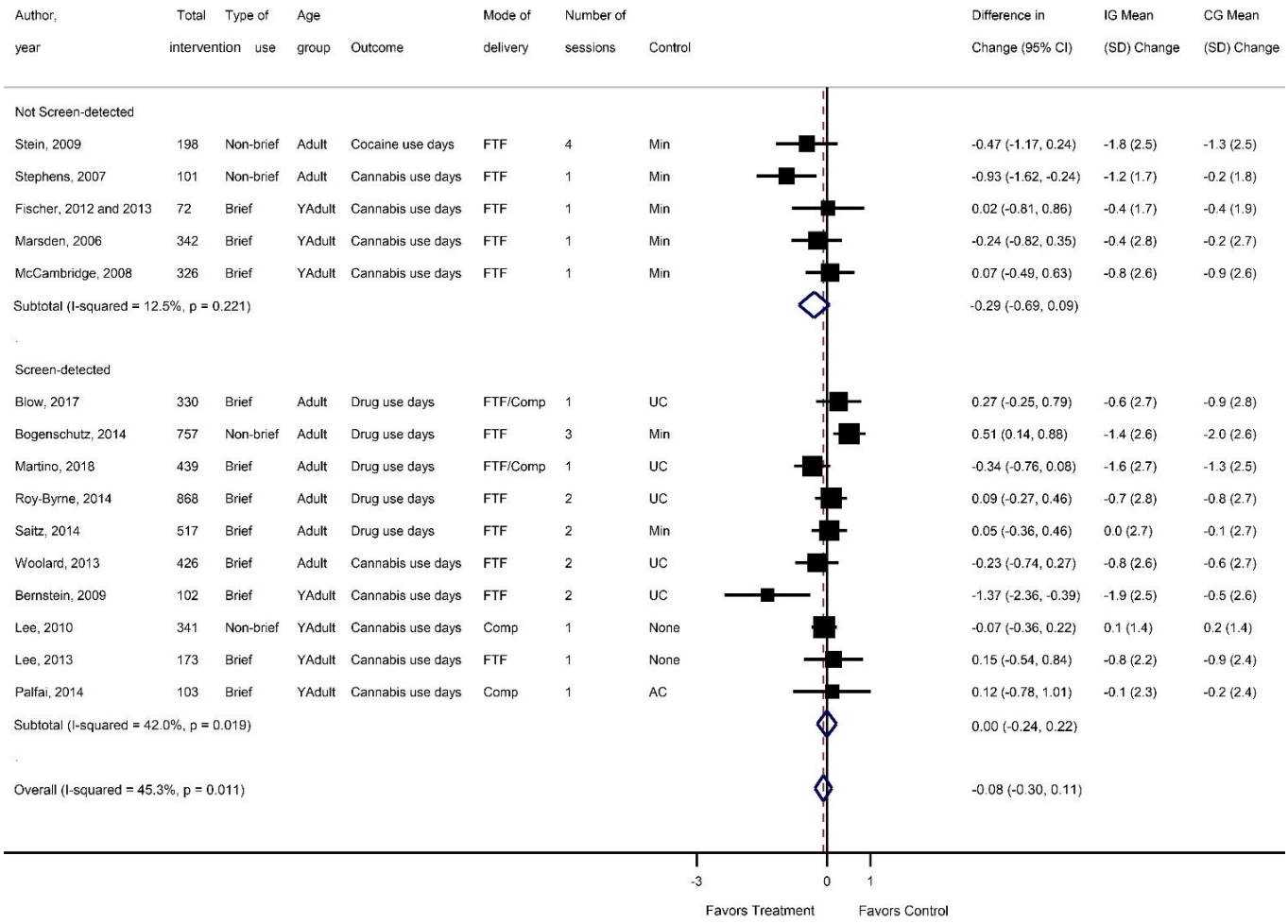
Abbreviations: Adul = adult; Adol = adolescent; ASID = Addiction Severity Index (drugs); ASSIST = Alcohol, Smoking, and Substance Involvement Screening Test; ATTS = amphetamine-type stimulant use; CA = cannabis; CI = confidence interval; Comp = computer; FTF = face-to-face; MA = marijuana subscale; MI = minimal intervention; MPS = Marijuana Problem Scale; NIP = Noteworthy Index of Problems; PAdul = postpartum adult; RAPI = Rutgers Alcohol Problems Index; RMPI = Rutgers Marijuana Problem Index; SD = standard deviation; SDS = Severity of Dependence Scale; SMD = standardized mean difference; UC = usual care; WL = waitlist; YAdul = young adult.

Figure 14. Psychosocial Interventions vs. Control Conditions—Abstinence at 6- to 12-Month Followup, Stratified by Population



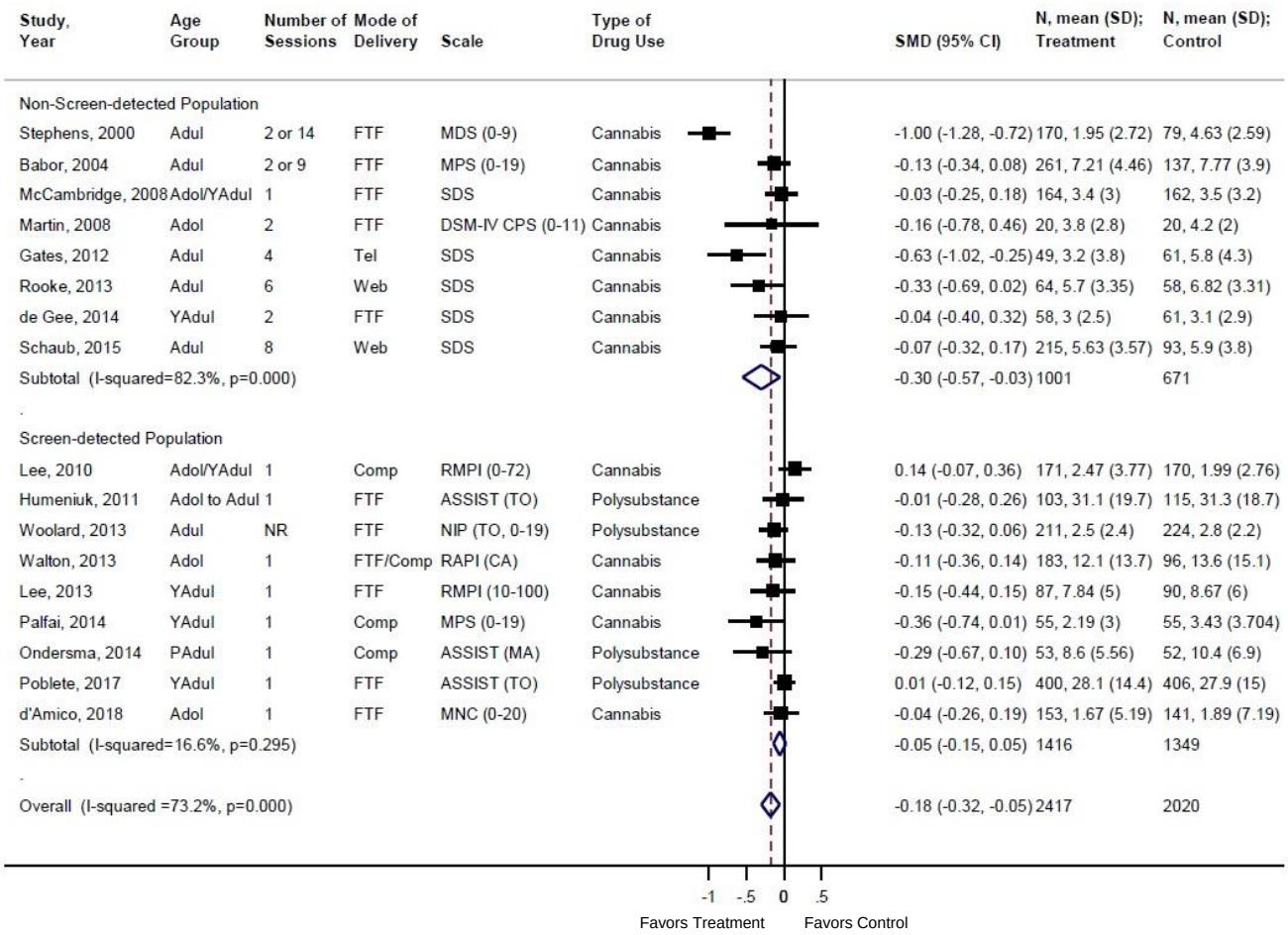
Abbreviations: Adol = adolescent; Adul = adult; CI = confidence interval; Comp = computer; FTF = face-to-face; MI = minimal intervention; Pp = postpartum; RR = relative risk; UC = usual care; WL = waitlist; YAdult = young adult.

Figure 15. Psychosocial Interventions vs. Control Conditions—Drug Use Days, Standardized to Drug Use in the Past 7 Days, at 6- to 12-Month Followup, Stratified by Population



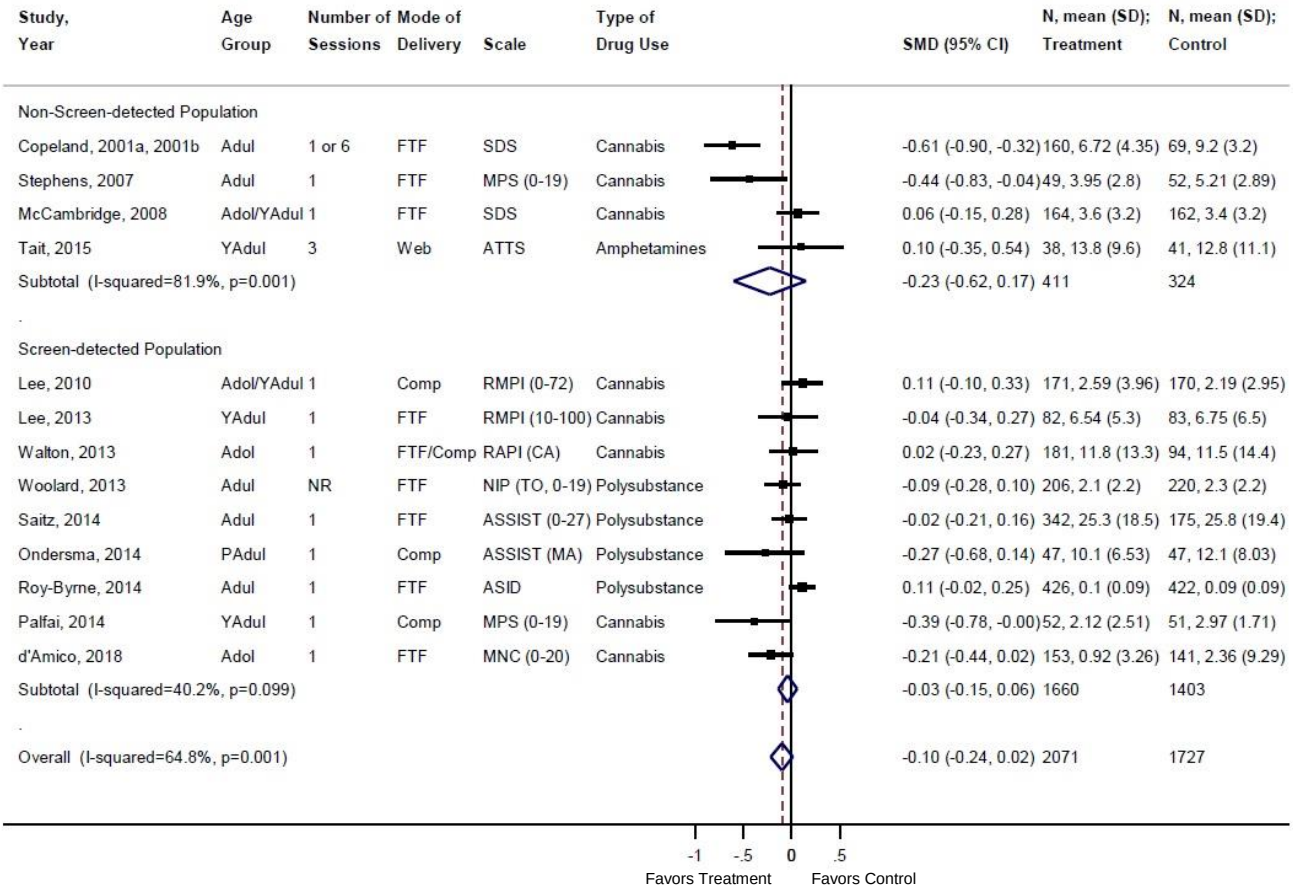
Abbreviations: AC = active control; CG = control group; CI = confidence interval; Comp = computer; FTF = face-to-face; IG = intervention group; Min = minimal intervention; SD = standard deviation; UC=usual care; YAdult = young adult.

Figure 16. Psychosocial Interventions vs. Control Conditions—Drug Use Severity at 3- to 4-Month Followup, Stratified by Population



Abbreviations: Adul = adult; Adol = adolescent; ASSIST = Alcohol, Smoking, and Substance Involvement Screening Test; CI = confidence interval; Comp = computer; DSM-IV CPS = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Compendium of Pharmaceuticals and Specialties; FTF = face-to-face; MA = marijuana subscale; MDS = Marijuana Dependence Scale; MNC = marijuana negative consequences; MPS = Marijuana Problem Scale; NIP = Noteworthy Index of Problems; NR = not reported; PAdul = postpartum adult; RAPI = Rutgers Alcohol Problems Index; RMPI = Rutgers Marijuana Problem Index; SD = standard deviation; SDS = Severity of Dependence Scale; SMD = standardized mean difference; Tel = telephone; TO = total (scale); YAdul = young adult.

Figure 17. Psychosocial Interventions vs. Control Conditions—Drug Use Severity at 6- to 12-Month Followup, Stratified by Population



Abbreviations: Adul = adult; Adol = adolescent; ASID = Addiction Severity Index (drugs); ASSIST = Alcohol, Smoking, and Substance Involvement Screening Test; ATTS = amphetamine-type stimulant use; CA = cannabis; CI = confidence interval; Comp = computer; FTF = face-to-face; MA = marijuana subscale; MPS = Marijuana Problem Scale; NIP = Noteworthy Index of Problems; PAdul = postpartum adult; RAPI = Rutgers Alcohol Problems Index; RMPI = Rutgers Marijuana Problem Index; SD = standard deviation; SDS = Severity of Dependence Scale; SMD = standardized mean difference; YAdul = young adult.

Table 1. Trials of Medications for Opioid Use Disorder vs. Placebo/No Medication

Drug	Author, year Country N *Quality*	Population Intervention vs. control	Intervention; route of administration	Dose	Duration of treatment	Relapse Intervention vs. control	Retention in treatment Intervention vs. control
Naltrexone	Cornish, 1997[71] U.S. N=51 *Fair*	*NR by intervention group* Mean age 39 years 10% female Primary opioid of use: heroin Duration of use: NR	Naltrexone; oral	25 mg, titrated to 100 mg on Tuesday and 150 mg on Friday	6 months	Proportion of opioid-positive urine tests 8% vs. 30% (n/N NR) p<0.05	52% (18/34) vs. 33% (6/17)*; RR 1.50; 95% CI 0.73 to 3.07
	Guo, 2001[5] China N=49 *Fair*	Mean age 25 vs. 27 years 11% vs. 7% female Primary opioid of use: heroin Duration of use: 3.6 vs. 3.6 years	Naltrexone; oral	50 mg	6 months	Not defined 71% (25/35) vs. 93% (13/14); RR 0.77; 95% CI 0.60 to 0.99	NR
	Hollister, 1978[72] U.S. N=192 *Fair*	Mean age NR 0% vs. 0% female Primary opioid of use: NR Duration of use: NR	Naltrexone; oral	50 mg to 100-150 mg	9 months	≥1 positive samples, among patients with ≥5 urine samples 35% (21/60) vs. 41% (26/64); RR 0.86; 95% CI 0.55 to 1.36	NR
	Krupitsky, 2004[73] Russia N=52 *Fair*	Mean age 23 vs. 21 years 11% vs. 28% female Primary opioid of use: heroin Duration of use: 2.3 vs. 2.9 years	Naltrexone; oral	50 mg	6 months	≥3 opioid-positive urine tests or signs/ symptoms of withdrawal 30% (8/27) vs. 72% (18/25); RR 0.41; 95% CI 0.22 to 0.77	44% (12/27) vs. 16% (4/25); RR 2.78; 95% CI 1.03 to 7.49
	Krupitsky, 2006[74] Russia N=280 *Fair*	Mean age 24 vs. 23 years 25% vs. 31% female Primary opioid of use: heroin Duration of use: 3.8 vs. 3.4 years	Naltrexone; oral	50 mg	6 months	Reported everyday heroin use, ≥3 consecutive opioid-positive urine tests, or signs/symptoms of withdrawal 31% (43/140) vs. 60% (84/140); RR 0.51 95% CI 0.39 to 0.68	39% (55/140) vs. 16% (22/140); RR 2.50; 95% CI 1.62 to 3.86
	Krupitsky, 2011[26] Russia N=250 *Good*	Mean age 29 vs. 30 years 10% vs. 14% female Primary opioid of use: heroin Duration of use: 9.1 vs. 10.0 years	Naltrexone; injectable	300 mg every 4 weeks	6 months	Positive urine drug test or self-reported opioid use 64% (81/126) vs. 77% (96/124); RR 0.83; 95% CI 0.71 to 0.98	53% (67/126) vs. 38% (47/124); RR 1.40; 95% CI 1.06 to 1.85

Table 1. Trials of Medications for Opioid Use Disorder vs. Placebo/No Medication

Drug	Author, year Country N *Quality*	Population Intervention vs. control	Intervention; route of administration	Dose	Duration of treatment	Relapse Intervention vs. control	Retention in treatment Intervention vs. control
Naltrexone	Krupitsky, 2012[25] and Krupitsky, 2016[76] Russia N=306 *Good*	Mean age 28 vs. 28 vs. 29 years 28% vs. 28% vs. 28% female Primary opioid of use: heroin Duration of use: 7.8 vs. 7.9 vs. 8.3 years	A: Naltrexone; implant B: Naltrexone; oral	A: 1,000 mg bimonthly B: 50 mg	6 months	Daily heroin use, signs and symptoms of withdrawal, or positive naloxone challenge A: 13% (13/102) vs. B: 57% (58/102) vs. placebo: 69% (70/102); A vs. placebo: RR 0.19; 95% CI 0.11 to 0.33; B vs. placebo: RR 0.84; 95% CI 0.66 to 1.09	A: 53% (54/102) vs. B: 16% (16/102) vs. placebo: 11% (11/102); A vs. placebo: RR 5.40; 95% CI 2.30 to 12.66; B vs. placebo: RR 1.33; 95% CI 0.56 to 3.20
	Krupitsky, 2013[75] Russia N=301 *Good*	Mean age 28 vs. 28 years 16% vs. 19% female Primary opioid of use: heroin Duration of use: 8.1 vs. 8.5 years	Naltrexone; oral	50 mg	6 months	Daily heroin use, 3 consecutive opioid-positive urine tests, or signs/ symptoms of withdrawal 36.4% (55/151) vs. 52.0% (78/150); RR 0.70; 95% CI 0.54 to 0.91	23% (35/151) vs. 8.7% (13/150); RR 2.67; 95% CI 1.47 to 4.85
	Lerner, 1992[77] Israel N=31 *Fair*	*NR by intervention group* Mean age 27 years % female: NR Primary opioid of use: heroin Duration of use: 2.8 years	Naltrexone; oral	12.5 mg, titrated to 50 mg, then 100 mg Monday and Wednesday, 150 mg Friday	2 months (12 month follow-up)	Positive urine drug test, 12 months 47% (7/15) vs. 62% (10/16); RR 0.75; 95% CI 0.39 to 1.45	NR (only reported through 2 months)
	San, 1991[78] Spain N=50 *Fair*	Mean age 26 vs. 27 years 21% vs. 27% female Primary opioid of use: heroin Duration of use: 6.5 vs. 8.0 years	Naltrexone; oral	100 mg Monday and Wednesday, 150 mg Friday	6 months (12 month follow-up)	Positive urine drug test, 12 months 57% (16/28) vs. 55% (12/22); RR 1.05; 95% CI 0.64 to 1.72	14% (4/28) vs. 36% (8/22); RR 0.39; 95% CI 0.14 to 1.14

Table 1. Trials of Medications for Opioid Use Disorder vs. Placebo/No Medication

Drug	Author, year Country N *Quality*	Population Intervention vs. control	Intervention; route of administration	Dose	Duration of treatment	Relapse Intervention vs. control	Retention in treatment Intervention vs. control
Naltrexone	Schottenfeld, 2008[70†] Malaysia N=82 (naltrexone and control arms) *Fair*	Mean age 38 vs. 36 years % female: NR Primary opioid of use: heroin Duration of use: 16.4 vs. 14.8 years	Naltrexone; oral	50 mg, titrated to 100-150 mg	6 months	3 consecutive positive urine tests or opiate positive test followed by two consecutive positive or missing tests: 91% (39/43) vs. 92% (36/39); RR 0.98; 95% CI 0.86 to 1.12	21% (9/43) vs. 13% (5/39); RR 1.63; 95% CI 0.60 to 4.45
	Shufman, 1994[79] Israel N=32 *Fair*	Mean age 34 vs. 32 years 0% vs. 0% female Primary opioid of use: heroin Duration of use: 6.7 vs. 5.9 years	Naltrexone; oral	25 mg, titrated to 50 mg	3 months	≥1 positive urine drug test: 62% (10/16) vs. 81% (13/16); RR 0.77; 95% CI 0.49 to 1.20	50% (8/16) vs. 56% (9/16); RR 0.89; 95% CI 0.46 to 1.71
	Stella, 2005[80] Italy N=42 *Fair*	Mean age: NR % female: NR Primary opioid of use: NR Duration of use: NR	Naltrexone; oral	50 mg	6 months	Not defined 57% (16/28) vs. 79% (11/14); RR 0.75; 95% CI 0.63 to 0.90	NR
Buprenorphine	Kakko, 2003[82] Sweden N=40 *Fair*	Mean age 29 vs. 32 years 25% vs. 30% female Primary opioid of use: heroin Duration of use: 5.8 vs. 4.8 years	Buprenorphine; sublingual	16 mg/day	12 months	≥2 positive urine samples within last 3 months 20% (4/20) vs. 100% (20/20); RR 0.20 (95% CI 0.08 to 0.48)	Voluntary or involuntary withdrawal: 75% (15/20) vs. 0% (0/20); RR 33.00 (95% CI 2.11 to 515.05)
	Krook, 2002[83] Norway N=106 *Fair*	Mean age 38 vs. 38 years 35% vs. 33% female Primary opioid of use: heroin Duration of use: 20 vs. 20 years	Buprenorphine; sublingual	16 mg/day	3 months	Self-reported heroin use, mean change from baseline (0-10 visual analog scale) -3.21 vs. 0.52; p<0.001	29% (16/55) vs. 2% (1/51); RR 14.84 (95% CI 2.04 to 107.89)
	Ling, 2010[84] U.S. N=163 *Fair*	Mean age 36 vs. 39 years 33% vs. 27% female Primary opioid of use: heroin (63%); prescription pain medication (37%) Duration of use: NR; duration >5 years: 16% vs. 14%	Buprenorphine; implant	320 mg	6 months	Mean proportion of negative urine tests (72 samples per patient): 36.6% (95% CI 30.5% to 42.6%) vs. 22.4% (15.3% to 29.5%); p=0.01	66% (71/108) vs. 31% (17/55); RR 2.13 (95% CI 1.40 to 3.23)

Table 1. Trials of Medications for Opioid Use Disorder vs. Placebo/No Medication

Drug	Author, year Country N *Quality*	Population Intervention vs. control	Intervention; route of administration	Dose	Duration of treatment	Relapse Intervention vs. control	Retention in treatment Intervention vs. control
Buprenorphine	Rosenthal, 2013[85] U.S. N=287 *Good*	Mean age 36 vs. 35 vs. 35 years 37% vs. 40% vs. 43% female Primary opioid of use: heroin (62%); prescription pain medication (37%); unspecified other (1%) Duration of use: NR; proportion with duration >5 years: 25% vs. 31% vs. 22%	A: Buprenorphine; implant B: Buprenorphine-naloxone; sublingual	A: 320 mg B: 12-16 mg/day	6 months	>50% of urine samples negative for opioids: A: 72.8% (83/114) vs. B: NR vs. placebo: 94.4% (51/54); A vs. placebo: RR 0.77 (95% CI 0.68 to 0.88	Completed trial A: 64% (73/114) vs. B: 64% (76/119) vs. placebo: 26% (14/54); (A or B) vs. placebo: RR 2.5 (95% CI 1.6 to 3.9)
	Schottenfeld, 2008[70†] Malaysia N=83 (buprenorphine and control arms) *Fair*	Mean age 38 vs. 36 years % female: NR Primary opioid of use: heroin Duration of use: 16.4 vs. 14.8 years	Buprenorphine; sublingual	8 mg/day, titrated to 16 to 24 mg/day	6 months	3 consecutive positive urine tests or opiate positive test followed by two consecutive positive or missing tests: 75% (33/44) vs. 92% (36/39); RR 0.81 (95% CI 0.67 to 0.99)	41% (18/44) vs. 13% (5/39); RR 3.19 (95% CI 1.31 to 7.79)
Methadone	Gruber, 2008[81] U.S. N=111 *Fair*	Mean age 43 vs. 40 vs. 43 years 46% vs. 46% vs. 26% female Primary opioid of use: heroin Duration of use: 16.6 vs. 16.9 vs. 20.4 years	A: Methadone; oral (+ minimal counseling) B: Methadone; oral (+ standard counseling)	Up to 90 mg/day	6 months	Self-reported heroin use (days) A: 5.9 (SD 7.7) vs. B: 4.2 (SD 6.7) vs. placebo: 18.4 (SD 12.8); A vs. placebo: p=0.0003	Retention at 8.5 months A: 48.6% (17/35) vs. B: 51.4% (19/37) vs. placebo: 38.5% (15/39): (A or B) vs. placebo: RR 1.30 (95% CI 0.82 to 2.06)
	Schwartz, 2007[86]; Schwartz, 2006[6]; Schwartz, 2009[87] U.S. N=319 *Good*	Mean age 41 vs. 42 years 42% vs. 38% female Primary opioid of use: heroin Duration of use: 18 vs. 19 years	Methadone; oral	Mean 78.4 mg/day	4 months	Opioid-positive drug test: 57% (99/175) vs. 79% (80/101); RR 0.71 (95% CI 0.61 to 0.84)	Entered into methadone treatment: 76% (151/199) vs. 21% (25/120); RR 3.64 (95% CI 2.55 to 5.21)

*n/N estimated from reported denominators and proportions.

†Study included naltrexone, buprenorphine and control arms; total N=126.

Abbreviations: CI = confidence interval; NR = not reported; RR = risk ratio; SD = standard deviation; U.S. = United States.

Table 2. Naltrexone Trials—Relapse and Retention in Treatment

Outcome Study Characteristics	Group analyzed	Number of trials	Relative risk (95% confidence interval)	I^2
Relapse, all trials	All participants	12	0.73 (0.62 to 0.85)	78%
Route of administration p for interaction=0.13	Oral	11	0.76 (0.65 to 0.88)	70%
	Injection or implant	2	0.41 (0.06 to 2.40)	98%
Timing of outcome assessment p for interaction=0.36	On treatment	10	0.71 (0.59 to 0.84)	82%
	Post intervention	2	0.93 (0.54 to 1.50)	0%
Study quality p for interaction=0.52	Good quality	3	0.67 (0.48 to 0.94)	84%
	Fair quality	9	0.76 (0.61 to 0.91)	78%
Naltrexone dose (oral administration) p for interaction=0.70	≤50 mg/day	7	0.69 (0.58 to 0.81)	47%
	>50 mg/day	4	0.97 (0.81 to 1.11)	0%
Retention in treatment, all trials	All participants	9	1.71 (1.13 to 2.49)	67%
Route of administration p for interaction=0.37	Oral	8	1.59 (1.00 to 2.38)	61%
	Injection or implant	2	2.48 (0.58 to 11.75)	94%
Timing of outcome assessment p for interaction=0.05	On treatment	8	1.89 (1.36 to 2.65)	59%
	Post intervention	1	0.39 (0.14 to 1.14)	--
Study quality p for interaction=0.33	Good quality	3	2.10 (1.21 to 4.13)	78%
	Fair quality	6	1.43 (0.78 to 2.47)	67%
Naltrexone dose (oral administration) p for interaction=0.18	≤50 mg/day	6	1.84 (1.22 to 2.71)	49%
	>50 mg/day	2	0.82 (0.14 to 4.48)	73%

Table 3. Opioid Agonist Trials—Relapse and Retention in Treatment

Outcome Study Characteristics	Group analyzed	Number of trials	Relative risk (95% confidence interval)	I^2
Relapse, all trials	All participants	4	0.75 (0.59 to 0.82)	75%
Drug p for interaction=0.78	Buprenorphine	3	0.59 (0.21 to 1.31)	84%
	Methadone	1	0.71 (0.61 to 0.84)	--
Type of counseling p for interaction=0.78	Standard counseling	3	0.59 (0.21 to 1.31)	84%
	No counseling	1	0.71 (0.61 to 0.84)	--
Study quality p for interaction=0.54	Good quality	2	0.75 (0.65 to 0.85)	0%
	Fair quality	2	0.46 (0.08 to 2.19)	93%
Buprenorphine route of administration p for interaction=0.70	Sublingual	2	0.46 (0.08 to 2.19)	93%
	Implant	1	0.77 (0.68 to 0.88)	--
Retention in treatment, all trials	All participants	7	2.58 (1.78 to 4.59)	71%
Drug p for interaction=0.54	Buprenorphine	5	2.52 (1.89 to 4.74)	51%
	Methadone	2	2.22 (0.63 to 7.56)	92%
Type of counseling p for interaction=0.79	Standard counseling	5	2.09 (1.54 to 3.33)	56%
	Minimal or no counseling	3	2.78 (0.93 to 13.74)	86%
Study quality p for interaction=0.72	Good quality	2	3.15 (1.90 to 4.81)	42%
	Fair quality	5	2.34 (1.41 to 9.20)	73%
Buprenorphine route of administration p for interaction=0.46	Sublingual	4	2.95 (1.97 to 12.06)	57%
	Implant	2	2.27 (1.58 to 3.31)	0%

Table 4. Psychosocial Intervention Trials—Study Characteristics

Author, year Country N *Quality*	Population Type of drug use	Screen-detected?	Type of intervention	Method of delivery	Number of sessions	Duration of sessions (hours, unless otherwise stated)	Control	Timing of outcome assessment (months)
Babor, 2004[30] U.S. N=450 *Good*	Adult Cannabis	No	A. Multicomponent (MET + CBT + case management) B. Brief MET	A. Face-to-face B. Face-to-face	A. 9 B. 2	A. NR B. 1	Waitlist	4
Baker, 2001a[88] and Baker, 2001b[89] Australia N=64 *Fair*	Adult Amphetamines	No	A. CBT + MI B. Brief CBT	A. Face-to-face B. Face-to-face	A. 4 B. 2	A. 0.5-1 B. 0.5-1	Minimal intervention	6
Baker, 2005[90] Australia N=214 *Fair*	Adult Amphetamines	No	A. CBT + MI B. Brief CBT	A. Face-to-face; some assessments conducted over the telephone B. Face-to-face; some assessments conducted over the telephone	A. 4 B. 2	A. 0.75-1 B. 0.75-1	Minimal intervention	6
Bernstein, 2005[4] U.S. N=1,175 *Fair*	Adults Cocaine; heroin	Yes*	Brief MI + telephone booster	Face-to-face; telephone	1	10-45 minutes	Minimal intervention	6
Bernstein, 2009[45] U.S. N=139 *Fair*	Adolescent/ Young Adult Cannabis	Yes	Brief MI	Face-to-face; telephone	1	20-30 minutes + 5-10 minute telephone booster call	Usual care	12
Blow, 2017[46] Bonar, 2018[91] U.S. N=780 *Good*	Adult Cannabis	Yes	A. Brief MI, computer-delivered B. Brief MI, therapist-delivered	A. Computer B. Face-to-face	A. 1 B. 1	A. 30 minutes B. 30 minutes	Usual care	12
Bogenschulz, 2014[47] and Bogenschulz, 2011[115] U.S. N=854 *Fair*	Adult Multiple drugs (18% street opioids; 5% prescription opioids)	Yes	Brief MI + telephone booster	Face-to-face; telephone	1 + 2 telephone booster calls	NR	Minimal intervention	12

Table 4. Psychosocial Intervention Trials—Study Characteristics

Author, year Country N *Quality*	Population Type of drug use	Screen-detected?	Type of intervention	Method of delivery	Number of sessions	Duration of sessions (hours, unless otherwise stated)	Control	Timing of outcome assessment (months)
Copeland, 2001a[31] and Copeland, 2001b[92] Australia N=229 *Fair*	Adult Cannabis	No	A. CBT B. CBT	A. Face-to-face B. Face-to-face	A. 6 B. 1	A. 1 B. 1.5	Waitlist	6
D'Amico, 2018[44] U.S. N=294 *Fair*	Adolescent Cannabis	Yes	Brief MI	Face-to-face	1	0.25-0.33	Minimal intervention	12
de Dios, 2012[93] U.S. N=34 *Fair*	Young Adult Cannabis	No	Brief MET + mindfulness meditation	Face-to-face	2	NR	Minimal intervention	3
de Gee, 2014[94] The Netherlands N=119 *Good*	Young Adult Cannabis	No	MI	Face to face	2	1.5	Minimal intervention	3
Dembo, 2016[95] U.S. N=300 *Fair*	Adolescent Cannabis	No	A. Brief MET + CBT (youth only) B. Brief MET (youth and parent)	Face-to-face	A. 2 B. 2	A. 1.5 B. 1.5	Usual care	18
Dupont, 2016[96] The Netherlands N=131 *Fair*	Adolescent/ Young Adult Cannabis	No	MET	Face-to-face	4	NR	Usual care	6
Fischer, 2012[98] and Fischer, 2013[97] Canada N=134 *Fair*	Young Adult Cannabis	No	Brief oral or written intervention consisting of short, fact-based and nonjudgmental information on cannabis-related health risks	Face-to-face	1	30 minutes	Minimal intervention	12
Gates, 2012[99] Australia N=149 *Fair*	Adult Cannabis	No	CBT + MI	Telephone	4	1	Waitlist	3

Table 4. Psychosocial Intervention Trials—Study Characteristics

Author, year Country N *Quality*	Population Type of drug use	Screen-detected?	Type of intervention	Method of delivery	Number of sessions	Duration of sessions (hours, unless otherwise stated)	Control	Timing of outcome assessment (months)
Gelberg, 2015[48] and Baumeister, 2014[114] U.S. N=334 *Fair*	Adult Multiple drugs (7% opioids)	Yes*	Brief MI + telephone booster	Face-to-face; telephone	1 + 2 telephone booster calls	3-4 minutes + 20-30 minute telephone booster	Minimal intervention	3
Gelberg, 2017[49] U.S. N=65 *Fair*	Adult Multiple drugs (11% opioids)	Yes*	Brief MI + telephone booster	Face-to-face; telephone	1 + 2 telephone booster calls	3-4 minutes + 20-30 minute telephone booster	Minimal intervention	3
Gryczynski, 2016[50] United States N=80 *Fair*	Adult Multiple drugs (24% opioids [proportion of patients at moderate risk])	Yes*	Brief computer intervention	Computer	1	10 minutes	Waitlist	3
Humeniuk, 2012[51] Australia, Brazil, India, U.S. N=389 *Fair*	Adolescent/ Adult Multiple drugs (13% opioids [proportion of patients at moderate risk])	Yes*	Brief MI	Face-to-face	1	15 minutes	Waitlist	3
Jones, 2005[100] U.S. N=130 *Fair*	Adult Opioids	No	Contingency management	Face-to-face	57	NR	Usual care	6
Lee, 2010[53] U.S. N=341 *Fair*	Adolescent/ Young Adult Cannabis	Yes	Brief MI	Computer	1	NR	Minimal intervention	6
Lee, 2013[52] U.S. N=212 *Fair*	Young Adult Cannabis	Yes	Brief MI	Face-to-face	1	1	Minimal intervention	6
Litt, 2005[103] U.S. N=450 *Fair*	Adult Cannabis	No	A. CBT + MET B. Brief MET	Face-to-face	A. 9 B. 2	NR	Waitlist	4

Table 4. Psychosocial Intervention Trials—Study Characteristics

Author, year Country N *Quality*	Population Type of drug use	Screen-detected?	Type of intervention	Method of delivery	Number of sessions	Duration of sessions (hours, unless otherwise stated)	Control	Timing of outcome assessment (months)
Litt, 2008[101] and Kadden, 2007[121] U.S. N=240 *Fair*	Adult Cannabis	No	A. CBT + MET + contingency management B. CBT + MET C. Contingency management	Face-to-face	A. 9 B. 9 C. 9	A. 1 B. 1 C. 15 minutes	Usual care	14
Litt, 2013[102] U.S. N=215 *Fair*	Adult Cannabis	No	A. CBT + MET + contingency management (for completing homework assignments) B. CBT + MET + contingency management (for cannabis-free urine samples)	Face-to-face	A. 9 B. 9	A. 1 B. 1	Usual care	9
Lozano, 2006[104] U.S. N=290 *Fair*	Adult Cannabis	No	A. CBT B. MET	Face-to-face	A. 14 B. 2	A. 2 B. 1.5	Waitlist	4
Marsden, 2006[105] U.K. N=342 *Good*	Adolescent/ Young Adult Stimulants	No	Brief MET	Face-to-face	1	45 minutes	Minimal intervention	6
Martin, 2008[106] Australia N=40 *Fair*	Adolescent Cannabis	No	Brief CBT	Face-to-face	2	NR	Waitlist	3
Martino, 2018[54] U.S. N=439 *Good*	Adults Multiple drugs (% opioids NR)	Yes*	A. Brief MI (in person) B. Brief MI (computer)	A. Face-to-face B. Computer	A. 1 B. 1	A. 20 minutes B. 20 minutes	Usual care	6
Mason, 2015[55] and Mason, 2017[119] U.S. N=119 *Fair*	Adolescent Cannabis and alcohol	Yes*	Brief MI	Face-to-face	1	20 minutes	Minimal intervention	6

Table 4. Psychosocial Intervention Trials—Study Characteristics

Author, year Country N *Quality*	Population Type of drug use	Screen-detected?	Type of intervention	Method of delivery	Number of sessions	Duration of sessions (hours, unless otherwise stated)	Control	Timing of outcome assessment (months)
McCambridge, 2004[108] and McCambridge, 2005[32] U.K. N=200 *Fair*	Adolescent/ Young Adult Cannabis Stimulants	No	Brief MET	Face-to-face	1	1	Minimal intervention	12
McCambridge, 2008[107] U.K. N=326 *Fair*	Adolescent/ Young Adult Cannabis	No	Brief MET	Face-to-face	1	≤1	Minimal intervention	6
Ondersma, 2007[56] U.S. N=107 *Fair*	Adult (Postpartum women) Multiple drugs (% opioids NR)	Yes	Brief MET + CBT	Computer	1	20 minutes	Minimal intervention	4
Ondersma, 2014[58] U.S. N=143 *Fair*	Adult (Postpartum women) Multiple drugs (% opioids NR)	Yes	Brief MET + CBT	Computer	1	20 minutes	Minimal intervention	6
Ondersma, 2018[57] U.S. N=500 *Fair*	Adult (Postpartum women) Multiple drugs (% opioids NR)	Yes	Brief MET + CBT	Computer	1	20 minutes	Minimal intervention	6
Palfai, 2014[59] U.S. N=123 *Fair*	Young Adult Cannabis	Yes	Brief MI	Computer	1	NR	Minimal intervention	6
Poblete, 2017[60] Chile N=806 *Fair*	Young Adult Multiple drugs (% opioids NR)	Yes*	Brief MI	Face-to-face	1	NR	Minimal intervention	3
Rooke, 2013[109] Australia N=230 *Fair*	Adult Cannabis	No	CBT + MI	Computer	6	NR	Minimal intervention	3
Roy-Byrne, 2014[61] and Krupski, 2012[118] U.S. N=868 *Good*	Adult Multiple drugs (26% opioids use in last 30 days)	Yes*	Brief MI	Face-to-face	1 + 1 telephone booster	0.5	Minimal intervention	12

Table 4. Psychosocial Intervention Trials—Study Characteristics

Author, year Country N *Quality*	Population Type of drug use	Screen-detected?	Type of intervention	Method of delivery	Number of sessions	Duration of sessions (hours, unless otherwise stated)	Control	Timing of outcome assessment (months)
Saitz, 2014[62], Fuster, 2016[116] and Kim, 2016[117] U.S. N=528 *Good*	Adult Multiple drugs (18% opioids; includes prescription opioids)	Yes*	A. Brief MI B. Brief MI + telephone booster	Face-to-face	A. 1 B. 1	A. 15 minutes B. 30-45 minutes + 20-30 minute telephone booster	Minimal intervention	6
Schaub, 2015[110] Germany N=308 *Fair*	Young Adult/ Adult Cannabis	No	A. CBT + MI + online chat B. CBT + MI	Computer	A. 8 B. 8	A. NR; online chat 20-30 minutes B. NR	Waitlist	3
Stein, 2009[111] U.S. N=198 *Fair*	Adult Stimulants	No	MI	Face-to-face	4	20-40 minutes	Minimal intervention	6
Stein, 2011[63] U.S. N=332 *Fair*	Young Adult Cannabis	Yes	Brief MI	Face-to-face	2	45 minutes	Minimal intervention	6
Stephens, 2000[33] U.S. N=291 *Fair*	Adult Cannabis	No	A. CBT + social support B. MI	Face-to-face	A. 14 B. 2	A. 2 B. 1.5	Waitlist	4
Stephens, 2007[112] U.S. N=188 *Good*	Adult Cannabis	No	Brief MI (review of personal feedback report)	Face-to-face	1	1.5	Minimal intervention	12
Tait, 2015[113] Australia N=160 *Fair*	Young Adult Stimulants	No	MET + CBT	Computer	3	NR	Waitlist	6
Tzilos Wernette, 2018[64] U.S. N=50 *Fair*	Adult (Pregnant women) Cannabis/ alcohol	Yes	Brief MI	Computer	1 + 1 booster	1	Minimal intervention	4
Walton, 2013[65] U.S. N=328 *Fair*	Adolescent Cannabis	Yes	A. Brief MI (computer) B. Brief MI (in person)	A. Computer B. Face-to-face	A. 1 B. 1	A. NR B. NR	Usual care	12

Table 4. Psychosocial Intervention Trials—Study Characteristics

Author, year Country N *Quality*	Population Type of drug use	Screen-detected?	Type of intervention	Method of delivery	Number of sessions	Duration of sessions (hours, unless otherwise stated)	Control	Timing of outcome assessment (months)
Watkins, 2017[66] U.S. N=397 *Fair*	Adult Multiple drugs (20% heroin; 10% prescription opioids)	Yes	Multicomponent (collaborative care)	Face-to-face	NA	NA	Usual care	6
Woolard, 2013[67] U.S. N=515 *Fair*	Adult Opioids/alcohol Cannabis	Yes	Brief MI	Face-to-face	NR	NR	Usual care	12
Yonkers, 2012[68] U.S. N=183 *Fair*	Adult (Pregnant women) Multiple drugs (% primary opioid use NR; 11% opioid use in past month)	Yes	MET + CBT	Computer	6	0.5	Minimal intervention	3
Zahradnik, 2009[69] and Otto, 2009[120] Germany N=126 *Fair*	Adult Multiple drugs (% opioids NR)	Yes	Brief MI	Face-to-face	2	0.5	Minimal intervention	12

*Study conducted in primary care setting.

Abbreviations: CBT = cognitive behavioral therapy; MET = motivational enhancement therapy; MI = motivational interviewing; NR = not reported; U.K. = United Kingdom; U.S. = United States.

Table 5. Psychosocial Intervention Trials—Abstinence at 3 to 4 Months or 6 to 12 Months

Timing Study Characteristics	Group analyzed	Number of trials	Relative risk (95% Confidence interval)	I^2
3-4 months, all trials	All participants	15	1.60 (1.24 to 2.13)	61%
Type of drug use p for interaction=0.10	Cannabis	7	2.08 (1.51 to 3.07)	28%
	Mixed drugs	7	1.24 (0.92 to 1.80)	60%
	Prescription drugs	1	2.08 (0.81 to 5.38)	--
Population p for interaction=0.05	Screen-detected population	8	1.28 (0.97 to 1.84)	57%
	Treatment-seeking population	7	2.08 (1.51 to 3.07)	28%
Type of intervention p for interaction=0.34	Brief interventions	10	1.46 (1.11 to 2.09)	56%
	Other (non-brief) interventions	6	2.01 (1.17 to 3.58)	70%
Age group p for interaction=0.77	Adolescent/young adult	2	1.54 (0.78 to 5.22)	61%
	Adult	13	1.58 (1.20 to 2.16)	64%
Pregnancy (adult only)	Pregnant or postpartum	5	1.24 (0.99 to 1.89)	41%
	Not pregnant or postpartum	8	1.77 (1.17 to 2.80)	71%
Mode of delivery p for interaction=0.61	Face-to-face	7	1.77 (1.13 to 3.02)	76%
	Other (web, computer, telephone)	8	1.43 (1.10 to 2.04)	35%
Study quality p for interaction=0.10	Good quality	1	4.34 (1.75 to 10.72)	--
	Fair quality	14	1.50 (1.18 to 1.98)	56%
6-12 months, all trials	All participants	14	1.25 (1.11 to 1.52)	38%
Type of drug use p for interaction=0.43	Cannabis	4	1.58 (1.17 to 3.06)	36%
	Stimulants	4	1.45 (0.86 to 2.56)	65%
	Mixed drugs	5	1.12 (0.92 to 1.36)	0%
	Prescription drugs	1	1.25 (0.65 to 2.40)	--
Population p for interaction=0.26	Screen-detected population	7	1.17 (0.99 to 1.41)	2%
	Treatment-seeking population	7	1.51 (1.14 to 2.37)	57%
Type of intervention p for interaction=0.22	Brief interventions	11	1.22 (1.08 to 1.42)	14%
	Other (non-brief) interventions	3	1.99 (0.55 to 7.80)	71%
Age group p for interaction=0.52	Adolescent/young adult	5	1.25 (1.04 to 1.64)	14%
	Adult	9	1.30 (1.05 to 1.80)	51%
Postpartum status (adult only)	Postpartum	2	1.07 (0.76 to 1.71)	0%
	Not postpartum	7	1.41 (1.04 to 2.16)	57%
Mode of delivery p for interaction=0.23	Face-to-face	11	1.31 (1.13 to 1.69)	43%
	Other (web, computer, telephone)	3	1.04 (0.73 to 1.45)	0%
Study quality p for interaction=0.21	Good quality	2	1.11 (0.58 to 1.51)	58%
	Fair quality	12	1.35 (1.15 to 1.73)	35%

Table 6. Psychosocial Intervention Trials—Drug Use Days at 3 to 4 Months or 6 to 12 Months

Timing Study Characteristics	Group analyzed	Number of trials	Mean difference (95% confidence interval)	I^2
3-4 months all trials	All participants	19	-0.49 (-0.85 to -0.13)	89%
Type of drug use p for interaction=0.11	Cannabis	14	-0.68 (-1.14 to -0.23)	89%
	Any drug use	5	-0.05 (-0.39 to 0.31)	58%
Population p for interaction=0.02	Screen-detected population	9	-0.10 (-0.31 to 0.12)	46%
	Treatment-seeking population	10	-0.91 (-1.52 to -0.31)	86%
Type of intervention p for interaction=0.03	Brief interventions	9	-0.13 (-0.36 to 0.12)	42%
	Other (more intensive) interventions	10	-0.88 (-1.50 to -0.28)	91%
Age group p for interaction=0.38	Adolescent	1	-1.47 (-2.99 to 0.06)	--
	Young adult or adolescent/young adult	8	-0.15 (-0.37 to 0.03)	0%
	Adult	10	-0.63 (-1.22 to -0.03)	93%
Mode of delivery p for interaction=0.66	Face-to-face	14	-0.54 (-1.01 to -0.08)	90%
	Other (web, computer, telephone)	5	-0.27 (-0.82 to 0.13)	49%
Study quality p for interaction=0.82	Good quality	5	-0.42 (-1.30 to 0.48)	93%
	Fair quality	14	-0.51 (-0.93 to -0.11)	86%
6-12 months, all trials	All participants	15	-0.08 (-0.30 to 0.11)	45%
Type of drug use p for interaction=0.42	Cannabis	7	-0.21 (-0.65 to 0.16)	41%
	Stimulants	1	-0.47 (-1.17 to 0.24)	--
	Any drug use	7	0.04 (-0.22 to 0.28)	43%
Population p for interaction=0.22	Screen-detected population	10	0.00 (-0.24 to 0.22)	42%
	Treatment-seeking population	5	-0.29 (-0.69 to 0.09)	12%
Type of intervention p for interaction=0.90	Brief interventions	11	-0.06 (-0.24 to 0.11)	0%
	Other (more intensive) interventions	4	-0.16 (-0.88 to 0.46)	79%
Age group p for interaction=0.80	Young adult or adolescent/young adult	7	-0.09 (-0.34 to 0.12)	0%
	Adult	8	-0.07 (-0.40 to 0.22)	66%
Mode of delivery p for interaction=0.80	Face-to-face	13	-0.10 (-0.36 to 0.12)	53%
	Other (web, computer, telephone)	2	-0.05 (-0.42 to 0.38)	0%
Study quality p for interaction=0.70	Good quality	6	-0.12 (-0.46 to 0.16)	36%
	Fair quality	9	-0.04 (-0.38 to 0.23)	45%

Note: Drug use days standardized to drug use in the past 7 days.

Table 7. Psychosocial Intervention Trials—Drug Use Severity at 3 to 4 Months or 6 to 12 Months

Timing Study Characteristics	Group analyzed	Number of trials	Standardized mean difference (95% confidence interval)	I^2
***3-4 month followup*, all trials**	All participants	17	-0.18 (-0.32 to -0.05)	73%
Type of drug use p for interaction=0.45	Cannabis use	13	-0.21 (-0.39 to -0.04)	78%
	Mixed substance use	4	-0.05 (-0.20 to 0.05)	1.3%
Population p for interaction=0.12	Screen-detected population	9	-0.05 (-0.15 to 0.05)	17%
	Treatment-seeking population	8	-0.30 (-0.57 to -0.03)	82%
Type of intervention p for interaction=0.18	Brief interventions	12	-0.09 (-0.20 to -0.002)	36%
	Other (non-brief) interventions	6	-0.32 (-0.70 to 0.06)	89%
Age group p for interaction=0.20	Adolescent	3	-0.08 (-0.26 to 0.10)	0%
	Young adult	6	-0.01 (-0.15 to 0.08)	22%
	Adult	8	-0.31 (-0.57 to -0.07)	82%
Mode of delivery p for interaction=0.66	Face-to-face	11	-0.15 (-0.33 to 0.02)	77%
	Other (web, computer, telephone)	7	-0.20 (-0.42 to -0.01)	64%
Study quality p for interaction=0.64	Good quality	2	-0.11 (-0.32 to 0.13)	0%
	Fair quality	15	-0.19 (-0.35 to -0.04)	76%
***6-12 month followup*, all trials**	All participants	13	-0.10 (-0.24 to 0.02)	65%
Type of drug use p for interaction=0.57	Amphetamine use	1	0.10 (-0.35 to 0.54)	--
	Cannabis use	8	-0.16 (-0.37 to 0.03)	72%
	Mixed substance use	4	-0.001 (-0.18 to 0.12)	42%
Population p for interaction=0.27	Screen-detected population	9	-0.03 (-0.15 to 0.06)	40%
	Treatment-seeking population	4	-0.23 (-0.62 to 0.17)	82%
Type of intervention p for interaction=0.03	Brief interventions	10	-0.02 (-0.13 to 0.06)	35%
	Other (non-brief) interventions	3	-0.36 (-0.80 to 0.14)	71%
Age group p for interaction=0.56	Adolescent	2	-0.10 (-0.37 to 0.18)	44%
	Young adult	5	0.02 (-0.16 to 0.15)	26%
	Adult	6	-0.18 (-0.44 to 0.04)	80%
Mode of delivery p for interaction=0.63	Face-to-face	9	-0.11 (-0.28 to 0.03)	70%
	Other (web, computer, telephone)	5	-0.03 (-0.28 to 0.16)	44%
Study quality p for interaction=0.69	Good-quality	3	-0.02 (-0.41 to 0.22)	72%
	Fair quality	10	-0.12 (-0.27 to 0.03)	62%

Table 8. Summary of Evidence

Key Question*	Intervention	Studies (k) Observations (n) Study Designs	Summary of Findings†	Consistency and Precision	Other Limitations	Strength of Evidence	Applicability
Efficacy of interventions (Key Questions 4a, b)	Naltrexone for opioid use disorder	13 trials (N=1,718)	• Drug use relapse: 11 trials, RR 0.73 (95% CI 0.62 to 0.85) I^2=78%; ARD -18% (95% CI -26% to -10%) • Retention in treatment: 9 trials, RR 1.71 (95% CI 1.13 to 2.49), I^2=67%; ARD 15% (95% CI 5% to 22%) • Mortality: Reported in 5 trials, with very few events Other health, legal, and social outcomes: Few trials, with inconsistent effects	For drug use relapse and retention in treatment, inconsistency in magnitude but not direction of effect. Estimates reasonably precise. Results consistent in stratified and sensitivity analyses.	Overall risk of bias moderate. Attrition was high. Methods for defining drug use relapse and retention in treatment varied. Reporting bias not detected.	Moderate	All trials enrolled treatment-seeking persons with opioid use disorder due to heroin use. Naltrexone administered in conjunction with drug use counseling. Most trials evaluated oral naltrexone, some trials recruited patients from the criminal justice system, and around half of naltrexone trials were conducted in countries in which opioid agonist therapy is not available
	Opioid agonist therapy (buprenorphine or methadone) for opioid use disorder	7 trials (N=1,109) • Buprenorphine: 5 trials (N=679) • Methadone: 2 trials (N=430) All trials conducted in treatment-seeking individuals	• Drug use relapse: 4 trials, RR 0.75 (95% CI 0.59 to 0.82), I^2=75%; ARD -35%, 95% CI -67% to -3%) • Retention in treatment: 7 trials, RR 2.58 (95% CI 1.78 to 4.59), I^2=71%; ARD 39% (95% CI 23% to 54%) • Results very similar when stratified by buprenorphine or methadone • Mortality: Reported in 2 trials, with very few events Other health, legal, and social outcomes: Few trials, with inconsistent effects	For drug use relapse and retention in treatment, inconsistency in magnitude but not direction of effect. Estimates reasonably precise. Results consistent in stratified and sensitivity analyses.	Overall risk of bias moderate. Attrition was high. Two trials used an open-label design. Methods for defining drug use relapse utilized urine drug test findings. Reporting bias not detected.	Moderate	All trials enrolled treatment-seeking persons with opioid use disorder, primarily due to heroin use. Opioid agonist therapy usually administered in conjunction with drug use counseling. Opioid agonist therapy usually administered in addiction treatment setting. No trial evaluated newly U.S. Food and Drug Administration-approved, injectable buprenorphine.

Table 8. Summary of Evidence

Key Question*	Intervention	Studies (k) Observations (n) Study Designs	Summary of Findings†	Consistency and Precision	Other Limitations	Strength of Evidence	Applicability
Efficacy of interventions (Key Questions 4a, b), continued	Psychosocial interventions	52 trials (N=15,659) • Screen-detected populations: 27 trials (N=10,227) • Treatment-seeking populations: 25 trials (N=5,432)	Drug use abstinence • 3 to 4 months: 15 trials, RR 1.60 (95% CI 1.24 to 2.13), I^2=61%; ARD 9% (95% CI 5% to 15%) • 6 to 12 months: 14 trials, RR 1.25 (95% CI 1.11 to 1.52), I^2=38%; ARD 10% (95% CI 3% to 16%) Drug use days (in last 7 days) • 3 to 4 months: 19 trials, mean difference -0.49 day (95% CI -0.85 to -0.13), I^2=89% • 6 to 12 months: 15 trials, mean difference -0.08 day (95% CI -0.30 to 0.11), I^2=45% Drug use severity • 3 to 4 months: 17 trials, SMD -0.18 (95% CI -0.32 to -0.05), I^2=73% • 6 to 12 months: 13 trials, SMD -0.10 (95% CI -0.24 to 0.02), I^2=65% Mortality: Reported in 4 trials with few events Other health, social, and legal outcomes: Few trials, with inconsistent effects	Substantial clinical heterogeneity and inconsistency. Effects present in trials of treatment-seeking but not screen-detected populations. Effects also generally stronger in trials that evaluated cannabis use than other type of drug use, trial of adult than trial of adolescents or young adults, and trial of more intensive than brief interventions. No stratified analysis explained inconsistency.	Overall risk of bias moderate. Attrition was high. Trials of psychosocial interventions could not be effectively blinded. Methods for measuring drug use outcomes varied. Reporting bias not detected.	Moderate	Studies varied in terms of whether patients were screen-detected or treatment-seeking, recruitment setting, and severity and type of drug use. Most trials evaluated psychosocial interventions that utilized cognitive behavioral therapy or motivational interventions, but treatment intensity varied. Brief interventions are usually designed to be feasible for delivery in primary care settings.

Table 8. Summary of Evidence

Key Question*	Intervention	Studies (k) Observations (n) Study Designs	Summary of Findings†	Consistency and Precision	Other Limitations	Strength of Evidence	Applicability
Harms of interventions (Key Question 5)	Naltrexone for opioid use disorder	11 trials (N=1,645)	• Withdrawal due to adverse events: 3 trials, RR 1.54 (95% CI 0.35 to 8.31), I^2=0% • Serious adverse events: 3 trials, RR 1.24 (95% CI 0.11 to 10.21, I^2=59% • Constipation: 2 trials, RR 0.97 (95% CI 0.37 to 2.39, I^2=0% • Diarrhea: 2 trials, RR 1.94 (95% CI 0.70 to 6.53, I^2=0%	Findings consistent but imprecise	Overall risk of bias moderate. Harms reporting was inconsistent and harms were NR by all trials	Low-moderate	See entry for efficacy of naltrexone
	Opioid agonist therapy (buprenorphine or methadone) for opioid use disorder	4 trials (N=639) on buprenorphine No studies on methadone	• Serious adverse events: 2 trials, RR 0.32 (95% CI 0.09 to 1.12), I^2=0% • Withdrawal due to adverse events: 1 trial (RR 0.89, 95% CI 0.06 to 13.7) • No hospitalizations due to serious medication-related adverse events: 1 trial • Constipation: 2 trials, RR 2.36 (95% CI 1.16 to 4.92), I^2=0%; ARD 12% (95% CI -5% to 41%) • Diaphoresis: 3 trials, RR 1.15 (95% CI 0.55 to 2.73), I^2=44% • Nausea: 2 trials, RR 1.13 (95% CI 0.41 to 6.07), I^2=30%	Some inconsistency and imprecision	Overall risk of bias moderate. Harms reporting was inconsistent and harms were NR by all trials	Low-moderate	See entry for efficacy of opioid agonist therapy
	Psychosocial interventions	4 trials (N=1,198)	• No harms were reported in either intervention of control groups No serious adverse events were noted	Findings consistent but imprecise	Overall risk of bias moderate. Harms were only reported in a few trials. However, serious harms are not expected with this type of intervention	Low-moderate	See entry for efficacy of psychosocial interventions

Table 8. Summary of Evidence

Key Question*	Intervention	Studies (k) Observations (n) Study Designs	Summary of Findings†	Consistency and Precision	Other Limitations	Strength of Evidence	Applicability
Efficacy of naloxone (Key Question 6)	-	No studies	--	--	--	--	--
Harms of naloxone (Key Question 7)	-	No studies	--	--	--	--	--

*The Key Question numbers are from the analytic framework in the screening report;[1] Key Questions 1-3 are addressed in that report.
†Comparisons are against placebo or no medication for pharmacological interventions, and against waitlist, a minimal intervention, or usual care for psychosocial interventions.

Abbreviations: ARD = absolute risk difference; CI = confidence interval; NR = not reported; RR = risk ratio; SMD = standardized mean difference; U.S. = United States.

Key Questions 4-5

Database: Ovid MEDLINE(R)
Pharmacologic interventions

1. substance-related disorders/ or amphetamine-related disorders/ or cocaine-related disorders/ or drug overdose/ or heroin dependence/ or inhalant abuse/ or marijuana abuse/ or opioid-related disorders/ or substance abuse, intravenous/ or substance abuse, oral/
2. exp Cannabinoids/
3. Cannabis/
4. exp "Marijuana Use"/
5. exp Analgesics, Opioid/
6. exp Cocaine/
7. exp Amphetamines/
8. exp Street Drugs/
9. (opioid* or opiate* or amphetamine* or methamphetamine* or cocaine or stimulant* or oxycodone or fentanyl or codeine or hydrocodone or hydromorphone or meperidine or methadone or morphine or heroin or cannabinoid or cannabis or marijuana or hash*).ti,ab.
10. (addict* or abus* or misuse* or mis-use* or misusing or mis-using or "non medical" or extramedical or "extra medical" or illicit* or illegal* or unlawful* or unsanction* or habit* or dependen* or disorder* or consumption or diversion*).ti,ab.
11. exp Buprenorphine/
12. exp Methadone/
13. Naltrexone/
14. (buprenorphine or probuphine or sublocade or subutex or suboxone or methadone or naltrexone or vivitrol).ti,ab,kw.
15. treatment outcome/
16. (treatment* or intervention*).ti,ab.
17. (dt or th or pc or rh).fs.
18. 1 and (or/11-14)
19. (or/2-9) and 10 and (or/11-14)
20. 18 or 19
21. 20 and (or/15-17)
22. Randomized Controlled Trials as Topic/
23. double-blind method/ or random allocation/
24. (random* or control* or trial or placebo or blind*).ti,ab,kw.
25. 21 and (or/22-24)
26. limit 21 to randomized controlled trial
27. 25 or 26
28. meta-analysis.pt.
29. meta-analysis/ or systematic review/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/
30. (medline or cochrane or "systematic review" or "meta analysis" or metaanalysis).ti,ab,kw.
31. 21 and (or/28-30)
32. limit 21 to (meta analysis or systematic reviews)
33. 31 or 32
34. 27 or 33
35. limit 34 to (english language and humans)

Database: Ovid MEDLINE(R)
Nonpharmacologic interventions – systematic reviews

1. substance-related disorders/ or amphetamine-related disorders/ or cocaine-related disorders/ or drug overdose/ or heroin dependence/ or inhalant abuse/ or marijuana abuse/ or opioid-related disorders/ or substance abuse, intravenous/ or substance abuse, oral/
2. exp Cannabinoids/
3. Cannabis/
4. exp "Marijuana Use"/

Appendix A1. Search Strategies

5. exp Analgesics, Opioid/
6. exp Cocaine/
7. exp Amphetamines/
8. exp Street Drugs/
9. (opioid* or opiate* or amphetamine* or methamphetamine* or cocaine or stimulant* or oxycodone or fentanyl or codeine or hydrocodone or hydromorphone or meperidine or methadone or morphine or heroin or cannabinoid or cannabis or marijuana or hash*).ti,ab.
10. (addict* or abus* or misuse* or mis-use* or misusing or mis-using or "non medical" or extramedical or "extra medical" or illicit* or illegal* or unlawful* or unsanction* or habit* or dependen* or disorder* or consumption or diversion*).ti,ab.
11. exp Behavior Therapy/
12. psychotherapy/
13. exp Psychotherapy, Group/
14. exp Counseling/
15. Self-Help Groups/
16. psychoanalytic therapy/
17. (brief adj3 intervention*).ti,ab.
18. ("cognitive behavior* therapy" or "cbt").ti,ab.
19. ("contingency management" or voucher* or prize*).ti,ab.
20. (motivation* adj3 enhanc*).ti,ab.
21. ("12 step" or "twelve step" or anonymous).ti,ab.
22. 21 not alcohol*.ti.
23. (family adj3 (counsel* or intervention* or therap*)).ti,ab.
24. psychotherapy, brief/
25. or/2-9
26. 10 and 25
27. 1 or 26
28. or/11-20
29. or/22-24
30. 28 or 29
31. 27 and 30
32. limit 31 to (meta analysis or systematic reviews)
33. meta-analysis.pt.
34. meta-analysis/ or systematic review/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/
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,hw.
45. (cochrane or (health adj2 technology assessment) or evidence report).jw.
46. (meta-analysis or systematic review).ti,ab.
47. (comparative adj3 (efficacy or effectiveness)).ti,ab.
48. (outcomes research or relative effectiveness).ti,ab.
49. ((indirect or indirect treatment or mixed-treatment) adj comparison*).ti,ab.
50. or/33-49
51. 31 and 50
52. 32 or 51

Appendix A1. Search Strategies

Database: Ovid MEDLINE(R)
Nonpharmacologic interventions - RCTs
1. substance-related disorders/ or amphetamine-related disorders/ or cocaine-related disorders/ or drug overdose/ or heroin dependence/ or inhalant abuse/ or marijuana abuse/ or opioid-related disorders/ or substance abuse, intravenous/ or substance abuse, oral/
2. exp Cannabinoids/
3. Cannabis/
4. exp "Marijuana Use"/
5. exp Analgesics, Opioid/
6. exp Cocaine/
7. exp Amphetamines/
8. exp Street Drugs/
9. (opioid* or opiate* or amphetamine* or methamphetamine* or cocaine or stimulant* or oxycodone or fentanyl or codeine or hydrocodone or hydromorphone or meperidine or methadone or morphine or heroin or cannabinoid or cannabis or marijuana or hash*).ti,ab.
10. (addict* or abus* or misuse* or mis-use* or misusing or mis-using or "non medical" or extramedical or "extra medical" or illicit* or illegal* or unlawful* or unsanction* or habit* or dependen* or disorder* or consumption or diversion*).ti,ab.
11. exp Behavior Therapy/
12. psychotherapy/
13. exp Psychotherapy, Group/
14. exp Counseling/
15. Self-Help Groups/
16. psychoanalytic therapy
17. (brief adj3 intervention*).ti,ab.
18. ("cognitive behavior* therapy" or "cbt").ti,ab.
19. ("contingency management" or voucher* or prize*).ti,ab.
20. (motivation* adj3 enhanc*).ti,ab.
21. ("12 step" or "twelve step" or anonymous).ti,ab.
22. 21 not alcohol*.ti.
23. (family adj3 (counsel* or intervention* or therap*)).ti,ab.
24. psychotherapy, brief/
25. or/2-9
26. 10 and 25
27. 1 or 26
28. or/11-20
29. or/22-24
30. 28 or 29
31. 27 and 30
32. limit 31 to randomized controlled trial
33. 31 and (random* or control* or trial or sham).ti,ab,kf.
34. 32 or 33

Database: PsycINFO
Pharmacologic interventions
1. drug abuse/ or drug usage/ or drug dependency/ or drug addiction/ or "substance use disorder"/
2. exp opiates/
3. exp cocaine/
4. marijuana usage/ or marijuana/
5. exp cannabis/ or cannabinoids/
6. exp cns stimulating drugs/
7. (opioid* or opiate* or amphetamine* or methamphetamine* or cocaine or stimulant* or oxycodone or fentanyl or codeine or hydrocodone or hydromorphone or meperidine or methadone or morphine or heroin or cannabinoid or cannabis or marijuana or hash*).ti,ab.

8. (addict* or abus* or misuse* or mis-use* or misusing or mis-using or "non medical" or extramedical or "extra medical" or illicit* or illegal* or unlawful* or unsanction* or habit* or dependen* or disorder* or consumption or diversion*).ti,ab.
9. (or/2-7) and 8
10. 1 or 9
11. buprenorphine/
12. methadone/
13. naltrexone/
14. (buprenorphine or probuphine or sublocade or subutex or suboxone or methadone or naltrexone or vivitrol).ti,ab.
15. 10 and (11 or 12 or 13 or 14)
16. exp Treatment Outcomes/
17. (treatment* or therap* or intervention*).ti,ab.
18. 15 and (16 or 17)
19. Clinical Trials/
20. (random* or control* or trial or placebo or sham or blind*).ti,ab.
21. exp Treatment Effectiveness Evaluation/ or exp "Literature Review"/
22. (systematic or "meta analysis" or metaanalysis or medline).ti,ab.
23. 18 and (or/19-22)
24. limit 23 to (human and english language)

Database: PsycINFO
Nonpharmacologic interventions – systematic reviews
1. drug abuse/ or drug usage/ or drug dependency/ or drug addiction/ or "substance use disorder"/ 2. exp opiates/
3. exp cocaine/
4. marijuana usage/ or marijuana/
5. exp cannabis/ or cannabinoids/
6. exp cns stimulating drugs/
7. (opioid* or opiate* or amphetamine* or methamphetamine* or cocaine or stimulant* or oxycodone or fentanyl or codeine or hydrocodone or hydromorphone or meperidine or methadone or morphine or heroin or cannabinoid or cannabis or marijuana or hash*).ti,ab.
8. (addict* or abus* or misuse* or mis-use* or misusing or mis-using or "non medical" or extramedical or "extra medical" or illicit* or illegal* or unlawful* or unsanction* or habit* or dependen* or disorder* or consumption or diversion*).ti,ab.
9. (or/2-7) and 8
10. 1 or 9
11. exp psychotherapy/
12. cognitive therapy/
13. exp COUNSELING/
14. exp family therapy/
15. exp behavior modification/
16. exp psychotherapeutic techniques/
17. exp psychotherapeutic processes/
18. (brief adj3 intervention*).ti,ab.
19. ("cognitive behavior* therapy" or "cbt").ti,ab.
20. ("contingency management" or voucher* or prize*).ti,ab.
21. (motivation* adj3 enhanc*).ti,ab.
22. (family adj3 (counsel* or intervention* or therap*)).ti,ab.
23. exp support groups/
24. ("12 step" or "twelve step" or anonymous).ti,ab.
25. 24 not alcohol*.ti.
26. 10 and (or/11-23)
27. 10 and 25
28. 26 or 27
29. (cinahl or cochrane or embase or medline or pubmed or scopus or "sociological abstracts" or "web of science").ab.
30. ("systematic review" or "meta analysis" or "metaanalysis").ti,ab.

31. ("systematic review" or "meta analysis").md.
32. exp "Literature Review"/
33. 28 and (or/29-32)

Database: PsycINFO
Nonpharmacologic interventions - RCTs
1. drug abuse/ or drug usage/ or drug dependency/ or drug addiction/ or "substance use disorder"/ 2. exp opiates/
3. exp cocaine/
4. marijuana usage/ or marijuana/
5. exp cannabis/ or cannabinoids/
6. exp cns stimulating drugs/
7. (opioid* or opiate* or amphetamine* or methamphetamine* or cocaine or stimulant* or oxycodone or fentanyl or codeine or hydrocodone or hydromorphone or meperidine or methadone or morphine or heroin or cannabinoid or cannabis or marijuana or hash*).ti,ab.
8. (addict* or abus* or misuse* or mis-use* or misusing or mis-using or "non medical" or extramedical or "extra medical" or illicit* or illegal* or unlawful* or unsanction* or habit* or dependen* or disorder* or consumption or diversion*).ti,ab.
9. (or/2-7) and 8
10. 1 or 9
11. exp psychotherapy/
12. cognitive therapy/
13. exp COUNSELING/
14. exp family therapy/
15. exp behavior modification/
16. exp psychotherapeutic techniques/
17. exp psychotherapeutic processes/
18. (brief adj3 intervention*).ti,ab.
19. ("cognitive behavior* therapy" or "cbt").ti,ab.
20. ("contingency management" or voucher* or prize*).ti,ab.
21. (motivation* adj3 enhanc*).ti,ab.
22. (family adj3 (counsel* or intervention* or therap*)).ti,ab.
23. (art or music* or acupuncture).ti,ab.
24. ("12 step" or "twelve step" or anonymous).ti,ab.
25. 24 not alcohol*.ti.
26. 10 and (or/11-23)
27. 10 and 25
28. 26 or 27
29. limit 28 to "0300 clinical trial"
30. exp Clinical Trials/
31. 28 and 30
32. 28 and (random* or control* or trial or sham).ti,ab,hw,id.
33. 29 or 31 or 32

Database: EBM Reviews - Cochrane Central Register of Controlled Trials
Pharmacologic interventions
1. substance-related disorders/ or amphetamine-related disorders/ or cocaine-related disorders/ or drug overdose/ or heroin dependence/ or inhalant abuse/ or marijuana abuse/ or opioid-related disorders/ or substance abuse, intravenous/ or substance abuse, oral/
2. exp Cannabinoids/
3. Cannabis/
4. exp Analgesics, Opioid/
5. exp Cocaine/
6. exp Amphetamines/
7. exp Street Drugs/

8. (opioid* or opiate* or amphetamine* or methamphetamine* or cocaine or stimulant* or oxycodone or fentanyl or codeine or hydrocodone or hydromorphone or meperidine or methadone or morphine or heroin or cannabinoid or cannabis or marijuana or hash*).ti,ab.
9. (addict* or abus* or misuse* or mis-use* or misusing or mis-using or "non medical" or extramedical or "extra medical" or illicit* or illegal* or unlawful* or unsanction* or habit* or dependen* or disorder* or consumption or diversion*).ti,ab.
10. exp Buprenorphine/
11. exp Methadone/
12. Naltrexone/
13. (buprenorphine or probuphine or sublocade or subutex or suboxone or methadone or naltrexone or vivitrol).ti,ab,kw.
14. treatment outcome/
15. (treatment* or intervention*).ti,ab.
16. (dt or th or pc or rh).fs.
17. 1 and (or/10-13)
18. (or/2-8) and 9 and (or/10-13)
19. 17 or 18
20. 19 and (or/14-16)
21. limit 20 to english language
22. limit 21 to medline records
23. 21 not 22

Database: EBM Reviews - Cochrane Central Register of Controlled Trials
Nonpharmacologic interventions
1. substance-related disorders/ or amphetamine-related disorders/ or cocaine-related disorders/ or drug overdose/ or heroin dependence/ or inhalant abuse/ or marijuana abuse/ or opioid-related disorders/ or substance abuse, intravenous/ or substance abuse, oral/
2. exp Cannabinoids/
3. Cannabis/
4. exp Analgesics, Opioid/
5. exp Cocaine/
6. exp Amphetamines/
7. exp Street Drugs/
8. (opioid* or opiate* or amphetamine* or methamphetamine* or cocaine or stimulant* or oxycodone or fentanyl or codeine or hydrocodone or hydromorphone or meperidine or methadone or morphine or heroin or cannabinoid or cannabis or marijuana or hash*).ti,ab.
9. (addict* or abus* or misuse* or mis-use* or misusing or mis-using or "non medical" or extramedical or "extra medical" or illicit* or illegal* or unlawful* or unsanction* or habit* or dependen* or disorder* or consumption or diversion*).ti,ab.
10. exp Behavior Therapy/
11. psychotherapy/
12. exp Psychotherapy, Group/
13. exp Counseling/
14. Self-Help Groups/
15. psychotherapy, brief/
16. (brief adj3 intervention*).ti,ab.
17. ("cognitive behavior* therapy" or "cbt").ti,ab.
18. ("contingency management" or voucher* or prize*).ti,ab.
19. (motivation* adj3 enhanc*).ti,ab.
20. ("12 step" or "twelve step" or anonymous).ti,ab.
21. 20 not alcohol*.ti.
22. (family adj3 (counsel* or intervention* or therap*)).ti,ab.
23. psychoanalytic therapy/
24. or/2-8
25. 9 and 24
26. 1 or 25

27. or/10-19
28. or/21-23
29. 27 or 28
30. 26 and 29
31. limit 30 to medline records
32. 30 not 31

Key Questions 4-7

Database: Elsevier Embase

('drug dependence treatment'/exp OR 'drug dependence treatment') AND ('buprenorphine'/exp OR buprenorphine OR 'naltrexone'/exp OR naltrexone OR 'methadone'/exp OR methadone OR 'naloxone'/exp OR naloxone) AND (random*:ab,ti OR placebo*:de,ab,ti OR ((double NEXT/1 blind*):ab,ti)) AND [embase]/lim NOT ([embase]/lim AND [medline]/lim) AND [english]/lim

Database: EBM Reviews - Cochrane Database of Systematic Reviews

1. (opioid* or opiate* or amphetamine* or methamphetamine* or cocaine or stimulant* or oxycodone or fentanyl or codeine or hydrocodone or hydromorphone or meperidine or methadone or morphine or heroin or cannabinoid or cannabis or marijuana or hash*).ti,ab.
2. (addict* or abus* or misuse* or mis-use* or misusing or mis-using or "non medical" or extramedical or "extra medical" or illicit* or illegal* or unlawful* or unsanction* or habit* or dependen* or disorder* or consumption or diversion*).ti,ab.
3. (treatment* or intervention*).ti,ab.
4. 1 and 2 and 3
5. limit 4 to full systematic reviews

Key Questions 6-7

Database: Ovid MEDLINE(R)

1. opioid-related disorders/
2. exp Analgesics, Opioid/ or Drug Overdose/
3. (opioid* or opiate* or oxycodone or fentanyl or codeine or hydrocodone or hydromorphone or meperidine or methadone or morphine or heroin).ti,ab.
4. (addict* or abus* or misuse* or mis-use* or misusing or mis-using or "non medical" or extramedical or "extra medical" or illicit* or illegal* or unlawful* or unsanction* or habit* or dependen* or disorder* or consumption or diversion*).ti,ab.
5. Naloxone/
6. (naloxone or evzio or narcan).ti,ab,kw.
7. treatment outcome/
8. (treatment* or intervention*).ti,ab.
9. (dt or th or pc or rh).fs.
10. Randomized Controlled Trials as Topic/
11. double-blind method/ or random allocation/
12. (random* or control* or trial or placebo or blind*).ti,ab,kw.
13. meta-analysis.pt.
14. meta-analysis/ or systematic review/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/
15. (medline or cochrane or "systematic review" or "meta analysis" or metaanalysis).ti,ab,kw.
16. 1 and (5 or 6)
17. (2 or 3) and 4 and (5 or 6)
18. 16 or 17
19. 18 and (7 or 8 or 9)
20. 19 and (or/10-15)
21. limit 19 to (meta analysis or randomized controlled trial or systematic reviews)
22. 20 or 21

23. limit 22 to (english language and humans)

Database: EBM Reviews - Cochrane Central Register of Controlled Trials
1. opioid-related disorders/
2. exp Analgesics, Opioid/ or Drug Overdose/
3. (opioid* or opiate* or oxycodone or fentanyl or codeine or hydrocodone or hydromorphone or meperidine or methadone or morphine or heroin).ti,ab.
4. (addict* or abus* or misuse* or mis-use* or misusing or mis-using or "non medical" or extramedical or "extra medical" or illicit* or illegal* or unlawful* or unsanction* or habit* or dependen* or disorder* or consumption or diversion*).ti,ab.
5. Naloxone/
6. (naloxone or evzio or narcan).ti,ab,kw.
7. treatment outcome/
8. (treatment* or intervention*).ti,ab.
9. (dt or th or pc or rh).fs.
10. 1 and (5 or 6)
11. (2 or 3) and 4 and (5 or 6)
12. 10 or 11
13. 12 and (or/7-9)
14. limit 13 to english language

Appendix A2. Inclusion and Exclusion Criteria

PICOTS	Inclusion criteria	Exclusion criteria
Conditions	Unhealthy drug use related to: KQs 4 and 5: Prescription or illicit opioids Cannabinoids Stimulants Polysubstance use involving prescription or illicit opioids, cannabinoids, or stimulants KQs 6 and 7: Prescription or illicit opioids	Other drugs
Populations	Adolescents and adults age 12 years and older Studies in which participants are identified as engaging in drug use (as defined above) A priori subpopulations at greater risk for drug use or its consequences will be examined based on the following factors: age (particularly young adults ages 18 to 25 years and adolescents ages 12 to 17 years), sex, race/ethnicity, socioeconomic status, pregnancy status, concurrent substance use (tobacco or alcohol), and severity of the disorder	Studies limited to: Persons with psychotic disorders (e.g., schizophrenia) Psychiatric inpatients, persons who are court-mandated to receive treatment (with the exception of adolescents), persons who are incarcerated) Persons who have failed standard treatments Persons prescribed opioids, stimulants, or using marijuana under medical supervision without a use disorder or misuse <70% SUD or unclear if majority is alcohol use
Interventions	KQs 4 and 5: Psychosocial interventions to reduce drug use, within the following broad categories, or combinations or adaptations of these categories: Brief interventions Cognitive behavioral therapy (including relapse prevention) Contingency management Motivational enhancement therapy 12-step facilitation therapy Family interventions (e.g., Adolescent Community Reinforcement Approach or Assertive Continuing Care) Within each approach, there may be variability in specific strategies (e.g., action plans, diaries), delivery method (e.g., face-to-face, electronic, individual, group-based), length of contact (e.g., brief, extended), and the number of contacts (e.g., single, multiple) FDA-approved medications to treat drug use disorder. FDA-approved medications are currently only available for treatment of opioid use disorder: buprenorphine (Probuphine®, Sublocade®, Subutex®, and generic forms), combined buprenorphine and naloxone (Suboxone®, Zubsolv®, Bunavail®), methadone, and extended release naltrexone (Vivitrol®) and oral naltrexone KQs 6 and 7: Naloxone (including Evzio®, Narcan®)	Psychosocial interventions not within the specified categories Psychosocial intervention is not described sufficiently to allow replication Interventions to prevent drug use initiation Management of persons prescribed opioids, stimulants, or using marijuana under medical supervision without a use disorder or misuse Vocational rehabilitation Housing interventions Neurostimulation/non-invasive brain stimulation techniques Medications for treatment of drug use not approved by the FDA for this indication Community-based, media, or policy interventions School-based interventions (university-based intervention included) Syringe exchange, supervision injection HIV-focused interventions Acupuncture, music therapy, art therapy, mindfulness-based interventions

Appendix A2. Inclusion and Exclusion Criteria

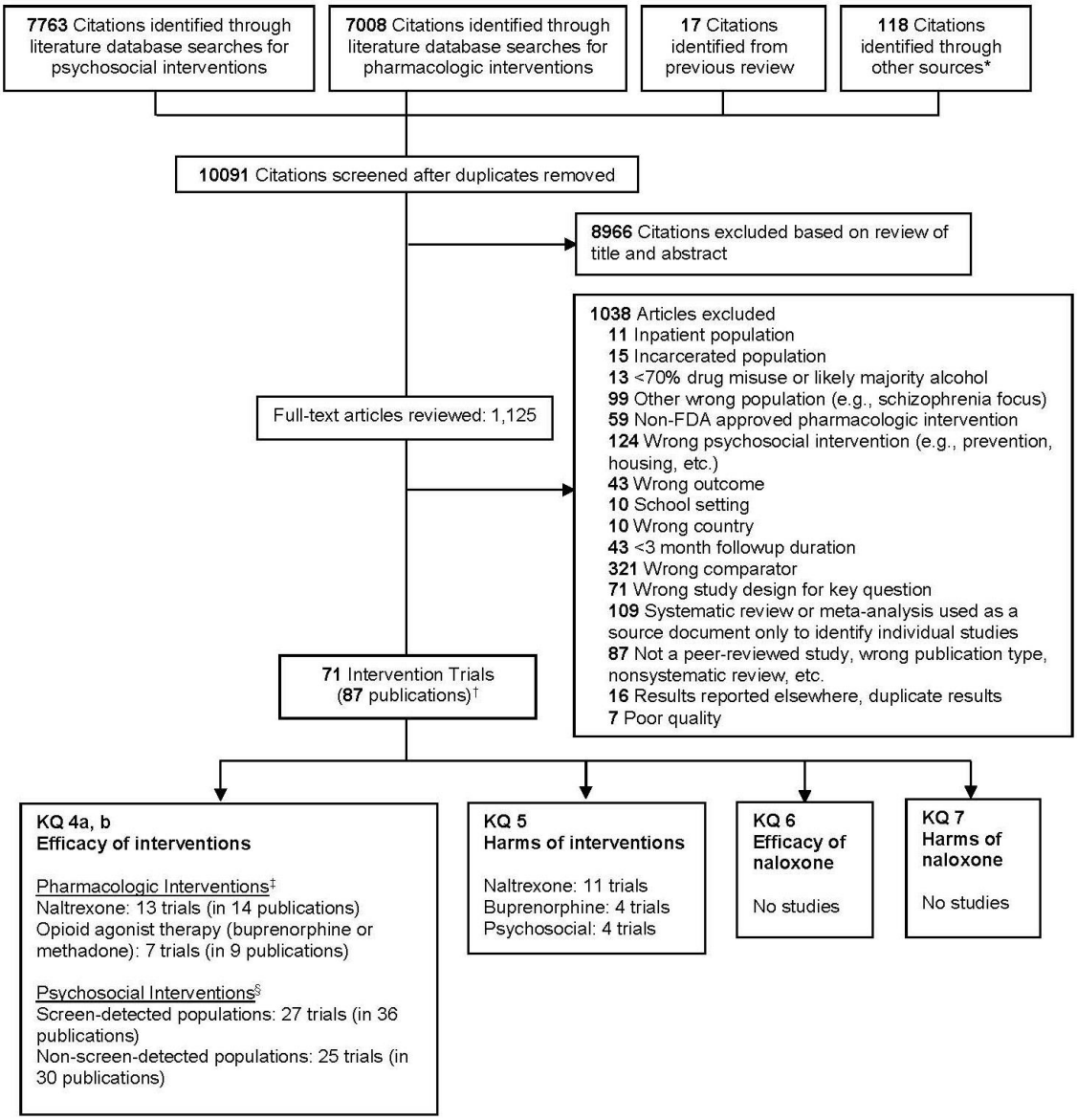
PICOTS	Inclusion criteria	Exclusion criteria
Comparisons	KQs 4-7: Included interventions vs: No intervention Placebo Usual care (unless the description of usual care is actually a head-to-head comparison) Waitlist Attention control (e.g., intervention is similar in format and intensity but is not thought to have a specific effect) Minimal intervention (e.g., no more than one single brief contact per year, brief written materials such as pamphlets) Medication + psychosocial intervention versus psychosocial intervention alone	Comparisons involving non-specified interventions Included intervention vs. included intervention Combinations of interventions vs. one intervention, other than specified Comparisons involving differing intensities of treatments
Settings	KQs 4-7: Any, aside from inpatient/residential or correctional facility	Inpatient/residential facility Correctional facility
Outcomes	KQs 4a: Drug use (self-report and/or biologic measures): Abstinence (use/no use) Frequency and/or quantity of drug use Severity of drug use disorder (reported as an index measured by a standardized questionnaire, such as the Short Inventory of Problems, Addiction Severity Index, Severity of Dependence Scale, or DSM-V severity) Polysubstance use Other risky behaviors (e.g., alcohol, tobacco, or other drug use; risky sexual behaviors) KQs4b: All-cause mortality Drug-related mortality (intentional and unintentional) Drug-related morbidity (e.g., mental health symptoms/disorders, STI/HIV transmission, hepatitis B or C virus transmission, respiratory infection, cardiovascular complications, stroke, seizure, nonfatal overdose, injuries and accidents, cognitive impairment, visit to emergency department, hospital inpatient stay) Obstetrical/perinatal/neonatal outcomes (e.g., perinatal mortality, preterm labor/delivery, low birth weight, placental abruption, intrauterine growth restriction, preeclampsia, antepartum or postpartum hemorrhage, gestational hypertension, decreased neonate length/head circumference, neonate neurobehavioral effects, congenital anomalies, neonatal abstinence syndrome, neonatal intensive care unit admission, length of neonate hospitalization) Quality of life Drug-related problems, such as legal problems, social and family relations, employment, and school/educational outcomes KQ5: Serious harms at any time point after the intervention began (e.g., death, seizure, cardiovascular event, other medical issue requiring urgent medical treatment, serious obstetrical/perinatal/neonatal complication attributable to included medications) Demoralization due to failed quit attempt Stigma, labeling, and/or discrimination Privacy issues (e.g., insurability status) Job loss Interference with the doctor-patient relationship	Attitudes, knowledge, and beliefs related to drug use Intention to change behavior

Appendix A2. Inclusion and Exclusion Criteria

PICOTS	Inclusion criteria	Exclusion criteria
Outcomes, continued	KQ 6: All-cause mortality Drug-related mortality (intentional and unintentional) Drug-related morbidity (e.g., nonfatal overdose and associated complications [e.g., seizure, cardiovascular, respiratory events], visit to emergency department, hospital inpatient stay) KQ 7: Serious harms, including withdrawal, agitation and associated injuries	Not applicable
Outcome assessment timing	At least 3 months after baseline measurement (except for studies in pregnant women, for which shorter lengths of followup will be included)	Not applicable
Study designs	KQs 4-7: Randomized, controlled trials and nonrandomized controlled trials; if evidence from controlled trials is lacking; large cohort and case-control studies for harms of medications	Time series studies, before-after studies with no comparison group, cross-sectional studies, case studies, case series, editorials/commentaries
Countries	Studies conducted in countries categorized as “Very High” on the 2014 Human Development Index (as defined by the United Nations Development Programme)	Studies conducted in countries that are not categorized as “Very High” on the 2014 Human Development Index
Language	English	Non-English

Abbreviations: DSM-V=Diagnostic and Statistical Manual of Mental Disorders Fifth Edition; FDA=food and drug administration; KQ=key question; PICOT=population, intervention, comparator, outcome, timing, study design/setting; STI=sexually transmitted infection; SUD=substance use disorder.

Appendix A3. Literature Flow Diagram



*Other sources include reference lists of relevant articles and systematic reviews, reviewer suggestions, etc.; includes background articles.
†The numbers in the bottom row do not sum to the total listed because some trials are included in multiple Key Questions or subcategories.
‡Two pharmacologic trials have been carried forward from the prior report.[2]
§Five psychosocial trials have been carried forward from the prior report.[2]
Note: Key Questions 1-3 are addressed in a separate report.[1]
Abbreviations: FDA = U.S. Food and Drug Administration; KQ = key question.

Appendix A4. List of Included Studies

Babor TF, Christiansen K, Donaldson J, et al. Brief treatments for cannabis dependence: Findings from a randomized multisite trial. J Consult Clin Psychol. 2004;72(3):455-66. doi: 10.1037/0022-006x.72.3.455. PMID: 15279529.

Baker A, Boggs TG, Lewin TJ. Randomized controlled trial of brief cognitive-behavioural interventions among regular users of amphetamine. Addiction. 2001;96(9):1279-87. doi: 10.1080/09652140120070337. PMID: 11672492.

Baker A, Boggs TG, Lewin TJ. Characteristics of regular amphetamine users and implications for treatment. Drug Alcohol Rev. 2001;20(1):49-56.

Baker A, Lee NK, Claire M, et al. Brief cognitive behavioural interventions for regular amphetamine users: a step in the right direction. Addiction. 2005;100(3):367-78. doi: 10.1111/j.1360-0443.2005.01002.x. PMID: 15733250.

Bernstein E, Edwards E, Dorfman D, et al. Screening and brief intervention to reduce marijuana use among youth and young adults in a pediatric emergency department. Acad Emerg Med. 2009;16(11):1174-85. doi: 10.1111/j.1553-2712.2009.00490.x. PMID: 20053238.

Bernstein J, Bernstein E, Tassiopoulos K, et al. Brief motivational intervention at a clinic visit reduces cocaine and heroin use. Drug Alcohol Depend. 2005;77(1):49-59. doi: 10.1016/j.drugalcdep.2004.07.006. PMID: 15607841.

Blow FC, Walton MA, Bohnert ASB, et al. A randomized controlled trial of brief interventions to reduce drug use among adults in a low-income urban emergency department: the HealthiER You study. Addiction. 2017;112(8):1395-405. doi: 10.1111/add.13773. PMID: 28127808.

Bonar EE, Walton MA, Barry KL, et al. Sexual HIV risk behavior outcomes of brief interventions for drug use in an inner-city emergency department: Secondary outcomes from a randomized controlled trial. Drug Alcohol Depend. 2018;183:217-24. doi: 10.1016/j.drugalcdep.2017.10.036. PMID: 29291549.

Bogenschutz MP, Donovan DM, Mandler RN, et al. Brief intervention for patients with problematic drug use presenting in emergency departments: a randomized clinical trial. JAMA Intern Med. 2014;174(11):1736-45. doi: 10.1001/jamainternmed.2014.4052. PMID: 25179753.

Bogenschutz MP, Donovan DM, Adinoff B, et al. Design of NIDA CTN Protocol 0047: screening, motivational assessment, referral, and treatment in emergency departments (SMART-ED). Am J Drug Alcohol Abuse. 2011;37(5):417-25. doi: 10.3109/00952990.2011.596971. PMID: 21854285.

Copeland J, Swift W, Roffman R, et al. A randomized controlled trial of brief cognitive-behavioral interventions for cannabis use disorder. J Subst Abuse Treat. 2001a;21(2):55-64; discussion 5-6. PMID: 11551733.

Copeland J, Swift W, Rees V. Clinical profile of participants in a brief intervention program for cannabis use disorder. J Subst Abuse Treat. 2001b;20(1):45-52. PMID: 11239727.

Cornish JW, Metzger D, Woody GE, et al. Naltrexone pharmacotherapy for opioid dependent federal probationers. J Subst Abuse Treat. 1997;14(6):529-34. PMID: 9437624.

D'Amico EJ, Parast L, Shadel WG, et al. Brief motivational interviewing intervention to reduce alcohol and marijuana use for at-risk adolescents in primary care. J Consult Clin Psychol. 2018;86(9):775-86. doi: 10.1037/ccp0000332. PMID: 30138016.

de Dios MA, Herman DS, Britton WB, et al. Motivational and mindfulness intervention for young adult female marijuana users. J Subst Abuse Treat. 2012;42(1):56-64. doi: 10.1016/j.jsat.2011.08.001. PMID: 21940136.

de Gee EA, Verdurmen JE, Bransen E, et al. A randomized controlled trial of a brief motivational enhancement for non-treatment-seeking adolescent cannabis users. J Subst Abuse Treat. 2014;47(3):181-8. PMID: 24969735.

Dembo R, Briones-Robinson R, Schmeidler J, et al. Brief intervention impact on truant youths' marijuana use: eighteen-month follow-up. J Child Adolesc Subst Abuse. 2016;25(1):18-32. doi: 10.1080/1067828X.2013.872068.

Dupont HB, Candel MJ, Kaplan CD, et al. Assessing the efficacy of MOTI-4 for reducing the use of cannabis among youth in the Netherlands: A randomized controlled trial. J Subst Abuse Treat. 2016;65:6-12. doi: 10.1016/j.jsat.2015.11.012. PMID: 26780988.

Fischer B, Jones W, Shuper P, et al. 12-month follow-up of an exploratory 'brief intervention' for high-frequency cannabis users among Canadian university students. Subst Abuse Treat Prev Policy. 2012;7:15. doi: 10.1186/1747-597x-7-15. PMID: 22538183.

Appendix A4. List of Included Studies

Fischer B, Dawe M, McGuire F, et al. Feasibility and impact of brief interventions for frequent cannabis users in Canada. J Subst Abuse Treat. 2013;44(1):132-8. doi: 10.1016/j.jsat.2012.03.006. PMID: 22520278.

Gates PJ, Norberg MM, Copeland J, et al. Randomized controlled trial of a novel cannabis use intervention delivered by telephone. Addiction. 2012;107(12):2149-58. doi: 10.1111/j.1360-0443.2012.03953.x. PMID: 22632139.

Gelberg L, Andersen RM, Afifi AA, et al. Project QUIT (Quit Using Drugs Intervention Trial): a randomized controlled trial of a primary care-based multi-component brief intervention to reduce risky drug use. Addiction. 2015;110(11):1777-90. doi: 10.1111/add.12993. PMID: 26471159.

Baumeister SE, Gelberg L, Leake BD, et al. Effect of a primary care based brief intervention trial among risky drug users on health-related quality of life. Drug Alcohol Depend. 2014;142:254-61. doi: 10.1016/j.drugalcdep.2014.06.034. PMID: 25042213.

Gelberg L, Andersen RM, Rico MW, et al. A pilot replication of QUIT, a randomized controlled trial of a brief intervention for reducing risky drug use, among Latino primary care patients. Drug Alcohol Depend. 2017;179:433-40. doi: 10.1016/j.drugalcdep.2017.04.022. PMID: 28844733.

Gruber VA, Delucchi KL, Kielstein A, et al. A randomized trial of 6-month methadone maintenance with standard or minimal counseling versus 21-day methadone detoxification. Drug Alcohol Depend. 2008;94(1-3):199-206. doi: 10.1016/j.drugalcdep.2007.11.021. PMID: 18243585.

Gryczynski J, O'Grady KE, Mitchell SG, et al. Immediate versus delayed computerized brief intervention for illicit drug misuse. J Addict Med. 2016;10(5):344-51. doi: 10.1097/ADM.0000000000000248. PMID: 27504925.

Guo S, Jiang Z, Wu Y. Efficacy of naltrexone hydrochloride for preventing relapse among opiate-dependent patients after detoxification. Hong Kong J Paediatr. 2001;11(4):2-8+28.

Hollister LE. Clinical evaluation of naltrexone treatment of opiate-dependent individuals. Report of the National Research Council Committee on Clinical Evaluation of Narcotic Antagonists. Arch Gen Psychiatry. 1978;35(3):335-40. PMID: 365122.

Humeniuk R, Ali R, Babor T, et al. A randomized controlled trial of a brief intervention for illicit drugs linked to the alcohol, smoking and substance involvement screening test (ASSIST) in clients recruited from primary health-care settings in four countries. Addiction. 2012;107(5):957-66. doi: 10.1111/j.1360-0443.2011.03740.x. PMID: 22126102.

Jones HE, Wong CJ, Tuten M, et al. Reinforcement-based therapy: 12-month evaluation of an outpatient drug-free treatment for heroin abusers. Drug Alcohol Depend. 2005;79(2):119-28. doi: 10.1016/j.drugalcdep.2005.01.006. PMID: 16002021.

Kakko J, Svanborg KD, Kreek MJ, et al. 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomised, placebo-controlled trial. Lancet. 2003;361(9358):662-8. PMID: 12606177.

Krook AL, Brors O, Dahlberg J, et al. A placebo-controlled study of high dose buprenorphine in opiate dependents waiting for medication-assisted rehabilitation in Oslo, Norway. Addiction. 2002;97(5):533-42. PMID: 12033654.

Krupitsky E, Nunes EV, Ling W, et al. Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomised trial. Lancet. 2011;377(9776):1506-13. doi: 10.1016/S0140-6736(11)60358-9. PMID: 21529928.

Krupitsky E, Zvartau E, Blokhina E, et al. Naltrexone with or without guanfacine for preventing relapse to opiate addiction in St. Petersburg, Russia. Drug Alcohol Depend. 2013;132(3):674-80. doi: 10.1016/j.drugalcdep.2013.04.021. PMID: 23683793.

Krupitsky EM, Zvartau EE, Masalov DV, et al. Naltrexone for heroin dependence treatment in St. Petersburg, Russia. J Subst Abuse Treat. 2004;26(4):285-94. PMID: 15182893.

Krupitsky EM, Zvartau EE, Masalov DV, et al. Naltrexone with or without fluoxetine for preventing relapse to heroin addiction in St. Petersburg, Russia. J Subst Abuse Treat. 2006;31(4):319-28. PMID: 17084785.

Krupski A, Joesch JM, Dunn C, et al. Testing the effects of brief intervention in primary care for problem drug use in a randomized controlled trial: rationale, design, and methods. Addict Sci Clin Pract. 2012;7:27. doi: 10.1186/1940-0640-7-27. PMID: 23237456.

Krupitsky E, Zvartau E, Blokhina E, et al. Anhedonia, depression, anxiety, and craving in opiate dependent patients stabilized on oral naltrexone or an extended release naltrexone implant. Am J Drug Alcohol Abuse. 2016;42(5):614-20. PMID: 27436632.

Appendix A4. List of Included Studies

Lee CM, Kilmer JR, Neighbors C, et al. Indicated prevention for college student marijuana use: a randomized controlled trial. J Consult Clin Psychol. 2013;81(4):702-9. doi: 10.1037/a0033285. PMID: 23750464.

Lee CM, Neighbors C, Kilmer JR, et al. A brief, web-based personalized feedback selective intervention for college student marijuana use: a randomized clinical trial. Psychol Addict Behav. 2010;24(2):265-73. doi: 10.1037/a0018859. PMID: 20565152.

Lerner A, Sigal M, Bacalu A, et al. A naltrexone double blind placebo controlled study in Israel. Isr J Psychiatry Relat Sci. 1992;29(1):36-43. PMID: 1568861.

Ling W, Casadonte P, Bigelow G, et al. Buprenorphine implants for treatment of opioid dependence: a randomized controlled trial. JAMA. 2010;304(14):1576-83. doi: 10.1001/jama.2010.1427. PMID: 20940383.

Litt MD, Kadden RM, Kabela-Cormier E, et al. Coping skills training and contingency management treatments for marijuana dependence: exploring mechanisms of behavior change. Addiction. 2008;103(4):638-48. doi: 10.1111/j.1360-0443.2008.02137.x. PMID: 18339108.

Kadden RM, Litt MD, Kabela-Cormier E, et al. Abstinence rates following behavioral treatments for marijuana dependence. Addict Behav. 2007;32(6):1220-36. doi: 10.1016/j.addbeh.2006.08.009. PMID: 16996224.

Litt MD, Kadden RM, Petry NM. Behavioral treatment for marijuana dependence: randomized trial of contingency management and self-efficacy enhancement. Addict Behav. 2013;38(3):1764-75. doi: 10.1016/j.addbeh.2012.08.011. PMID: 23254227.

Litt MD, Kadden RM, Stephens RS. Coping and self-efficacy in marijuana treatment: results from the marijuana treatment project. J Consult Clin Psychol. 2005;73(6):1015-25. doi: 10.1037/0022-006x.73.6.1015. PMID: 16392975.

Lozano BE, Stephens RS, Roffman RA. Abstinence and moderate use goals in the treatment of marijuana dependence. Addiction. 2006;101(11):1589-97. PMID: 17034438.

Marsden J, Stillwell G, Barlow H, 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(7):1014-26. PMID: 16771893.

Martin G, Copeland J. The adolescent cannabis check-up: randomized trial of a brief intervention for young cannabis users. J Subst Abuse Treat. 2008;34(4):407-14. PMID: 17869051.

Martino S, Ondersma SJ, Forray A, et al. A randomized controlled trial of screening and brief interventions for substance misuse in reproductive health. Am J Obstet Gynecol. 2018;218(3):322.e1-.e12. doi: 10.1016/j.ajog.2017.12.005. PMID: 29247636.

Mason M, Light J, Campbell L, et al. Peer network counseling with urban adolescents: a randomized controlled trial with moderate substance users. J Subst Abuse Treat. 2015;58:16-24. doi: 10.1016/j.jsat.2015.06.013. PMID: 26234955.

Mason MJ, Sabo R, Zaharakis NM. Peer network counseling as brief treatment for urban adolescent heavy cannabis users. J Stud Alcohol Drugs. 2017;78(1):152-7. PMID: 27936376.

McCambridge J, Slym RL, Strang J. Randomized controlled trial of motivational interviewing compared with drug information and advice for early intervention among young cannabis users. Addiction. 2008;103(11):1809-18. PMID: 18778385.

McCambridge J, Strang J. The efficacy of single-session motivational interviewing in reducing drug consumption and perceptions of drug-related risk and harm among young people: results from a multi-site cluster randomized trial. Addiction. 2004;99(1):39-52. PMID: 14678061.

McCambridge J, Strang J. Deterioration over time in effect of motivational interviewing in reducing drug consumption and related risk among young people. Addiction. 2005;100(4):470-8. PMID: 15784061.

Ondersma SJ, Svikis DS, Schuster CR. Computer-based brief intervention a randomized trial with postpartum women. Am J Prev Med. 2007;32(3):231-8. PMID: 17236741.

Ondersma SJ, Svikis DS, Thacker C, et al. Computer-delivered indirect screening and brief intervention for drug use in the perinatal period: a randomized trial. Drug Alcohol Depend. 2018;185:271-7. doi: 10.1016/j.drugalcdep.2017.12.022. PMID: 29482051.

Ondersma SJ, Svikis DS, Thacker LR, et al. Computer-delivered screening and brief intervention (e-SBI) for postpartum drug use: a randomized trial. J Subst Abuse Treat. 2014;46(1):52-9. doi: 10.1016/j.jsat.2013.07.013. PMID: 24051077.

Appendix A4. List of Included Studies

Palfai TP, Saitz R, Winter M, et al. Web-based screening and brief intervention for student marijuana use in a university health center: Pilot study to examine the implementation of eCHECKUP TO GO in different contexts. Addict Behav. 2014;39(9):1346-52. doi: 10.1016/j.addbeh.2014.04.025. PMID: 24845164.

Poblete F, Barticevic NA, Zuzulich MS, et al. A randomized controlled trial of a brief intervention for alcohol and drugs linked to the alcohol, smoking and substance involvement screening test (ASSIST) in primary health care in Chile. Addiction. 2017;112(8):1462-9. doi: 10.1111/add.13808. PMID: 28239995.

Rooke S, Copeland J, Norberg M, et al. Effectiveness of a self-guided web-based cannabis treatment program: randomized controlled trial. J Med Internet Res. 2013;15(2):e26. doi: 10.2196/jmir.2256. PMID: 23470329.

Rosenthal RN, Ling W, Casadonte P, et al. Buprenorphine implants for treatment of opioid dependence: randomized comparison to placebo and sublingual buprenorphine/naloxone. Addiction. 2013;108(12):2141-9. doi: 10.1111/add.12315. PMID: 23919595.

Roy-Byrne P, Bumgardner K, Krupski A, et al. Brief intervention for problem drug use in safety-net primary care settings: a randomized clinical trial. JAMA. 2014;312(5):492-501. doi: 10.1001/jama.2014.7860. PMID: 25096689.

Krupitsky E, Zvartau E, Blokhina E, et al. Randomized trial of long-acting sustained-release naltrexone implant vs oral naltrexone or placebo for preventing relapse to opioid dependence. Arch Gen Psychiatry. 2012;69(9):973-81. doi: 10.1001/archgenpsychiatry.2012.1a. PMID: 22945623.

Saitz R, Palfai TP, Cheng DM, et al. Screening and brief intervention for drug use in primary care: the ASPIRE randomized clinical trial. JAMA. 2014;312(5):502-13. doi: 10.1001/jama.2014.7862. PMID: 25096690.

Fuster D, Cheng DM, Wang N, et al. Brief intervention for daily marijuana users identified by screening in primary care: a subgroup analysis of the ASPIRE randomized clinical trial. Subst Abus. 2016;37(2):336-42. doi: 10.1080/08897077.2015.1075932. PMID: 26453188.

Kim TW, Bernstein J, Cheng DM, et al. Receipt of addiction treatment as a consequence of a brief intervention for drug use in primary care: a randomized trial. Addiction. 2016;112(5):818-27. doi: 10.1111/add.13701. PMID: 27886657.

San L, Pomarol G, Peri JM, et al. Follow-up after a six-month maintenance period on naltrexone versus placebo in heroin addicts. Br J Addict. 1991;86(8):983-90. PMID: 1912753.

Schaub MP, Wenger A, Berg O, et al. A web-based self-help intervention with and without chat counseling to reduce cannabis use in problematic cannabis users: three-arm randomized controlled trial. J Med Internet Res. 2015;17(10):e232. doi: 10.2196/jmir.4860. PMID: 26462848.

Schottenfeld RS, Chawarski MC, Mazlan M. Maintenance treatment with buprenorphine and naltrexone for heroin dependence in Malaysia: a randomised, double-blind, placebo-controlled trial. Lancet. 2008;371(9631):2192-200. doi: 10.1016/S0140-6736(08)60954-X. PMID: 18586174.

Schwartz RP, Jaffe JH, Highfield DA, et al. A randomized controlled trial of interim methadone maintenance: 10-month follow-up. Drug Alcohol Depend. 2007;86(1):30-6. PMID: 16793221.

Schwartz RP, Highfield DA, Jaffe JH, et al. A randomized controlled trial of interim methadone maintenance. Arch Gen Psychiatry. 2006;63(1):102-9. PMID: 16389204.

Schwartz RP, Jaffe JH, O'Grady KE, et al. Interim methadone treatment: impact on arrests. Drug Alcohol Depend. 2009;103(3):148-54. doi: 10.1016/j.drugalcdep.2009.03.007. PMID: 19443133.

Shufman EN, Porat S, Witztum E, et al. The efficacy of naltrexone in preventing reabuse of heroin after detoxification. Biol Psychiatry. 1994;35(12):935-45. PMID: 8080893.

Stein MD, Hagerty CE, Herman DS, et al. A brief marijuana intervention for non-treatment-seeking young adult women. J Subst Abuse Treat. 2011;40(2):189-98. doi: 10.1016/j.jsat.2010.11.001. PMID: 21185685.

Stein MD, Herman DS, Anderson BJ. A motivational intervention trial to reduce cocaine use. J Subst Abuse Treat. 2009;36(1):118-25.

Stella L, D'Ambra C, Mazzeo F, et al. Naltrexone plus benzodiazepine aids abstinence in opioid-dependent patients. Life Sci. 2005;77(21):2717-22. PMID: 15979652.

Appendix A4. List of Included Studies

Stephens RS, Roffman RA, Curtin L. Comparison of extended versus brief treatments for marijuana use. J Consult Clin Psychol. 2000;68(5):898-908. PMID: 11068976.

Stephens RS, Roffman RA, Fearer SA, et al. The marijuana check-up: promoting change in ambivalent marijuana users. Addiction. 2007;102(6):947-57. doi: 10.1111/j.1360-0443.2007.01821.x. PMID: 17523990.

Tait RJ, McKetin R, Kay-Lambkin F, et al. Six-month outcomes of a Web-based intervention for users of amphetamine-type stimulants: randomized controlled trial. J Med Internet Res. 2015;17(4):e105. doi: 10.2196/jmir.3778. PMID: 25925801.

Tzilos Wernette G, Plegue M, Kahler CW, et al. A pilot randomized controlled trial of a computer-delivered brief intervention for substance use and risky sex during pregnancy. J Womens Health (Larchmt). 2018;27(1):83-92. doi: 10.1089/jwh.2017.6408. PMID: 28981379.

Walton MA, Bohnert K, Resko S, et al. Computer and therapist based brief interventions among cannabis-using adolescents presenting to primary care: one year outcomes. Drug Alcohol Depend. 2013;132(3):646-53. doi: 10.1016/j.drugalcdep.2013.04.020. PMID: 23711998.

Watkins KE, Ober AJ, Lamp K, et al. Collaborative care for opioid and alcohol use disorders in primary care: the SUMMIT randomized clinical trial. JAMA Intern Med. 2017;177(10):1480-8. doi: 10.1001/jamainternmed.2017.3947. PMID: 28846769.

Woolard R, Baird J, Longabaugh R, et al. Project reduce: reducing alcohol and marijuana misuse: effects of a brief intervention in the emergency department. Addict Behav. 2013;38(3):1732-9. doi: 10.1016/j.addbeh.2012.09.006. PMID: 23261491.

Yonkers KA, Forray A, Howell HB, et al. Motivational enhancement therapy coupled with cognitive behavioral therapy versus brief advice: a randomized trial for treatment of hazardous substance use in pregnancy and after delivery. Gen Hosp Psychiatry. 2012;34(5):439-49. doi: 10.1016/j.genhosppsych.2012.06.002. PMID: 22795046.

Zahradnik A, Otto C, Crackau B, et al. Randomized controlled trial of a brief intervention for problematic prescription drug use in non-treatment-seeking patients. Addiction. 2009;104(1):109-17. doi: 10.1111/j.1360-0443.2008.02421.x. PMID: 19133895.

Otto C, Crackau B, Lohrmann I, et al. Brief intervention in general hospital for problematic prescription drug use: 12-month outcome. Drug Alcohol Depend. 2009;105(3):221-6. doi: 10.1016/j.drugalcdep.2009.07.010. PMID: 19726140.

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Abbott PJ, Weller SB, Delaney HD, et al. Community reinforcement approach in the treatment of opiate addicts. Am J Drug Alcohol Abuse. 1998;24(1):17-30. PMID: 9513627. Excluded: Wrong comparator

Aboujaoude E, Salame WO. Naltrexone: A pan-addiction treatment? CNS Drugs. 2016;30(8):719-33. doi: 10.1007/s40263-016-0373-0. PMID: 27401883. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Abrahms JL. A Cognitive-behavioural versus nondirective group treatment program for opioid addicted persons: an adjunct to methadone maintenance. Int J Addict. 1979;14(4):503-11. Excluded: Wrong comparator

Abramowitz SI, Pantleo PM. The effectiveness of brief methadone withdrawal among urban opiate addicts. Int J Addict. 1972;7(4):629-35. doi: 10.3109/10826087209028116. PMID: 4659588. Excluded: Wrong study design for key question

Achmad YM, Istiqomah AN, Iskandar S, et al. Integration of methadone maintenance treatment and HIV care for injecting drug users: a cohort study in Bandung, Indonesia. Acta Med Indones. 2009;41 Suppl 1:23-7. PMID: 19920294. Excluded: Wrong study design for key question

Adi Y, Juarez-Garcia A, Wang D, et al. Oral naltrexone as a treatment for relapse prevention in formerly opioid-dependent drug users: a systematic review and economic evaluation. Health Technol Assess. 2007;11(6):iii-iv, 1-85. PMID: 17280624. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Aghataher A, Mahani KN. The effect of rational emotive behavior group therapy on self-concept and depression of self-introduced drug abusers referred to ofogh addiction treatment center in Zarand (Kerman, Iran). Biomed Pharmacol J. 2014;7(1):317-23. doi: 10.13005/bpj/493. Excluded: Wrong country

Ahmad-Abadi FK, Maarefvand M, Aghaei H, et al. Effectiveness of Satir-informed family-therapy on the codependency of drug dependents' family members in Iran: A randomized controlled trial. J Evid Inf Soc Work. 2017;14(4):301-10. doi: 10.1080/23761407.2017.1331147. PMID: 28644761. Excluded: Wrong country

Ahmadi J. A controlled trial of buprenorphine treatment for opium dependence: the first experience from Iran. Drug Alcohol Depend. 2002;66(2):111-4. PMID: 11906798. Excluded: <3 month followup duration

Ahmadi J, Ahmadi K, Ohaeri J. Controlled, randomized trial in maintenance treatment of intravenous buprenorphine dependence with naltrexone, methadone or buprenorphine: a novel study. Eur J Clin Invest. 2003;33(9):824-9. PMID: 12925043. Excluded: Wrong comparator

Ahmadi J, Babaee-Beigi M, Alishahi M, et al. Twelve-month maintenance treatment of opium-dependent patients. J Subst Abuse Treat. 2004;26(1):363-6. PMID: 14698800. Excluded: Wrong study design for key question

Ainscough TS, McNeill A, Strang J, et al. Contingency management interventions for non-prescribed drug use during treatment for opiate addiction: A systematic review and meta-analysis. Drug Alcohol Depend. 2017;178:318-39. doi: 10.1016/j.drugalcdep.2017.05.028. PMID: 28688295. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Alessi SM, Hanson T, Wieners M, et al. Low-cost contingency management in community clinics: delivering incentives partially in group therapy. Exp Clin Psychopharmacol. 2007;15(3):293-300. PMID: 17563216. Excluded: Incarcerated population

Alessi SM, Rash C, Petry NM. Contingency management is efficacious and improves outcomes in cocaine patients with pretreatment marijuana use. Drug Alcohol Depend. 2011;118(1):62-7. doi: 10.1016/j.drugalcdep.2011.03.001. PMID: 21440999. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Alexander JF, Parsons BV. Short-term behavioral intervention with delinquent families: Impact on family process and recidivism. J Abnorm Psychol. 1973;81(3):219-25. PMID: 4710043. Excluded: Wrong outcome

Ali S, Tahir B, Jabeen S, et al. Methadone treatment of opiate addiction: A systematic review of comparative studies. Innov Clin Neurosci. 2017;14(7-8):8-19. PMID: 29616150. Excluded: Wrong comparator

Amass L, Bickel WK, Higgins ST, et al. Alternate-day dosing during buprenorphine treatment of opioid dependence. Life Sci. 1994;54(17):1215-28. PMID: 8164503. Excluded: Wrong comparator

Amass L, Kamien JB, Mikulich SK. Efficacy of daily and alternate-day dosing regimens with the combination buprenorphine-naloxone tablet. Drug Alcohol Depend. 2000;58(1-2):143-52. PMID: 10669065. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Amato L, Davoli M, Perucci CA, et al. An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. J Subst Abuse Treat. 2005;28(4):321-9. PMID: 15925266. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Amato L, Minozzi S, Davoli M, et al. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. Cochrane Database Syst Rev. 2011 (10):CD004147. doi: 10.1002/14651858.CD004147.pub4. PMID: 21975742. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Amato L, Minozzi S, Davoli M, et al. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. Cochrane Database Syst Rev. 2004 (4):CD004147. PMID: 15495081. Excluded: Wrong comparator

Andrade LF, Alessi SM, Petry NM. The impact of contingency management on quality of life among cocaine abusers with and without alcohol dependence. Am J Addict. 2012;21(1):47-54. doi: 10.1111/j.1521-0391.2011.00185.x. PMID: 22211346. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Anglin M. The efficacy of civil commitment in treating narcotics addiction. J Drug Issues. 1988;18(4):527-45. doi: 10.1177/002204268801800403. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Annis HM, Peachey JE. The use of calcium carbimide in relapse prevention counselling: results of a randomized controlled trial. Br J Addict. 1992;87(1):63-72. PMID: 1543940. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Anton RF, Moak DH, Latham P, et al. Naltrexone combined with either cognitive behavioral or motivational enhancement therapy for alcohol dependence. J Clin Psychopharmacol. 2005;25(4):349-57. PMID: 16012278. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Anton RF, O'Malley SS, Ciraulo DA, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. JAMA. 2006;295(17):2003-17. doi: 10.1001/jama.295.17.2003. PMID: 16670409. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Arlt VK. Clinician mindfulness, motivational interviewing and treatment outcomes for substance-using adolescents. Dissertation Abstracts International: Section B: The Sciences and Engineering. 2017;78(2-B(E)):No Pagination Specified. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Arndt IO, Dorozynsky L, Woody GE, et al. Desipramine treatment of cocaine dependence in methadone-maintained patients. Arch Gen Psychiatry. 1992;49(11):888-93. PMID: 1444727. Excluded: Non-FDA approved pharmacologic intervention

Ashraf I, Ashraf S, Asif JA, et al. Metabolic effects of opiate use during pregnancy: A reappraisal. IMJ. 2016;23(5):481-4. Excluded: Wrong study design for key question

Assadi SM, Radgoodarzi R, Ahmadi-Abhari SA. Baclofen for maintenance treatment of opioid dependence: a randomized double-blind placebo-controlled clinical trial [ISRCTN32121581]. BMC Psychiatry. 2003;3:16. doi: 10.1186/1471-244x-3-16. PMID: 14624703. Excluded: Non-FDA approved pharmacologic intervention

Aubrey LL. Motivational interviewing with adolescents presenting for outpatient substance abuse treatment: ProQuest Information & Learning; 1998. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Avants SK, Margolin A, Holford TR, et al. A randomized controlled trial of auricular acupuncture for cocaine dependence. Arch Intern Med. 2000;160(15):2305-12. PMID: 10927727. Excluded: Non-FDA approved pharmacologic intervention

Avants SK, Margolin A, Usubiaga MH, et al. Targeting HIV-related outcomes with intravenous drug users maintained on methadone: a randomized clinical trial of a harm reduction group therapy. J Subst Abuse Treat. 2004;26(2):67-78. PMID: 15050083. Excluded: Wrong comparator

Ayres R, Ingram J, Rees A, et al. Enhancing motivation within a rapid opioid substitution treatment feasibility RCT: A nested qualitative study. Subst Abuse Treat Prev Policy. 2014;9:44. doi: 10.1186/1747-597X-9-44. PMID: 25407020. Excluded: Wrong outcome

Azrin N, Donohue B, Besalel V, et al. Youth drug abuse treatment: A controlled outcome study. J Child Adolesc Subst Abuse. 1994;3(3):1-16. Excluded: Wrong comparator

Azrin NH, Acierno R, Kogan ES, et al. Follow-up results of supportive versus behavioral therapy for illicit drug use. Behav Res Ther. 1996;34(1):41-6. PMID: 8561763. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Azrin NH, Donohue B, Teichner GA, et al. A controlled evaluation and description of individual-cognitive problem solving and family-behavior therapies in dually-diagnosed conduct-disordered and substance-dependent youth. J Child Adolesc Subst Abuse. 2001;11(1):1-43. Excluded: Wrong comparator

Azrin NH, McMahon PT, Donohue B, et al. Behavior therapy for drug abuse: a controlled treatment outcome study. Behav Res Ther. 1994;32(8):857-66. PMID: 7993330. Excluded: Wrong comparator

Babowitch JD, Antshel KM. Adolescent treatment outcomes for comorbid depression and substance misuse: A systematic review and synthesis of the literature. J Affect Disord. 2016;201:25-33. doi: 10.1016/j.jad.2016.04.018. PMID: 27156096. Excluded: Other wrong population (e.g., schizophrenia focus)

Back SE, Gentilin S, Brady KT. Cognitive-behavioral stress management for individuals with substance use disorders: a pilot study. J Nerv Ment Dis. 2007;195(8):662-8. PMID: 17700298. Excluded: Wrong outcome

Baer JS, Garrett SB, Beadnell B, et al. Brief motivational intervention with homeless adolescents: evaluating effects on substance use and service utilization. Psychol Addict Behav. 2007;21(4):582-6. PMID: 18072842. Excluded: Other wrong population (e.g., schizophrenia focus)

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Baewert A, Gombas W, Schindler SD, et al. Influence of peak and trough levels of opioid maintenance therapy on driving aptitude. Eur Addict Res. 2007;13(3):127-35. PMID: 17570908. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Bahrami S, Asghari F. A controlled trial of acceptance and commitment therapy for addiction severity in methamphetamine users: Preliminary study. Arch Psychiatry Psychother. 2017;19(2):49-55. doi: 10.12740/APP/68159. Excluded: Wrong country

Baker TE, Chang G. The use of auricular acupuncture in opioid use disorder: A systematic literature review. Am J Addict. 2016;25(8):592-602. doi: 10.1111/ajad.12453. PMID: 28051842. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Bale RN, Van Stone WW, Kuldau JM, et al. Therapeutic communities vs methadone maintenance. A prospective controlled study of narcotic addiction treatment: design and one-year follow-up. Arch Gen Psychiatry. 1980;37(2):179-93. PMID: 7352849. Excluded: Wrong comparator

Ball SA, Martino S, Nich C, et al. Site matters: multisite randomized trial of motivational enhancement therapy in community drug abuse clinics. J Consult Clin Psychol. 2007;75(4):556-67. PMID: 17663610. Excluded: <70% drug misuse or likely majority alcohol

Bandstra ES. Maternal opioid treatment: Human experimental research (MOTHER) Study: maternal, fetal and neonatal outcomes from secondary analyses. Addiction. 2012;107 Suppl 1:1-4. doi: 10.1111/j.1360-0443.2012.04059.x. PMID: 23106922. Excluded: Wrong comparator

Bandstra ES, Morrow CE, Mansoor E, et al. Prenatal drug exposure: infant and toddler outcomes. J Addict Dis. 2010;29(2):245-58. doi: 10.1080/10550881003684871. PMID: 20407980. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Bao YP, Liu ZM, Epstein DH, et al. A meta-analysis of retention in methadone maintenance by dose and dosing strategy. Am J Drug Alcohol Abuse. 2009;35(1):28-33. doi: 10.1080/00952990802342899. PMID: 19152203. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Baranok N. Treatment of family codependency as a factor promoting remission in opiate addicts. The international psychiatry and behavioral neurosciences yearbook - 2012, Vol 2. Hauppauge, NY: Nova Biomedical Books; US; 2013:275-80. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Barlow J, Sembi S, Gardner F, et al. An evaluation of the parents under pressure programme: a study protocol for an RCT into its clinical and cost effectiveness. Trials. 2013;14:210. doi: 10.1186/1745-6215-14-210. PMID: 23841920. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Barnett PG, Masson CL, Sorensen JL, et al. Linking opioid-dependent hospital patients to drug treatment: Health care use and costs 6 months after randomization. Addiction. 2006;101(12):1797-804. PMID: 17156179. Excluded: Wrong comparator

Barrett K, Chang YP. Behavioral interventions targeting chronic pain, depression, and substance use disorder in primary care. J Nurs Scholarsh. 2016;48(4):345-53. doi: 10.1111/jnu.12213. PMID: 27149578. Excluded: Other wrong population (e.g., schizophrenia focus)

Batki SL, Washburn AM, Delucchi K, et al. A controlled trial of fluoxetine in crack cocaine dependence. Drug Alcohol Depend. 1996;41(2):137-42. PMID: 8809502. Excluded: Non-FDA approved pharmacologic intervention

Bawor M, Dennis BB, Bhalerao A, et al. Sex differences in outcomes of methadone maintenance treatment for opioid use disorder: A systematic review and meta-analysis. CMAJ Open. 2015;3(3):E344-51. doi: 10.9778/cmajo.20140089. PMID: 26457294. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Beck AK, Forbes E, Baker AL, et al. Systematic review of SMART recovery: Outcomes, process variables, and implications for research. Psychol Addict Behav. 2017;31(1):1-20. doi: 10.1037/adb0000237. PMID: 28165272. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Becker SJ, Curry JF. Outpatient interventions for adolescent substance abuse: a quality of evidence review. J Consult Clin Psychol. 2008;76(4):531-43. doi: 10.1037/0022-006X.76.4.531. PMID: 18665683. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Beebe KL, Chavoustie S, Ling W, et al. Buprenorphine implants for the treatment of opioid dependence: Six and 12 month outcomes. Neuropsychopharmacology. 2012;38(2). Excluded: Results reported elsewhere, duplicate results

Beitel M, Genova M, Schuman-Olivier Z, et al. Reflections by inner-city drug users on a Buddhist-based spirituality-focused therapy: a qualitative study. Am J Orthopsychiatry. 2007;77(1):1-9. PMID: 17352579. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Bell J. Buprenorphine in the treatment of heroin addiction. Dusunen Adam. 2012;25(2):93-100. doi: 10.5350/DAJPN20122502001. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Bell J, Hall W, Byth K. Changes in criminal activity after entering methadone maintenance. Br J Addict. 1992;87(2):251-8. PMID: 1313321. Excluded: Wrong study design for key question

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Bell MD, Laws HB, Petrakis IB. A randomized controlled trial of cognitive remediation and work therapy in the early phase of substance use disorder recovery for older veterans: Neurocognitive and substance use outcomes. Psychiatr Rehabil J. 2017;40(1):94-102. doi: 10.1037/prj0000211. PMID: 27732034. Excluded: Wrong comparator

Bellack AS, Bennett ME, Gearon JS, et al. A randomized clinical trial of a new behavioral treatment for drug abuse in people with severe and persistent mental illness. Arch Gen Psychiatry. 2006;63(4):426-32. doi: 10.1001/archpsyc.63.4.426. PMID: 16585472. Excluded: Other wrong population (e.g., schizophrenia focus)

Benishek LA, Dugosh KL, Kirby KC, et al. Prize-based contingency management for the treatment of substance abusers: a meta-analysis. Addiction. 2014;109(9):1426-36. doi: 10.1111/add.12589. PMID: 24750232. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Bennett GA, Withers J, Thomas PW, et al. A randomised trial of early warning signs relapse prevention training in the treatment of alcohol dependence. Addict Behav. 2005;30(6):1111-24. doi: 10.1016/j.addbeh.2004.10.008. PMID: 15925121. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Berman AH, Wennberg P, Sinadinovic K. Changes in mental and physical well-being among problematic alcohol and drug users in 12-month Internet-based intervention trials. Psychol Addict Behav. 2015;29(1):97-105. doi: 10.1037/a0038420. PMID: 25664387. Excluded: <70% drug misuse or likely majority alcohol

Bernard JP, Havnes I, Slordal L, et al. Methadone-related deaths in Norway. Forensic Sci Int. 2013;224(1-3):111-6. doi: 10.1016/j.forsciint.2012.11.010. PMID: 23246070. Excluded: Wrong study design for key question

Bernstein SL, D'Onofrio G. Screening, treatment initiation, and referral for substance use disorders. Addict Sci Clin Pract. 2017;12(1):18. doi: 10.1186/s13722-017-0083-z. PMID: 28780906. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Bertrand K, Roy E, Vaillancourt E, et al. Randomized controlled trial of motivational interviewing for reducing injection risk behaviours among people who inject drugs. Addiction. 2015;110(5):832-41. doi: 10.1111/add.12867. PMID: 25641704. Excluded: Wrong comparator

Bickel WK, Amass L, Higgins ST, et al. Effects of adding behavioral treatment to opioid detoxification with buprenorphine. J Consult Clin Psychol. 1997;65(5):803-10. PMID: 9337499. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Bickel WK, Marsch LA, Buchhalter AR, et al. Computerized behavior therapy for opioid-dependent outpatients: a randomized controlled trial. Exp Clin Psychopharmacol. 2008;16(2):132-43. doi: 10.1037/1064-1297.16.2.132. PMID: 18489017. Excluded: Wrong comparator

Binder T, Vavrinkova B. Prospective randomised comparative study of the effect of buprenorphine, methadone and heroin on the course of pregnancy, birthweight of newborns, early postpartum adaptation and course of the neonatal abstinence syndrome (NAS) in women followed up in the outpatient department. Neuro Endocrinol Lett. 2008;29(1):80-6. PMID: 18283247. Excluded: Wrong comparator

Blokhina E, Krupitsky E, Bushara N, et al. Implantable and oral naltrexone for preventing relapse in opiate addicts: A psychometric evaluation. Drug Alcohol Depend. 2015;146(14). Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Blow F, Bohnert AS, Ignacio R, et al. Efficacy of computer and therapist brief interventions for drug users. Drug Alcohol Depend. 2015;156(13). Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Blumberg D, Carrizales F, Kazanis W, et al. Changes in quality of life in cocaine-dependent participants provided treatment with buprenorphine + naloxone & extended release naltrexone. Drug Alcohol Depend. 2017;171. Excluded: Non-FDA approved pharmacologic intervention

Bogenschutz MP, Rice SL, Tonigan J, et al. 12-step facilitation for the dually diagnosed: A randomized clinical trial. J Subst Abuse Treat. 2014;46(4):403-11. doi: 10.1016/j.jsat.2013.12.009. PMID: 24462479. Excluded: Other wrong population (e.g., schizophrenia focus)

Bohnert AS, Blow F, Cunningham R, et al. A randomized clinical trial of a behavioral intervention to reduce opioid overdose risk behavior. Drug Alcohol Depend. 2015;156(13). Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Bohnert ASB, Bonar EE, Cunningham R, et al. A pilot randomized clinical trial of an intervention to reduce overdose risk behaviors among emergency department patients at risk for prescription opioid overdose. Drug Alcohol Depend. 2016;163:40-7. doi: 10.1016/j.drugalcdep.2016.03.018. PMID: 27062245. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Bonsack C, Gibellini Manetti S, Favrod J, et al. Motivational intervention to reduce cannabis use in young people with psychosis: a randomized controlled trial. Psychother Psychosom. 2011;80(5):287-97. doi: 10.1159/000323466. PMID: 21646823. Excluded: Other wrong population (e.g., schizophrenia focus)

Bowen S, Chawla N, Collins SE, et al. Mindfulness-based relapse prevention for substance use disorders: a pilot efficacy trial. Substance Abuse. 2009;30(4):295-305. doi: 10.1080/08897070903250084. PMID: 19904665. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Bowen S, Witkiewitz K, Clifasefi SL, et al. Relative efficacy of mindfulness-based relapse prevention, standard relapse prevention, and treatment as usual for substance use disorders: a randomized clinical trial. JAMA Psychiatry. 2014;71(5):547-56. PMID: 24647726. Excluded: Wrong comparator

Bradford A, Hurley F, Golondzowski O, et al. Interim report on clinic intake and safety data collected from 17 NIDA-funded naltrexone studies. NIDA Res Monogr. 1976 (9):163-71. PMID: 794717. Excluded: Wrong study design for key question

Brewer S, Godley MD, Hulvershorn LA. Treating mental health and substance use disorders in adolescents: What is on the menu? Curr Psychiatry Rep. 2017;19(1)doi: 10.1007/s11920-017-0755-0. PMID: 28120255. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Brigham GS, Slesnick N, Winhusen TM, et al. A randomized pilot clinical trial to evaluate the efficacy of community reinforcement and family training for treatment retention (CRAFT-T) for improving outcomes for patients completing opioid detoxification. Drug Alcohol Depend. 2014;138:240-3. doi: 10.1016/j.drugalcdep.2014.02.013. PMID: 24656054. Excluded: Other wrong population (e.g., schizophrenia focus)

Britton PC, Conner KR. Suicide attempts within 12 months of treatment for substance use disorders. Suicide Life Threat Behav. 2010;40(1):14-21. doi: 10.1521/suli.2010.40.1.14. PMID: 20170258. Excluded: Wrong study design for key question

Brogly SB, Saia KA, Walley AY, et al. Prenatal buprenorphine versus methadone exposure and neonatal outcomes: systematic review and meta-analysis. Am J Epidemiol. 2014;180(7):673-86. doi: 10.1093/aje/kwu190. PMID: 25150272. Excluded: Wrong comparator

Brooner RK, Kidorf MS, King VL, et al. Behavioral contingencies improve counseling attendance in an adaptive treatment model. J Subst Abuse Treat. 2004;27(3):223-32. PMID: 15501375. Excluded: Wrong comparator

Brown HL, Britton KA, Mahaffey D, et al. Methadone maintenance in pregnancy: a reappraisal. Am J Obstet Gynecol. 1998;179(2):459-63. PMID: 9731853. Excluded: Wrong study design for key question

Brown SM. A mindfulness-based intervention to improve family functioning among child welfare-involved families with substance use. Dissertation Abstracts International Section A: Humanities and Social Sciences. 2016;77(11-A(E)):No Pagination Specified. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Brown TG, Seraganian P, Tremblay J, et al. Matching substance abuse aftercare treatments to client characteristics. Addict Behav. 2002;27(4):585-604. PMID: 12188594. Excluded: Wrong comparator

Brown TL, Henggeler SW, Schoenwald SK, et al. Multisystemic treatment of substance abusing and dependent juvenile delinquents: Effects on school attendance at posttreatment and 6-month follow-up. Child Serv Soc Pol Res Pract. 1999;2(2):81-93. Excluded: Other wrong population (e.g., schizophrenia focus)

Budney AJ, Higgins ST, Radonovich KJ, et al. Adding voucher-based incentives to coping skills and motivational enhancement improves outcomes during treatment for marijuana dependence. J Consult Clin Psychol. 2000;68(6):1051-61. PMID: 11142539. Excluded: Wrong comparator

Budney AJ, Higgins ST, Radotrovich KJ, et al. Abstinence-based vouchers increase marijuana abstinence during outpatient treatment for marijuana dependence. NIDA Res Monogr. 2000. Excluded: Wrong comparator

Budney AJ, Moore BA, Rocha HL, et al. Clinical trial of abstinence-based vouchers and cognitive-behavioral therapy for cannabis dependence. J Consult Clin Psychol. 2006;74(2):307-16. doi: 10.1037/0022-006x.4.2.307. PMID: 16649875. Excluded: Wrong comparator

Budney AJ, Vandrey RG, Stanger C. [Pharmacological and psychosocial interventions for cannabis use disorders]. Rev Bras Psiquiatr. 2010;32 Suppl 1:S46-55. PMID: 20512270. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Burch AE, Rash CJ, Petry NM. Cocaine-using substance abuse treatment patients with and without HIV respond well to contingency management treatment. J Subst Abuse Treat. 2017;77:21-5. doi: 10.1016/j.jsat.2017.03.001. PMID: 28476266. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Busch S, Hawk K, Fiellin D, et al. Health service use in a randomized clinical trial comparing three methods of emergency department interventions for opioid dependence. Drug Alcohol Depend. 2015;156(13). Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Calsyn DA, Crits-Christoph P, Hatch-Maillette MA, et al. Reducing sex under the influence of drugs or alcohol for patients in substance abuse treatment. Addiction. 2010;105(1):100-8. doi: 10.1111/j.1360-0443.2009.02812.x. PMID: 20078464. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Calsyn DA, Hatch-Maillette M, Tross S, et al. Motivational and skills training HIV/sexually transmitted infection sexual risk reduction groups for men. J Subst Abuse Treat. 2009;37(2):138-50. doi: 10.1016/j.jsat.2008.11.008. PMID: 19150206. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Campbell AN, Nunes EV, Matthews AG, et al. "Internet-delivered treatment for substance abuse: A multisite randomized controlled trial": Correction. Am J Psychiatry. 2014;171(12):1339-40. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Campbell AN, Nunes EV, Matthews AG, et al. Internet-delivered treatment for substance abuse: a multisite randomized controlled trial. Am J Psychiatry. 2014;171(6):683-90. doi: 10.1176/appi.ajp.2014.13081055. PMID: 24700332. Excluded: Wrong comparator

Campbell AN, Nunes EV, Pavlicova M, et al. Gender-based outcomes and acceptability of a computer-assisted psychosocial intervention for substance use disorders. J Subst Abuse Treat. 2015;53:9-15. doi: 10.1016/j.jsat.2014.12.006. PMID: 25613105. Excluded: Wrong outcome

Carney T, Myers BJ, Louw J, et al. Brief school-based interventions and behavioural outcomes for substance-using adolescents. Cochrane Database Syst Rev. 2016 (1)doi: 10.1002/14651858.CD008969.pub3. PMID: 26787125. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Carroll KM, Ball SA, Martino S, et al. Computer-assisted delivery of cognitive-behavioral therapy for addiction: a randomized trial of CBT4CBT. Am J Psychiatry. 2008;165(7):881-8. doi: 10.1176/appi.ajp.2008.07111835. PMID: 18450927. Excluded: Wrong comparator

Carroll KM, Ball SA, Martino S, et al. Enduring effects of a computer-assisted training program for cognitive behavioral therapy: A 6-month follow-up of CBT4CBT. Drug Alcohol Depend. 2009;100(1-2):178-81. doi: 10.1016/j.drugalcdep.2008.09.015. PMID: 19041197. Excluded: Wrong comparator

Carroll KM, Ball SA, Nich C, et al. Motivational interviewing to improve treatment engagement and outcome in individuals seeking treatment for substance abuse: a multisite effectiveness study. Drug Alcohol Depend. 2006;81(3):301-12. doi: 10.1016/j.drugalcdep.2005.08.002. PMID: 16169159. Excluded: <70% drug misuse or likely majority alcohol

Carroll KM, Ball SA, Nich C, et al. Targeting behavioral therapies to enhance naltrexone treatment of opioid dependence: efficacy of contingency management and significant other involvement. Arch Gen Psychiatry. 2001;58(8):755-61. PMID: 11483141. Excluded: Wrong comparator

Carroll KM, Easton CJ, Nich C, et al. The use of contingency management and motivational/skills-building therapy to treat young adults with marijuana dependence. J Consult Clin Psychol. 2006;74(5):955-66. doi: 10.1037/0022-006x.74.5.955. PMID: 17032099. Excluded: Wrong comparator

Carroll KM, Martino S, Ball SA, et al. A multisite randomized effectiveness trial of motivational enhancement therapy for Spanish-speaking substance users. J Consult Clin Psychol. 2009;77(5):993-9. doi: 10.1037/a0016489. PMID: 19803579. Excluded: <70% drug misuse or likely majority alcohol

Carroll KM, Nich C, Ball SA, et al. Treatment of cocaine and alcohol dependence with psychotherapy and disulfiram. Addiction. 1998;93(5):713-27. PMID: 9692270. Excluded: Wrong comparator

Carroll KM, Onken LS. Behavioral therapies for drug abuse. Am J Psychiatry. 2005;162(8):1452-60. doi: 10.1176/appi.ajp.162.8.1452. PMID: 16055766. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Carroll KM, Rounsaville BJ, Nich C, et al. One-year follow-up of psychotherapy and pharmacotherapy for cocaine dependence. Delayed emergence of psychotherapy effects. Arch Gen Psychiatry. 1994;51(12):989-97. PMID: 7979888. Excluded: Wrong comparator

Carroll KM, Sinha R, Nich C, et al. Contingency management to enhance naltrexone treatment of opioid dependence: a randomized clinical trial of reinforcement magnitude. Exp Clin Psychopharmacol. 2002;10(1):54-63. PMID: 11866252. Excluded: Wrong comparator

Castells X, Cunill R, PerezMana C, et al. Psychostimulant drugs for cocaine dependence. Cochrane Database Syst Rev. 2016 (9)doi: 10.1002/14651858.CD007380.pub4. PMID: 27670244. Excluded: Non-FDA approved pharmacologic intervention

Centers for Disease C, Prevention. Integrated prevention services for HIV infection, viral hepatitis, sexually transmitted diseases, and tuberculosis for persons who use drugs illicitly: summary guidance from CDC and the U.S. Department of Health and Human Services. MMWR Recomm Rep. 2012;61(RR-5):1-40. PMID: 23135062. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Chaparro LE, Furlan AD, Deshpande A, et al. Opioids compared to placebo or other treatments for chronic low-back pain. Cochrane Database Syst Rev. 2013 (8):CD004959. doi: 10.1002/14651858.CD004959.pub4. PMID: 23983011. Excluded: Other wrong population (e.g., schizophrenia focus)

Chaparro LE, Furlan AD, Deshpande A, et al. Opioids compared with placebo or other treatments for chronic low back pain: an update of the Cochrane review.[Reprint of Cochrane Database Syst Rev. 2013;8:CD004959; PMID: 23983011]. Spine. 2014;39(7):556-63. doi: 10.1097/BRS.0000000000000249. PMID: 24480962. Excluded: Other wrong population (e.g., schizophrenia focus)

Chatters R, Cooper K, Day E, et al. Psychological and psychosocial interventions for cannabis cessation in adults: A systematic review. Addict Res Theory. 2016;24(2):93-110. doi: 10.3109/16066359.2015.1073719. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Chawarski MC, Mazlan M, Schottenfeld RS. Behavioral drug and HIV risk reduction counseling (BDRC) with abstinence-contingent take-home buprenorphine: a pilot randomized clinical trial. Drug Alcohol Depend. 2008;94(1-3):281-4. doi: 10.1016/j.drugalcdep.2007.11.008. PMID: 18164145. Excluded: Wrong comparator

Chawarski MC, Zhou W, Schottenfeld RS. Behavioral drug and HIV risk reduction counseling (BDRC) in MMT programs in Wuhan, China: a pilot randomized clinical trial. Drug Alcohol Depend. 2011;115(3):237-9. doi: 10.1016/j.drugalcdep.2010.09.024. PMID: 21159452. Excluded: Wrong comparator

Chen W, Hong Y, Zou X, et al. Effectiveness of prize-based contingency management in a methadone maintenance program in China. Drug Alcohol Depend. 2013;133(1):270-4. doi: 10.1016/j.drugalcdep.2013.05.028. PMID: 23831409. Excluded: Wrong comparator

Cheng AL, Lin H, Kasprow W, et al. Impact of supported housing on clinical outcomes: analysis of a randomized trial using multiple imputation technique. J Nerv Ment Dis. 2007;195(1):83-8. PMID: 17220745. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Chiesa A, Serretti A. Are mindfulness-based interventions effective for substance use disorders? A systematic review of the evidence. Subst Use Misuse. 2014;49(5):492-512. doi: 10.3109/10826084.2013.770027. PMID: 23461667. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Chindalore VL, Craven RA, Yu KP, et al. Adding ultralow-dose naltrexone to oxycodone enhances and prolongs analgesia: a randomized, controlled trial of Oxytrex. J Pain. 2005;6(6):392-9. PMID: 15943961. Excluded: Other wrong population (e.g., schizophrenia focus)

Chopra MP, Landes RD, Gatchalian KM, et al. Buprenorphine medication versus voucher contingencies in promoting abstinence from opioids and cocaine. Exp Clin Psychopharmacol. 2009;17(4):226-36. doi: 10.1037/a0016597. PMID: 19653788. Excluded: Wrong comparator

Christoff AO, Boerngen-Lacerda R. Reducing substance involvement in college students: a three-arm parallel-group randomized controlled trial of a computer-based intervention. Addict Behav. 2015;45:164-71. doi: 10.1016/j.addbeh.2015.01.019. PMID: 25679364. Excluded: Wrong country

Church SH, Rothenberg JL, Sullivan MA, et al. Concurrent substance use and outcome in combined behavioral and naltrexone therapy for opiate dependence. Am J Drug Alcohol Abuse. 2001;27(3):441-52. PMID: 11506261. Excluded: Wrong study design for key question

Chutuape MA, Silverman K, Stitzer ML. Effects of urine testing frequency on outcome in a methadone take-home contingency program. Drug Alcohol Depend. 2001;62(1):69-76. PMID: 11173169. Excluded: Wrong comparator

Cochran G, Field C, Karp J, et al. A community pharmacy intervention for opioid medication misuse: a pilot randomized clinical trial. J Am Pharm Assoc. 2018 PMID: 29691197. Excluded: Wrong comparator

Cochran G, Stitzer M, Campbell AN, et al. Web-based treatment for substance use disorders: differential effects by primary substance. Addict Behav. 2015;45:191-4. doi: 10.1016/j.addbeh.2015.02.002. PMID: 25697725. Excluded: <70% drug misuse or likely majority alcohol

Coffin PO, Santos GM, Hern J, et al. Extended-release naltrexone for methamphetamine dependence among men who have sex with men: a randomized placebo-controlled trial. Addiction. 2018;113(2):268-78. doi: 10.1111/add.13950. PMID: 28734107. Excluded: Non-FDA approved pharmacologic intervention

Comer SD, Sullivan MA, Yu E, et al. Injectable, sustained-release naltrexone for the treatment of opioid dependence: a randomized, placebo-controlled trial. Arch Gen Psychiatry. 2006;63(2):210-8. PMID: 16461865. Excluded: <3 month followup duration

Comulada WS, Weiss RE, Cumberland W, et al. Reductions in drug use among young people living with HIV. Am J Drug Alcohol Abuse. 2007;33(3):493-501. PMID: 17613977. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Conrod PJ, Stewart SH, Pihl RO, et al. Efficacy of brief coping skills interventions that match different personality profiles of female substance abusers. Psychol Addict Behav. 2000;14(3):231-42. PMID: 10998949. Excluded: Other wrong population (e.g., schizophrenia focus)

Cooper K, Chatters R, Kaltenthaler E, et al. Psychological and psychosocial interventions for cannabis cessation in adults: A systematic review short report. Health Technol Assess. 2015;19(56):1-130. doi: 10.3310/hta19560. PMID: 26202542. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Cornelius JR, Bukstein OG, Wood DS, et al. Double-blind placebo-controlled trial of fluoxetine in adolescents with comorbid major depression and an alcohol use disorder. Addict Behav. 2009;34(10):905-9. doi: 10.1016/j.addbeh.2009.03.008. PMID: 19321268. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Courbasson C, Nishikawa Y, Dixon L. Outcome of dialectical behaviour therapy for concurrent eating and substance use disorders. Clin Psychol Psychother. 2012;19(5):434-49. doi: 10.1002/cpp.748. PMID: 21416557. Excluded: Other wrong population (e.g., schizophrenia focus)

Crits-Christoph P, Ring-Kurtz S, McClure B, et al. A randomized controlled study of a web-based performance improvement system for substance abuse treatment providers. J Subst Abuse Treat. 2010;38(3):251-62. doi: 10.1016/j.jsat.2010.01.001. PMID: 20116964. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Cropsey KL, Lane PS, Hale GJ, et al. Results of a pilot randomized controlled trial of buprenorphine for opioid dependent women in the criminal justice system. Drug Alcohol Depend. 2011;119(3):172-8. doi: 10.1016/j.drugalcdep.2011.06.021. PMID: 21782352. Excluded: Incarcerated population

Curran S, Savage C. Patient response to naltrexone: issues of acceptance, treatment effects, and frequency of administration. NIDA Res Monogr. 1976 (9):67-9. PMID: 794722. Excluded: Wrong study design for key question

Czuchry M, Newbern-McFarland D, Dansereau DF. Visual representation tools for improving addiction treatment outcomes. J Psychoactive Drugs. 2009;41(2):181-7. PMID: 19705680. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Dakof GA, Henderson CE, Rowe CL, et al. A randomized clinical trial of family therapy in juvenile drug court. J Fam Psychol. 2015;29(2):232-41. doi: 10.1037/fam0000053. PMID: 25621927. Excluded: Wrong comparator

D'Amico EJ, Hunter SB, Miles JN, et al. A randomized controlled trial of a group motivational interviewing intervention for adolescents with a first time alcohol or drug offense. J Subst Abuse Treat. 2013;45(5):400-8. doi: 10.1016/j.jsat.2013.06.005. PMID: 23891459. Excluded: Other wrong population (e.g., schizophrenia focus)

D'Amico EJ, Miles JN, Stern SA, et al. Brief motivational interviewing for teens at risk of substance use consequences: a randomized pilot study in a primary care clinic. J Subst Abuse Treat. 2008;35(1):53-61. PMID: 18037603. Excluded: Poor quality

Danaee-far M, Maarefvand M, Rafiey H. Effectiveness of a brief home-based social work motivational intervention for male methamphetamine users in Tehran: A randomized clinical trial. Subst Use Misuse. 2016;51(14):1863-9. doi: 10.1080/10826084.2016.1200620. PMID: 27608368. Excluded: Wrong country

Danielson CK. Reducing risk for substance use problems among adolescents with a child maltreatment history. J Am Acad Child Adolesc Psychiatry. 2016;Conference: 63rd annual meeting of the american academy of child and adolescent psychiatry. United states. Conference start:. 20161024. Conference end: 20161029 55(10 Supplement 1):S293. Excluded: Other wrong population (e.g., schizophrenia focus)

Danielson CK, McCart MR, Walsh K, et al. Reducing substance use risk and mental health problems among sexually assaulted adolescents: a pilot randomized controlled trial. J Fam Psychol. 2012;26(4):628-35. doi: 10.1037/a0028862. PMID: 22686269. Excluded: Other wrong population (e.g., schizophrenia focus)

Darker CD, Sweeney BP, Barry JM, et al. Psychosocial interventions for benzodiazepine harmful use, abuse or dependence. Cochrane Database Syst Rev. 2015 (5)doi: 10.1002/14651858.CD009652.pub2. PMID: 26106751. Excluded: Other wrong population (e.g., schizophrenia focus)

Das JK, Salam RA, Arshad A, et al. Interventions for adolescent substance abuse: An overview of systematic reviews. J Adolesc Health. 2016;59(4s):S61-s75. doi: 10.1016/j.jadohealth.2016.06.021. PMID: 27664597. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Davis ML, Powers MB, Handelsman P, et al. Behavioral therapies for treatment-seeking cannabis users: a meta-analysis of randomized controlled trials. Eval Health Prof. 2015;38(1):94-114. doi: 10.1177/0163278714529970. PMID: 24695072. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Deady M, Teesson M, Kay-Lambkin FJ. Treatments for co-occurring depression and substance use in young people: a systematic review. Curr Drug Abuse Rev. 2014;7(1):3-17. PMID: 25323123. Excluded: Other wrong population (e.g., schizophrenia focus)

Dees SM, Dansereau DF, Simpson DD. Mapping-enhanced drug abuse counseling: urinalysis results in the first year of methadone treatment. J Subst Abuse Treat. 1997;14(1):45-54. PMID: 9218236. Excluded: Wrong comparator

DeMarce JM, Stephens RS, Roffman RA. Psychological distress and marijuana use before and after treatment: testing cognitive-behavioral matching hypotheses. Addict Behav. 2005;30(5):1055-9. PMID: 15893104. Excluded: Wrong outcome

Dennis BB, Bawor M, Paul J, et al. Pain and opioid addiction: A systematic review and evaluation of pain measurement in patients with opioid dependence on methadone maintenance treatment. Curr Drug Abuse Rev. 2016;9(1):49-60. PMID: 27021147. Excluded: Wrong outcome

Dennis M, Godley SH, Diamond G, et al. The cannabis youth treatment (CYT) study: main findings from two randomized trials. J Subst Abuse Treat. 2004;27(3):197-213. doi: 10.1016/j.jsat.2003.09.005. PMID: 15501373. Excluded: Wrong comparator

Diakogiannis IA, Steinberg M, Kosten TR. Mazindol treatment of cocaine abuse. A double-blind investigation. NIDA Res Monogr. 1990;105:514. PMID: 1876105. Excluded: Non-FDA approved pharmacologic intervention

Dole VP, Robinson JW, Orraca J, et al. Methadone treatment of randomly selected criminal addicts. N Engl J Med. 1969;280(25):1372-5. PMID: 4890477. Excluded: Incarcerated population

D'Onofrio G, Chawarski MC, O'Connor PG, et al. Emergency department-initiated buprenorphine for opioid dependence with continuation in primary care: Outcomes during and after treatment. Acad Emerg Med. 2017;24. Excluded: Results reported elsewhere, duplicate results

Appendix A5. List of Excluded Studies With Reasons For Exclusion

D'Onofrio G, Chawarski MC, O'Connor PG, et al. Emergency department-initiated buprenorphine for opioid dependence with continuation in primary care: Outcomes during and after intervention. J Gen Intern Med. 2017;32(6):660-6. doi: 10.1007/s11606-017-3993-2. PMID: 28194688. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

D'Onofrio G, O'Connor P, Pantalon M, et al. A randomized clinical trial of emergency department initiated treatment for opioid dependence: Two and six month outcomes. Drug Alcohol Depend. 2015;156(13). Excluded: Results reported elsewhere, duplicate results

D'Onofrio G, O'Connor PG, Pantalon MV, et al. Emergency department-initiated buprenorphine/naloxone treatment for opioid dependence: A randomized clinical trial. JAMA. 2015;313(16):1636-44. doi: 10.1001/jama.2015.3474. PMID: 25919527. Excluded: <3 month followup duration

Donovan DM, Daley DC, Brigham GS, et al. Stimulant abuser groups to engage in 12-step: A multisite trial in the National Institute on Drug Abuse clinical trials network. J Subst Abuse Treat. 2013;44(1):103-14. doi: 10.1016/j.jsat.2012.04.004. PMID: 22657748. Excluded: Wrong comparator

Dowling NA, Merkouris SS, Lorains FK. Interventions for comorbid problem gambling and psychiatric disorders: Advancing a developing field of research. Addict Behav. 2016;58:21-30. doi: 10.1016/j.addbeh.2016.02.012. PMID: 26900888. Excluded: Other wrong population (e.g., schizophrenia focus)

Downey KK, Helmus TC, Schuster CR. Treatment of heroin-dependent poly-drug abusers with contingency management and buprenorphine maintenance. Exp Clin Psychopharmacol. 2000;8(2):176-84. PMID: 10843300. Excluded: Wrong comparator

Drummond C, Perryman K. Psychosocial interventions in pharmacotherapy of opioid dependence: a literature review. World Health Organization. London, UK: 2007. http://www.who.int/substance_abuse/activities/psychosocial_interventions.pdf?ua=1 Accessed September 10, 2018. Excluded: Wrong comparator

Dugosh K, Abraham A, Seymour B, et al. A systematic review on the use of psychosocial interventions in conjunction with medications for the treatment of opioid addiction. J Addict Med. 2016;10(2):93-103. doi: 10.1097/ADM.0000000000000193. PMID: 26808307. Excluded: Wrong comparator

Dunn C, Deroo L, Rivara FP. The use of brief interventions adapted from motivational interviewing across behavioral domains: a systematic review. Addiction. 2001;96(12):1725-42. PMID: 11784466. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Dunn K, DeFulio A, Everly JJ, et al. Employment-based reinforcement of adherence to oral naltrexone in unemployed injection drug users: 12-month outcomes. Psychol Addict Behav. 2015;29(2):270-6. doi: 10.1037/adb0000010. PMID: 25134047. Excluded: Wrong comparator

Dunn KE, Defulio A, Everly JJ, et al. Employment-based reinforcement of adherence to oral naltrexone treatment in unemployed injection drug users. Exp Clin Psychopharmacol. 2013;21(1):74-83. doi: 10.1037/a0030743. PMID: 23205722. Excluded: Wrong comparator

Dupont HB, Candel M, Lemmens P, et al. Stages of Change Model has Limited Value in Explaining the Change in Use of Cannabis among Adolescent Participants in an Efficacious Motivational Interviewing Intervention. J Psychoactive Drugs. 2017;49(5):363-72. doi: 10.1080/02791072.2017.1325030. PMID: 28548619. Excluded: Wrong outcome

Dutra L, Stathopoulou G, Basden SL, et al. A meta-analytic review of psychosocial interventions for substance use disorders. Am J Psychiatry. 2008;165(2):179-87. doi: 10.1176/appi.ajp.2007.06111851. PMID: 18198270. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Easton C, Swan S, Sinha R. Motivation to change substance use among offenders of domestic violence. J Subst Abuse Treat. 2000;19(1):1-5. PMID: 10867294. Excluded: Other wrong population (e.g., schizophrenia focus)

Eccleston C, Fisher E, Thomas KH, et al. Interventions for the reduction of prescribed opioid use in chronic non-cancer pain. Cochrane Database Syst Rev. 2017 (11)doi: 10.1002/14651858.CD010323.pub3. PMID: 29130474. Excluded: Other wrong population (e.g., schizophrenia focus)

ED-based counseling sessions reduce risky opioid use among certain patients. ED Management. 2016;28(7):81-3. PMID: 27439227. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Edwards J, Elkins K, Hinton M, et al. Randomized controlled trial of a cannabis-focused intervention for young people with first-episode psychosis. Acta Psychiatr Scand. 2006;114(2):109-17. doi: 10.1111/j.1600-0447.2006.00783.x. PMID: 16836598. Excluded: Other wrong population (e.g., schizophrenia focus)

Eisenberg K, Woodruff SI. Randomized controlled trial to evaluate screening and brief intervention for drug-using multiethnic emergency and trauma department patients. Addict Sci Clin Pract. 2013;8(1):8. doi: 10.1186/1940-0640-8-8. PMID: 23566363. Excluded: Results reported elsewhere, duplicate results

Elk R, Mangus L, Rhoades H, et al. Cessation of cocaine use during pregnancy: effects of contingency management interventions on maintaining abstinence and complying with prenatal care. Addict Behav. 1998;23(1):57-64. PMID: 9468743. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Elliott JC, Carey KB, Vanable PA. A preliminary evaluation of a web-based intervention for college marijuana use. Psychol Addict Behav. 2014;28(1):288-93. doi: 10.1037/a0034995. PMID: 24731118. Excluded: <3 month followup duration

Epstein DH, Hawkins WE, Covi L, et al. Cognitive-behavioral therapy plus contingency management for cocaine use: findings during treatment and across 12-month follow-up. Psychol Addict Behav. 2003;17(1):73-82. PMID: 12665084. Excluded: Wrong comparator

Epstein DH, Schmittner J, Umbricht A, et al. Promoting abstinence from cocaine and heroin with a methadone dose increase and a novel contingency. Drug Alcohol Depend. 2009;101(1-2):92-100. doi: 10.1016/j.drugalcdep.2008.11.006. PMID: 19101098. Excluded: Wrong comparator

Erickson SJ, Tonigan J, Winhusen T. Therapist effects in a NIDA CTN intervention trial with pregnant substance abusing women: Findings from a RCT with MET and TAU conditions. Alcohol Treat Q. 2012;30(2):224-37. doi: 10.1080/07347324.2012.663295. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Esposito-Smythers C, Spirito A, Kahler CW, et al. Treatment of co-occurring substance abuse and suicidality among adolescents: A randomized trial. J Consult Clin Psychol. 2011;79(6):728-39. doi: 10.1037/a0026074. PMID: 22004303. Excluded: Other wrong population (e.g., schizophrenia focus)

Everly JJ, DeFulio A, Koffarnus MN, et al. Employment-based reinforcement of adherence to depot naltrexone in unemployed opioid-dependent adults: A randomized controlled trial. Addiction. 2011;106(7):1309-18. doi: 10.1111/j.1360-0443.2011.03400.x. PMID: 21320227. Excluded: Wrong comparator

Fals-Stewart W, Lam WK. Computer-assisted cognitive rehabilitation for the treatment of patients with substance use disorders: a randomized clinical trial. Exp Clin Psychopharmacol. 2010;18(1):87-98. doi: 10.1037/a0018058. PMID: 20158298. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Fals-Stewart W, O'Farrell TJ. Behavioral family counseling and naltrexone for male opioid-dependent patients. J Consult Clin Psychol. 2003;71(3):432-42. PMID: 12795568. Excluded: Wrong comparator

Fals-Stewart W, Schafer J. The treatment of substance abusers diagnosed with obsessive-compulsive disorder: An outcome study. J Subst Abuse Treat. 1992;9(4):365-70. doi: 10.1016/0740-5472%2892%2990032-J. PMID: 1479631. Excluded: Other wrong population (e.g., schizophrenia focus)

Feaster DJ, Mitrani VB, Burns MJ, et al. A randomized controlled trial of structural ecosystems therapy for HIV medication adherence and substance abuse relapse prevention. Drug Alcohol Depend. 2010;111(3):227-34. doi: 10.1016/j.drugalcdep.2010.04.017. PMID: 20538417. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Feingold A, Oliveto A, Schottenfeld R, et al. Utility of crossover designs in clinical trials: efficacy of desipramine vs. placebo in opioid-dependent cocaine abusers. Am J Addict. 2002;11(2):111-23. PMID: 12028741. Excluded: Non-FDA approved pharmacologic intervention

Fernandes S, Ferigolo M, Benchaya MC, et al. Brief Motivational Intervention and telemedicine: a new perspective of treatment to marijuana users. Addict Behav. 2010;35(8):750-5. doi: 10.1016/j.addbeh.2010.03.001. PMID: 20385444. Excluded: Wrong country

Festinger DS, Dugosh KL, Kirby KC, et al. Contingency management for cocaine treatment: cash vs. vouchers. J Subst Abuse Treat. 2014;47(2):168-74. doi: 10.1016/j.jsat.2014.03.001. PMID: 24746956. Excluded: Wrong comparator

Fiellin DA, O'Connor PG, Chawarski M, et al. Methadone maintenance in primary care: a randomized controlled trial. JAMA. 2001;286(14):1724-31. PMID: 11594897. Excluded: Wrong comparator

Fiellin DA, Pantalon MV, Chawarski MC, et al. Counseling plus buprenorphine-naloxone maintenance therapy for opioid dependence. N Engl J Med. 2006;355(4):365-74. PMID: 16870915. Excluded: Wrong comparator

Filges T, Andersen D, Jorgensen A-MK. Effects of multidimensional family therapy (MDFT) on nonopioid drug abuse: a systematic review and meta-analysis. Res Soc Work Pract. 2018;28(1):68-83. doi: 10.1177/1049731515608241. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Filges T, Jorgensen AMK. Cognitive–behavioral therapies for young people in outpatient treatment for nonopioid drug use. Res Soc Work Pract. 2018;28(3):363-85. doi: 10.1177/1049731516629803. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Findling RL, Pagano ME, McNamara NK, et al. The short-term safety and efficacy of fluoxetine in depressed adolescents with alcohol and cannabis use disorders: a pilot randomized placebo-controlled trial. Child Adolesc Psychiatry Ment Health. 2009;3(1):11. doi: 10.1186/1753-2000-3-11. PMID: 19298659. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Fletcher JB, Shoptaw S, Peck JA, et al. Contingency management reduces symptoms of psychological and emotional distress among homeless, substance-dependent men who have sex with men. Ment Health Serv Res. 2014;7(4):420-30. doi: 10.1080/17523281.2014.892897. PMID: 25364379. Excluded: <70% drug misuse or likely majority alcohol

Foxcroft DR, Callen H, Davies EL, et al. Effectiveness of the strengthening families programme 10-14 in Poland: cluster randomized controlled trial. Eur J Public Health. 2017;27(3):494-500. doi: 10.1093/eurpub/ckw195. PMID: 28339547. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

French MT, Sacks S, de Leon G, et al. Modified therapeutic community for mentally ill chemical abusers: Outcomes and costs. Eval Health Prof. 1999;22(1):60-85. doi: 10.1177/016327879902200104. PMID: 10350964. Excluded: Other wrong population (e.g., schizophrenia focus)

Frisman L, Ford J, Lin H-J, et al. Outcomes of trauma treatment using the TARGET model. J Groups Addict Recover. 2008;3(3-4):285-303. doi: 10.1080/15560350802424910. Excluded: Other wrong population (e.g., schizophrenia focus)

Fudala PJ, Bridge TP, Herbert S, et al. Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. N Engl J Med. 2003;349(10):949-58. PMID: 12954743. Excluded: <3 month followup duration

Galanter M, Dermatis H, Glickman L, et al. Network therapy: decreased secondary opioid use during buprenorphine maintenance. J Subst Abuse Treat. 2004;26(4):313-8. PMID: 15182896. Excluded: Wrong comparator

Garland EL, Roberts-Lewis A, Tronnier CD, et al. Mindfulness-oriented recovery enhancement versus CBT for co-occurring substance dependence, traumatic stress, and psychiatric disorders: Proximal outcomes from a pragmatic randomized trial. Behav Res Ther. 2016;77:7-16. doi: 10.1016/j.brat.2015.11.012. PMID: 26701171. Excluded: Other wrong population (e.g., schizophrenia focus)

Garland EL, Roberts-Lewis A, Tronnier CD, et al. "Mindfulness-oriented recovery enhancement versus CBT for co-occurring substance dependence, traumatic stress, and psychiatric disorders: Proximal outcomes from a pragmatic randomized trial": Corrigendum. Behav Res Ther. 2018;100:78. doi: 10.1016/j.brat.2017.09.007. PMID: 28964403. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Garrett SB, Doyle SR, Peavy K, et al. Age differences in outcomes among patients in the "Stimulant Abuser Groups to Engage in 12-Step" (STAGE-12) intervention. J Subst Abuse Treat. 2018;84:21-9. doi: 10.1016/j.jsat.2017.10.012. PMID: 29195590. Excluded: Wrong outcome

Gastfriend D, Silverman B, Memisoglu A, et al. Continuity of clinical efficacy with injectable extended-release naltrexone (XR-NTX). J Addict Med. 2013;7(4):E4. Excluded: Results reported elsewhere, duplicate results

Gates PJ, Sabioni P, Copeland J, et al. Psychosocial interventions for cannabis use disorder. Cochrane Database Syst Rev. 2016 (5):Cd005336. doi: 10.1002/14651858.CD005336.pub4. PMID: 27149547. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

George TP, Chawarski MC, Pakes J, et al. Disulfiram versus placebo for cocaine dependence in buprenorphine-maintained subjects: a preliminary trial. Biol Psychiatry. 2000;47(12):1080-6. PMID: 10862808. Excluded: Non-FDA approved pharmacologic intervention

Gerra G, Marcato A, Caccavari R, et al. Clonidine and opiate receptor antagonists in the treatment of heroin addiction. J Subst Abuse Treat. 1995;12(1):35-41. PMID: 7752296. Excluded: Non-FDA approved pharmacologic intervention

Ghitza UE, Epstein DH, Preston KL. Contingency management reduces injection-related HIV risk behaviors in heroin and cocaine using outpatients. Addict Behav. 2008;33(4):593-604. PMID: 18068905. Excluded: Wrong comparator

Ghitza UE, Epstein DH, Schmittner J, et al. Randomized trial of prize-based reinforcement density for simultaneous abstinence from cocaine and heroin. J Consult Clin Psychol. 2007;75(5):765-74. PMID: 17907858. Excluded: Wrong comparator

Gibbons CJ, Nich C, Steinberg K, et al. Treatment process, alliance and outcome in brief versus extended treatments for marijuana dependence. Addiction. 2010;105(10):1799-808. doi: 10.1111/j.1360-0443.2010.03047.x. PMID: 20840200. Excluded: Wrong outcome

Gilbert L, El-Bassel N, Manuel J, et al. An integrated relapse prevention and relationship safety intervention for women on methadone: testing short-term effects on intimate partner violence and substance use. Violence Vict. 2006;21(5):657-72. PMID: 17022356. Excluded: Wrong comparator

Gilchrist LD, Schinke SP, Trimble JE, et al. Skills enhancement to prevent substance abuse among American Indian adolescents. Int J Addict. 1987;22(9):869-79. PMID: 3679639. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Glasner S, Mooney LJ, Ang A, et al. Mindfulness-based relapse prevention for stimulant dependent adults: A pilot randomized clinical trial. Mindfulness (N Y). 2017;8(1):126-35. doi: 10.1007/s12671-016-0586-9. PMID: 28191264. Excluded: Wrong comparator

Glasner-Edwards S, Mooney L, Ang A, et al. Mindfulness based relapse prevention improves stimulant use among adults with major depression and generalized anxiety disorder. Drug Alcohol Depend. 2015;156. Excluded: Other wrong population (e.g., schizophrenia focus)

Gmel G, Gaume J, Bertholet N, et al. Effectiveness of a brief integrative multiple substance use intervention among young men with and without booster sessions. J Subst Abuse Treat. 2013;44(2):231-40. doi: 10.1016/j.jsat.2012.07.005. PMID: 22885010. Excluded: Other wrong population (e.g., schizophrenia focus)

Godley MD, Godley SH, Dennis ML, et al. The effect of assertive continuing care on continuing care linkage, adherence and abstinence following residential treatment for adolescents with substance use disorders. Addiction. 2007;102(1):81-93. doi: 10.1111/j.1360-0443.2006.01648.x. PMID: 17207126. Excluded: Wrong comparator

Godley MD, Godley SH, Dennis ML, et al. A randomized trial of assertive continuing care and contingency management for adolescents with substance use disorders. J Consult Clin Psychol. 2014;82(1):40-51. doi: 10.1037/a0035264. PMID: 24294838. Excluded: Wrong comparator

Godley SH, Garner BR, Passetti LL, et al. Adolescent outpatient treatment and continuing care: main findings from a randomized clinical trial. Drug Alcohol Depend. 2010;110(1-2):44-54. doi: 10.1016/j.drugalcdep.2010.02.003. PMID: 20219293. Excluded: Wrong comparator

Goldstein MF, Deren S, Kang SY, et al. Evaluation of an alternative program for MMTP drop-outs: impact on treatment re-entry. Drug Alcohol Depend. 2002;66(2):181-7. PMID: 11906805. Excluded: Other wrong population (e.g., schizophrenia focus)

Goti J, Diaz R, Serrano L, et al. Brief intervention in substance-use among adolescent psychiatric patients: a randomized controlled trial. Eur Child Adolesc Psychiatry. 2010;19(6):503-11. doi: 10.1007/s00787-009-0060-5. PMID: 19779855. Excluded: Other wrong population (e.g., schizophrenia focus)

Gottheil E, Rieger JA, Farwell B, et al. An outpatient drug program for adolescent students: preliminary evaluation. Am J Drug Alcohol Abuse. 1977;4(1):31-41. PMID: 612189. Excluded: School setting

Gottheil E, Thornton C, Weinstein S. Effectiveness of high versus low structure individual counseling for substance abuse. Am J Addict. 2002;11(4):279-90. PMID: 12584871. Excluded: Wrong comparator

Gowing L, Farrell MF, Bornemann R, et al. Oral substitution treatment of injecting opioid users for prevention of HIV infection. Cochrane Database Syst Rev. 2011 (8):CD004145. doi: 10.1002/14651858.CD004145.pub4. PMID: 21833948. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Gowing LR, Hickman M, Degenhardt L. Mitigating the risk of HIV infection with opioid substitution treatment. Bull World Health Organ. 2013;91(2):148-9. doi: 10.2471/BLT.12.109553. PMID: 23554530. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Grabowski J, Rhoades H, Stotts A, et al. Agonist-like or antagonist-like treatment for cocaine dependence with methadone for heroin dependence: two double-blind randomized clinical trials. Neuropsychopharmacology. 2004;29(5):969-81. PMID: 15039761. Excluded: Non-FDA approved pharmacologic intervention

Grant JE, Odlaug BL, Kim SW. A double-blind, placebo-controlled study of N-acetyl cysteine plus naltrexone for methamphetamine dependence. Eur Neuropsychopharmacol. 2010;20(11):823-8. doi: 10.1016/j.euroneuro.2010.06.018. PMID: 20655182. Excluded: Non-FDA approved pharmacologic intervention

Grant S, Colaiaco B, Motala A, et al. Mindfulness-based relapse prevention for substance use disorders: A systematic review and meta-analysis. J Addict Med. 2017;11(5):386-96. doi: 10.1097/adm.0000000000000338. PMID: 28727663. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Grenard JL, Ames SL, Wiers RW, et al. Brief intervention for substance use among at-risk adolescents: a pilot study. J Adolesc Health. 2007;40(2):188-91. doi: 10.1016/j.jadohealth.2006.08.008. PMID: 17259065. Excluded: School setting

Gross A, Marsch LA, Badger GJ, et al. A comparison between low-magnitude voucher and buprenorphine medication contingencies in promoting abstinence from opioids and cocaine. Exp Clin Psychopharmacol. 2006;14(2):148-56. PMID: 16756418. Excluded: Wrong comparator

Gruber K, Chutuape MA, Stitzer ML. Reinforcement-based intensive outpatient treatment for inner city opiate abusers: a short-term evaluation. Drug Alcohol Depend. 2000;57(3):211-23. doi: 10.1016/S0376-8716%2899%2900054-X. PMID: 10661672. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Gunne LM, Gronbladh L. The Swedish methadone maintenance program: a controlled study. Drug Alcohol Depend. 1981;7(3):249-56. PMID: 7261900. Excluded: Poor quality

Haber PS, Elsayed M, Espinoza D, et al. Constipation and other common symptoms reported by women and men in methadone and buprenorphine maintenance treatment. Drug Alcohol Depend. 2017;181:132-9. doi: 10.1016/j.drugalcdep.2017.09.024. PMID: 29054032. Excluded: Wrong study design for key question

Hagedorn HJ, Noorbaloochi S, Simon AB, et al. Rewarding early abstinence in Veterans Health Administration addiction clinics. J Subst Abuse Treat. 2013;45(1):109-17. doi: 10.1016/j.jsat.2013.01.006. PMID: 23453480. Excluded: Wrong comparator

Hall SM, Bass A, Hargreaves WA, et al. Contingency management and information feedback in outpatient heroin detoxification. Behav Ther. 1979;10(4):443-51. doi: 10.1016/S0005-7894%2879%2980049-0. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Haller DM, Meynard A, Lefebvre D, et al. Effectiveness of training family physicians to deliver a brief intervention to address excessive substance use among young patients: a cluster randomized controlled trial. CMAJ. 2014;186(8):E263-72. doi: 10.1503/cmaj.131301. PMID: 24616136. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Hand DJ, Ellis JD, Carr MM, et al. Contingency management interventions for tobacco and other substance use disorders in pregnancy. Psychol Addict Behav. 2017;31(8):907-21. doi: 10.1037/adb0000291. PMID: 28639813. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Handelsman L, Rosenblum A, Palij M, et al. Bromocriptine for cocaine dependence. A controlled clinical trial. Am J Addict. 1997;6(1):54-64. PMID: 9097872. Excluded: Non-FDA approved pharmacologic intervention

Haney M, Ramesh D, Glass A, et al. Naltrexone maintenance decreases cannabis self-administration and subjective effects in daily cannabis smokers. Neuropsychopharmacology. 2015;40(11):2489-98. doi: 10.1038/npp.2015.108. PMID: 25881117. Excluded: Non-FDA approved pharmacologic intervention

Hanson T, Alessi SM, Petry NM. Contingency management reduces drug-related human immunodeficiency virus risk behaviors in cocaine-abusing methadone patients. Addiction. 2008;103(7):1187-97. doi: 10.1111/j.1360-0443.2008.02216.x. PMID: 18494842. Excluded: Wrong comparator

Harris J. Mindfulness training: Impact of coping and self-efficacy in adolescent substance use: Seattle Pacific University; 2012. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Hartnett D, Carr A, Hamilton E, et al. The effectiveness of functional family therapy for adolescent behavioral and substance misuse problems: A meta-analysis. Fam Process. 2017;56(3):607-19. doi: 10.1111/famp.12256. PMID: 27731494. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Hartnett D, Carr A, Sexton T. The effectiveness of functional family therapy in reducing adolescent mental health risk and family adjustment difficulties in an irish context. Fam Process. 2016;55(2):287-304. doi: 10.1111/famp.12195. PMID: 26542420. Excluded: Wrong outcome

Havassy B, Hargreaves WA. Allowing methadone clients control over dosage: A 48-week controlled trial. Addict Behav. 1981;6(4):283-8. doi: 10.1016/0306-4603%2881%2990041-1. Excluded: Wrong comparator

Hawkins JD, Catalano RF, Jr., Gillmore MR, et al. Skills training for drug abusers: generalization, maintenance, and effects on drug use. J Consult Clin Psychol. 1989;57(4):559-63. PMID: 2671072. Excluded: Wrong comparator

Hawkins JD, Catalano RF, Jr., Wells EA. Measuring effects of a skills training intervention for drug abusers. J Consult Clin Psychol. 1986;54(5):661-4. PMID: 3771883. Excluded: Wrong comparator

Hayes SC, Wilson KG, Gifford EV, et al. A preliminary trial of twelve-step facilitation and acceptance and commitment therapy with polysubstance-abusing methadone-maintained opiate addicts. Behav Ther. 2004;35(4):667-88. doi: 10.1016/S0005-7894%2804%2980014-5. Excluded: Wrong comparator

He F, Jiang Y, Li L. The effect of naloxone treatment on opioid-induced side effects: A meta-analysis of randomized and controlled trails. Medicine (Baltimore). 2016;95(37):e4729. doi: 10.1097/MD.0000000000004729. PMID: 27631221. Excluded: Other wrong population (e.g., schizophrenia focus)

Heinzerling KG, Gadzhyan J, van Oudheusden H, et al. Pilot randomized trial of bupropion for adolescent methamphetamine abuse/dependence. J Adolesc Health. 2013;52(4):502-5. doi: 10.1016/j.jadohealth.2012.10.275. PMID: 23333007. Excluded: Non-FDA approved pharmacologic intervention

Helmer SM, Muellmann S, Zeeb H, et al. Development and evaluation of the efficacy of a web-based 'social norms'-intervention for the prevention and reduction of substance use in a cluster-controlled trial conducted at eight German universities. BMC Public Health. 2016;16:252. doi: 10.1186/s12889-016-2898-z. PMID: 26969585. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Henggeler SW, Clingempeel WG, Brondino MJ, et al. Four-year follow-up of multisystemic therapy with substance-abusing and substance-dependent juvenile offenders. J Am Acad Child Adolesc Psychiatry. 2002;41(7):868-74. PMID: 12108813. Excluded: Other wrong population (e.g., schizophrenia focus)

Henggeler SW, McCart MR, Cunningham PB, et al. Enhancing the effectiveness of juvenile drug courts by integrating evidence-based practices. J Consult Clin Psychol. 2012;80(2):264-75. doi: 10.1037/a0027147. PMID: 22309470. Excluded: Wrong comparator

Henggeler SW, Melton GB, Smith LA. Family preservation using multisystemic therapy: an effective alternative to incarcerating serious juvenile offenders. J Consult Clin Psychol. 1992;60(6):953-61. PMID: 1460157. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Henggeler SW, Pickrel SG, Brondino MJ. Multisystemic treatment of substance-abusing and dependent delinquents: outcomes, treatment fidelity, and transportability. Ment Health Serv Res. 1999;1(3):171-84. PMID: 11258740. Excluded: Other wrong population (e.g., schizophrenia focus)

Hennessey EA, Fisher BW. A meta-analysis exploring the relationship between 12-step attendance and adolescent substance use relapse. J Groups Addict Recover. 2015;10(1):79-96. doi: 10.1080/1556035X.2015.999621. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Hersh D, Van Kirk JR, Kranzler HR. Naltrexone treatment of comorbid alcohol and cocaine use disorders. Psychopharmacology (Berl). 1998;139(1-2):44-52. PMID: 9768541. Excluded: Non-FDA approved pharmacologic intervention

Hien DA, Cohen LR, Miele GM, et al. Promising treatments for women with comorbid PTSD and substance use disorders. Am J Psychiatry. 2004;161(8):1426-32. doi: 10.1176/appi.ajp.161.8.1426. PMID: 15285969. Excluded: Other wrong population (e.g., schizophrenia focus)

Hien DA, Morgan-Lopez AA, Campbell AN, et al. Attendance and substance use outcomes for the seeking safety program: sometimes less is more. J Consult Clin Psychol. 2012;80(1):29-42. doi: 10.1037/a0026361. PMID: 22182262. Excluded: Other wrong population (e.g., schizophrenia focus)

Hien DA, Wells EA, Jiang H, et al. Multisite randomized trial of behavioral interventions for women with co-occurring PTSD and substance use disorders. J Consult Clin Psychol. 2009;77(4):607-19. doi: 10.1037/a0016227. PMID: 19634955. Excluded: Other wrong population (e.g., schizophrenia focus)

Higgins ST, Budney AJ, Bickel WK, et al. Outpatient behavioral treatment for cocaine dependence: One-year outcome. Exp Clin Psychopharmacol. 1995;3(2):205-12. Excluded: Wrong comparator

Higgins ST, Budney AJ, Bickel WK, et al. Outpatient behavioral treatment for cocaine dependence: One-year outcome. Addictive behaviors: Readings on etiology, prevention, and treatment. Washington, DC: American Psychological Association; US; 1997:629-45. Excluded: Wrong comparator

Higgins ST, Budney AJ, Bickel WK, et al. Achieving cocaine abstinence with a behavioral approach. Am J Psychiatry. 1993;150(5):763-9. doi: 10.1176/ajp.150.5.763. PMID: 8480823. Excluded: Wrong comparator

Higgins ST, Stitzer ML, Bigelow GE, et al. Contingent methadone delivery: effects on illicit-opiate use. Drug Alcohol Depend. 1986;17(4):311-22. PMID: 3757767. Excluded: <3 month followup duration

Hjorthoj CR, Fohlmann A, Larsen AM, et al. Specialized psychosocial treatment plus treatment as usual (TAU) versus TAU for patients with cannabis use disorder and psychosis: The CapOpus randomized trial. Psychol Med. 2013;43(7):1499-510. doi: 10.1017/S0033291712002255. PMID: 23040144. Excluded: Other wrong population (e.g., schizophrenia focus)

Hoch E, Buhringer G, Pixa A, et al. CANDIS treatment program for cannabis use disorders: findings from a randomized multi-site translational trial. Drug Alcohol Depend. 2014;134:185-93. doi: 10.1016/j.drugalcdep.2013.09.028. PMID: 24176199. Excluded: Wrong study design for key question

Hoch E, Noack R, Henker J, et al. Efficacy of a targeted cognitive-behavioral treatment program for cannabis use disorders (CANDIS). Eur Neuropsychopharmacol. 2012;22(4):267-80. doi: 10.1016/j.euroneuro.2011.07.014. PMID: 21865014. Excluded: Wrong study design for key question

Hogue A, Henderson CE, Ozechowski TJ, et al. Evidence base on outpatient behavioral treatments for adolescent substance use: updates and recommendations 2007-2013. J Clin Child Adolesc Psychol. 2014;43(5):695-720. doi: 10.1080/15374416.2014.915550. PMID: 24926870. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Hogue A, Liddle HA. Family-based treatment for adolescent substance abuse: Controlled trials and new horizons in services research. J Fam Ther. 2009;31(2):126-54. doi: 10.1111/j.1467-6427.2009.00459.x. PMID: 21113237. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Hohmann L, Bradt J, Stegemann T, et al. Effects of music therapy and music-based interventions in the treatment of substance use disorders: A systematic review. PLoS ONE. 2017;12(11):e0187363. doi: 10.1371/journal.pone.0187363. PMID: 29141012. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Hops H, Ozechowski TJ, Waldron HB, et al. Adolescent health-risk sexual behaviors: effects of a drug abuse intervention. Aids Behav. 2011;15(8):1664-76. doi: 10.1007/s10461-011-0019-7. PMID: 21833690. Excluded: Wrong comparator

Horigian VE, Anderson AR, Szapocznik J. Family-based treatments for adolescent substance use. Child Adolesc Psychiatr Clin N Am. 2016;25(4):603-28. doi: 10.1016/j.chc.2016.06.001. PMID: 27613341. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Horigian VE, Robbins MS, Dominguez R, et al. Principles for defining adverse events in behavioral intervention research: lessons from a family-focused adolescent drug abuse trial. Clin Trials. 2010;7(1):58-68. doi: 10.1177/1740774509356575. PMID: 20156957. Excluded: Wrong comparator

Horigian VE, Weems CF, Robbins MS, et al. Reductions in anxiety and depression symptoms in youth receiving substance use treatment. Am J Addict. 2013;22(4):329-37. doi: 10.1111/j.1521-0391.2013.12031.x. PMID: 23795871. Excluded: Wrong study design for key question

Hoseiny H, Jadidi M, Habiballah Nataj L, et al. The effect of methadone-maintenance therapy with and without interactive treatment on improving emotion-regulation strategies and resilience among opiate-dependent clients. Int J High Risk Behav Addict. 2015;4(1):e23526. doi: 10.5812/ijhrba.23526. PMID: 25821751. Excluded: Wrong study design for key question

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Hser YI, Li J, Jiang H, et al. Effects of a randomized contingency management intervention on opiate abstinence and retention in methadone maintenance treatment in China. Addiction. 2011;106(10):1801-9. doi: 10.1111/j.1360-0443.2011.03490.x. PMID: 21793958. Excluded: Wrong comparator

Hsu SH, Collins SE, Marlatt GA. Examining psychometric properties of distress tolerance and its moderation of mindfulness-based relapse prevention effects on alcohol and other drug use outcomes. Addict Behav. 2013;38(3):1852-8. doi: 10.1016/j.addbeh.2012.11.002. PMID: 23266526. Excluded: Wrong outcome

Huang YS, Tang TC, Lin CH, et al. Effects of motivational enhancement therapy on readiness to change MDMA and methamphetamine use behaviors in Taiwanese adolescents. Subst Use Misuse. 2011;46(4):411-6. doi: 10.3109/10826084.2010.501664. PMID: 20735217. Excluded: <3 month followup duration

Hubbard RL, Leimberger JD, Haynes L, et al. Telephone enhancement of long-term engagement (TELE) in continuing care for substance abuse treatment: a NIDA clinical trials network (CTN) study. Am J Addict. 2007;16(6):495-502. PMID: 18058417. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Humeniuk R, Dennington V, Ali R. The effectiveness of a brief intervention for illicit drugs linked to the alcohol, smoking and substance involvement screening test (ASSIST) in primary health care settings: a technical report of phase III findings of the WHO ASSIST randomized controlled trial. Geneva: World Health Organization. 2008. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Humeniuk R, Newcombe DAL, Dennington V, et al. A randomised controlled trial of a brief intervention for illicit drug use linked to ASSIST screening in a primary healthcare setting: results from the Australian component of the World Health Organization Phase III ASSIST studies. Aust J Prim Health. 2018;24(2):149-54. doi: 10.1071/PY17056. PMID: 29481765. Excluded: Results reported elsewhere, duplicate results

Hunt GE, Siegfried N, Morley K, et al. Psychosocial interventions for people with both severe mental illness and substance misuse. Cochrane Database Syst Rev. 2013 (10):CD001088. doi: 10.1002/14651858.CD001088.pub3. PMID: 24092525. Excluded: Other wrong population (e.g., schizophrenia focus)

Hunter SB, Ramchand R, Griffin BA, et al. The effectiveness of community-based delivery of an evidence-based treatment for adolescent substance use. J Subst Abuse Treat. 2012;43(2):211-20. doi: 10.1016/j.jsat.2011.11.003. PMID: 22209657. Excluded: Wrong comparator

Hunter SB, Watkins KE, Hepner KA, et al. Treating depression and substance use: a randomized controlled trial. J Subst Abuse Treat. 2012;43(2):137-51. doi: 10.1016/j.jsat.2011.12.004. PMID: 22301087. Excluded: Wrong comparator

Hwang VS. A brief motivational intervention for marijuana use in college students. Dissertation Abstracts International: Section B: The Sciences and Engineering. 2018;78(9-B(E)):No Pagination Specified. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Iguchi MY, Belding MA, Morral AR, et al. Reinforcing operants other than abstinence in drug abuse treatment: An effective alternative for reducing drug use. J Consult Clin Psychol. 1997;65(3):421-8. PMID: 9170765. Excluded: Wrong comparator

Indave B, Amato L, Minozzi S, et al. Antipsychotic medications for cocaine dependence. Cochrane Database Syst Rev. 2016 (6)doi: 10.1002/14651858.CD006306.pub3. PMID: 26992929. Excluded: Non-FDA approved pharmacologic intervention

Ingersoll KS, Dillingham RA, Hettema JE, et al. Pilot RCT of bidirectional text messaging for ART adherence among nonurban substance users with HIV. Health Psychol. 2015;34S:1305-15. doi: 10.1037/hea0000295. PMID: 26651472. Excluded: Other wrong population (e.g., schizophrenia focus)

Ingersoll KS, Farrell-Carnahan L, Cohen-Filipic J, et al. A pilot randomized clinical trial of two medication adherence and drug use interventions for HIV+ crack cocaine users. Drug Alcohol Depend. 2011;116(1-3):177-87. doi: 10.1016/j.drugalcdep.2010.12.016. PMID: 21306837. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Irvin JE, Bowers CA, Dunn ME, et al. Efficacy of relapse prevention: a meta-analytic review. J Consult Clin Psychol. 1999;67(4):563-70. PMID: 10450627. Excluded: Wrong outcome

Jacobus J, Taylor CT, Gray KM, et al. A multi-site proof-of-concept investigation of computerized approach-avoidance training in adolescent cannabis users. Drug Alcohol Depend. 2018;187:195-204. doi: 10.1016/j.drugalcdep.2018.03.007. PMID: 29679914. Excluded: <3 month followup duration

Jaffe AJ, Rounsaville B, Chang G, et al. Naltrexone, relapse prevention, and supportive therapy with alcoholics: an analysis of patient treatment matching. J Consult Clin Psychol. 1996;64(5):1044-53. PMID: 8916634. Excluded: Other wrong population (e.g., schizophrenia focus)

Jaffray M, Matheson C, Bond CM, et al. A cluster randomised controlled trial of enhanced pharmacy services (EPS) to improve outcomes for patients on methadone maintenance therapy (MMT). Int J Pharm Pract. 2011;19:4. doi: 10.1111/j.2042-7174.2011.00098.x. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Jalling C, Bodin M, Romelsjo A, et al. Parent programs for reducing adolescent's antisocial behavior and substance use: A randomized controlled trial. J Child Fam Stud. 2016;25:811-26. doi: 10.1007/s10826-015-0263-y. PMID: 26900316. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Jarvis BP, Holtyn AF, DeFulio A, et al. Effects of incentives for naltrexone adherence on opiate abstinence in heroin-dependent adults. Addiction. 2017;112(5):830-7. doi: 10.1111/add.13724. PMID: 27936293. Excluded: Wrong comparator

Jarvis BP, Holtyn AF, Subramaniam S, et al. Extended-release injectable naltrexone for opioid use disorder: a systematic review. Addiction. 2018;113(7):1188-209. doi: 10.1111/add.14180. PMID: 29396985. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Jayaram-Lindstrom N, Hammarberg A, Beck O, et al. Naltrexone for the treatment of amphetamine dependence: a randomized, placebo-controlled trial. Am J Psychiatry. 2008;165(11):1442-8. doi: 10.1176/appi.ajp.2008.08020304. PMID: 18765480. Excluded: Non-FDA approved pharmacologic intervention

Jeal N, Macleod J, Turner K, et al. Systematic review of interventions to reduce illicit drug use in female drug-dependent street sex workers. BMJ Open. 2015;5(11):e009238. doi: 10.1136/bmjopen-2015-009238. PMID: 26582403. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Jenaabadi H, Jahangir AH. Comparing the effectiveness of mindfulness-based group therapy and methadone maintenance therapy on psychological symptoms (obsession, interpersonal sensitivity, depression, anxiety, and aggression) among opioid-dependent patients. Shiraz E Med J. 2017;18(6). Excluded: Wrong comparator

Jensen CD, Cushing CC, Aylward BS, et al. Effectiveness of motivational interviewing interventions for adolescent substance use behavior change: a meta-analytic review. J Consult Clin Psychol. 2011;79(4):433-40. doi: 10.1037/a0023992. PMID: 21728400. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Jiang H, Du J, Wu F, et al. Efficacy of contingency management in improving retention and compliance to methadone maintenance treatment: a random controlled study. Shanghai Arch Psychiatry. 2012;24(1):11-9. doi: 10.3969/j.issn.1002-0829.2012.01.002. PMID: 25324596. Excluded: Wrong comparator

Jiang S, Wu L, Gao X. Beyond face-to-face individual counseling: a systematic review on alternative modes of motivational interviewing in substance abuse treatment and prevention. Addict Behav. 2017;73:216-35. doi: 10.1016/j.addbeh.2017.05.023. PMID: 28554033. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Joanning H, Quinn W, Thomas F, et al. Treating adolescent drug abuse: A comparison of family systems therapy, group therapy, and family drug education. J Marital Fam Ther. 1992;18(4):345-56. Excluded: Wrong comparator

Johnson JD. The effects of a brief cognitive-behavioral group intervention on the depression and hopelessness of drug dependent, human immunodeficiency virus-positive, African-American women (immune deficiency). Dissertation Abstracts International: Section B: The Sciences and Engineering. 2001;62(1-B):551. Excluded: Wrong outcome

Johnson RE, Eissenberg T, Stitzer ML, et al. A placebo controlled clinical trial of buprenorphine as a treatment for opioid dependence. Drug Alcohol Depend. 1995;40(1):17-25. PMID: 8746920. Excluded: <3 month followup duration

Johnson S, Sheridan Rains L, Marwaha S, et al. A randomised controlled trial of the clinical and cost-effectiveness of a contingency management intervention compared to treatment as usual for reduction of cannabis use and of relapse in early psychosis (CIRCLE): a study protocol for a randomised controlled trial. Trials. 2016;17(1)doi: 10.1186/s13063-016-1620-x. PMID: 27770820. Excluded: Other wrong population (e.g., schizophrenia focus)

Jones HE, Haug N, Silverman K, et al. The effectiveness of incentives in enhancing treatment attendance and drug abstinence in methadone-maintained pregnant women. Drug Alcohol Depend. 2001;61(3):297-306. PMID: 11164694. Excluded: Wrong comparator

Jones HE, Haug NA, Stitzer ML, et al. Improving treatment outcomes for pregnant drug-dependent women using low-magnitude voucher incentives. Addict Behav. 2000;25(2):263-7. PMID: 10795950. Excluded: Wrong comparator

Jones HE, Johnson RE, Bigelow GE, et al. Safety and efficacy of L-tryptophan and behavioral incentives for treatment of cocaine dependence: a randomized clinical trial. Am J Addict. 2004;13(5):421-37. doi: 10.1080/10550490490512753. PMID: 15764421. Excluded: Wrong comparator

Jones HE, O'Grady KE, Tuten M. Reinforcement-based treatment improves the maternal treatment and neonatal outcomes of pregnant patients enrolled in comprehensive care treatment. Am J Addict. 2011;20(3):196-204. doi: 10.1111/j.1521-0391.2011.00119.x. PMID: 21477047. Excluded: Wrong comparator

Jones SL, Kanfer R, Lanyon RI. Skill training with alcoholics: A clinical extension. Addict Behav. 1982;7(3):285-90. PMID: 7180623. Excluded: Other wrong population (e.g., schizophrenia focus)

Jordan JB. Acupuncture treatment for opiate addiction: a systematic review. J Subst Abuse Treat. 2006;30(4):309-14. PMID: 16716845. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Judson BA, Goldstein A. Naltrexone treatment of heroin addiction: one-year follow-up. Drug Alcohol Depend. 1984;13(4):357-65. PMID: 6479015. Excluded: Wrong study design for key question

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Jungerman FS, Andreoni S, Laranjeira R. Short term impact of same intensity but different duration interventions for cannabis users. Drug Alcohol Depend. 2007;90(2-3):120-7. doi: 10.1016/j.drugalcdep.2007.02.019. PMID: 17412530. Excluded: Wrong country

Kadden RM, Litt MD, Cooney NL, et al. Prospective matching of alcoholic clients to cognitive-behavioral or interactional group therapy. J Stud Alcohol. 2001;62(3):359-69. PMID: 11414346. Excluded: Other wrong population (e.g., schizophrenia focus)

Kakko J, Gronbladh L, Svanborg KD, et al. A stepped care strategy using buprenorphine and methadone versus conventional methadone maintenance in heroin dependence: a randomized controlled trial. Am J Psychiatry. 2007;164(5):797-803. PMID: 17475739. Excluded: Wrong comparator

Kaminer Y, Burleson JA. Psychotherapies for adolescent substance abusers: 15-month follow-up of a pilot study. Am J Addict. 1999;8(2):114-9. PMID: 10365191. Excluded: Wrong comparator

Kaminer Y, Burleson JA, Blitz C, et al. Psychotherapies for adolescent substance abusers: a pilot study. J Nerv Ment Dis. 1998;186(11):684-90. PMID: 9824170. Excluded: Wrong comparator

Kaminer Y, Burleson JA, Burke R, et al. The efficacy of contingency management for adolescent cannabis use disorder: a controlled study. Substance Abuse. 2014;35(4):391-8. doi: 10.1080/08897077.2014.933724. PMID: 25010430. Excluded: Wrong comparator

Kaminer Y, Burleson JA, Goldberger R. Cognitive-behavioral coping skills and psychoeducation therapies for adolescent substance abuse. J Nerv Ment Dis. 2002;190(11):737-45. doi: 10.1097/01.nmd.0000038168.51591.b6. PMID: 12436013. Excluded: Wrong comparator

Kamon J, Budney A, Stanger C. A contingency management intervention for adolescent marijuana abuse and conduct problems. J Am Acad Child Adolesc Psychiatry. 2005;44(6):513-21. PMID: 15908833. Excluded: Wrong study design for key question

Kampman KM, Pettinati HM, Lynch KG, et al. Modafinil and naltrexone for the treatment of comorbid cocaine and alcohol dependence. Drug Alcohol Depend. 2014;146(14). Excluded: Non-FDA approved pharmacologic intervention

Kaner EF, Brown N, Jackson K. A systematic review of the impact of brief interventions on substance use and co-morbid physical and mental health conditions. Ment Health Serv Res. 2011;4(1):38-61. doi: 10.1080/17523281.2011.533449. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Kang SY, Kleinman PH, Woody GE, et al. Outcomes for cocaine abusers after once-a-week psychosocial therapy. Am J Psychiatry. 1991;148(5):630-5. PMID: 1850208. Excluded: Wrong study design for key question

Karno M, Farabee D, Brecht ML, et al. Patient reactance moderates the effect of directive telephone counseling for methamphetamine users. J Stud Alcohol Drugs. 2012;73(5):844-50. PMID: 22846250. Excluded: Wrong outcome

Katz D, Toner B. A systematic review of gender differences in the effectiveness of mindfulness-based treatments for substance use disorders. Mindfulness (N Y). 2013;4(4):318-31. doi: 10.1007/s12671-012-0132-3. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Katz EC, Chutuape MA, Jones HE, et al. Voucher reinforcement for heroin and cocaine abstinence in an outpatient drug-free program. Exp Clin Psychopharmacol. 2002;10(2):136-43. PMID: 12022799. Excluded: Wrong comparator

Kay-Lambkin FJ, Baker AL, Kelly BJ, et al. It's worth a try: The treatment experiences of rural and urban participants in a randomized controlled trial of computerized psychological treatment for comorbid depression and alcohol/other drug use. J Dual Diagn. 2012;8(4):262-76. doi: 10.1080/15504263.2012.723315. Excluded: Other wrong population (e.g., schizophrenia focus)

Keegan J, Lavenduski C, Schooff K. Comments and findings from a naltrexone double blind study. NIDA Res Monogr. 1976 (9):74-6. PMID: 794724. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Kelly AB, Halford WK, Young RM. Maritally distressed women with alcohol problems: the impact of a short-term alcohol-focused intervention on drinking behaviour and marital satisfaction. Addiction. 2000;95(10):1537-49. PMID: 11070529. Excluded: Other wrong population (e.g., schizophrenia focus)

Kelly JF, Kaminer Y, Kahler CW, et al. A pilot randomized clinical trial testing integrated 12-Step facilitation (iTSF) treatment for adolescent substance use disorder. Addiction. 2017;112(12):2155-66. doi: 10.1111/add.13920. PMID: 28742932. Excluded: Wrong comparator

Kelly SM, O'Grady K E, Jaffe JH, et al. Improvements in outcomes in methadone patients on probation/parole regardless of counseling early in treatment. J Addict Med. 2013;7(2):133-8. doi: 10.1097/ADM.0b013e318284a0c1. PMID: 23455877. Excluded: Wrong comparator

Kelly SM, O'Grady KE, Gryczynski J, et al. Methadone patients in patient-centered treatment: one-year arrest data. Drug Alcohol Depend. 2016;171:e100-e1. Excluded: Wrong comparator

Kelly SM, Schwartz RP, O'Grady K E, et al. Impact of methadone with versus without drug abuse counseling on HIV risk: 4- and 12-month findings from a clinical trial. J Addict Med. 2012;6(2):145-52. doi: 10.1097/ADM.0b013e31823ae556. PMID: 22134175. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Kelty E, Hulse G. A retrospective cohort study of birth outcomes in neonates exposed to naltrexone in utero: A comparison with methadone-, buprenorphine- and non-opioid-exposed neonates. Drugs. 2017;77(11):1211-9. doi: 10.1007/s40265-017-0763-8. PMID: 28536981. Excluded: Wrong study design for key question

Kelty E, Hulse G. A retrospective cohort study of obstetric outcomes in opioid-dependent women treated with implant naltrexone, oral methadone or sublingual buprenorphine, and non-dependent controls. Drugs. 2017;77(11):1199-210. doi: 10.1007/s40265-017-0762-9. PMID: 28536980. Excluded: Wrong study design for key question

Kemp R, Harris A, Vurel E, et al. Stop Using Stuff: trial of a drug and alcohol intervention for young people with comorbid mental illness and drug and alcohol problems. Australas Psychiatry. 2007;15(6):490-3. doi: 10.1080/10398560701439665. PMID: 17852064. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Kennedy AP, Phillips KA, Epstein DH, et al. A randomized investigation of methadone doses at or over 100 mg/day, combined with contingency management. Drug Alcohol Depend. 2013;130(1-3):77-84. doi: 10.1016/j.drugalcdep.2012.10.025. PMID: 23195924. Excluded: Wrong comparator

Keoleian V, Stalcup SA, Polcin DL, et al. A cognitive behavioral therapy-based text messaging intervention for methamphetamine dependence. J Psychoactive Drugs. 2013;45(5):434-42. PMID: 24592670. Excluded: <3 month followup duration

Khatami M, Woody G, O'Brien C, et al. Biofeedback treatment of narcotic addiction: a double-blind study. Drug Alcohol Depend. 1982;9(2):111-7. PMID: 7094834. Excluded: Wrong comparator

Khusid MA, Vythilingam M. The emerging role of mindfulness meditation as effective self-management strategy, Part 2: Clinical implications for chronic pain, substance misuse, and insomnia. Mil Med. 2016;181(9):969-75. doi: 10.7205/MILMED-D-14-00678. PMID: 27612339. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Kidorf M, Brooner RK, Gandotra N, et al. Reinforcing integrated psychiatric service attendance in an opioid-agonist program: A randomized and controlled trial. Drug Alcohol Depend. 2013;133(1):30-6. doi: 10.1016/j.drugalcdep.2013.06.005. PMID: 23866988. Excluded: Other wrong population (e.g., schizophrenia focus)

Kidorf M, King VL, Gandotra N, et al. Improving treatment enrollment and re-enrollment rates of syringe exchangers: 12-month outcomes. Drug Alcohol Depend. 2012;124(1-2):162-6. doi: 10.1016/j.drugalcdep.2011.12.008. PMID: 22209388. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Kidorf M, King VL, Neufeld K, et al. Improving substance abuse treatment enrollment in community syringe exchangers. Addiction. 2009;104(5):786-95. doi: 10.1111/j.1360-0443.2009.02560.x. PMID: 19413790. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Kidorf M, King VL, Peirce J, et al. A treatment reengagement intervention for syringe exchangers. J Subst Abuse Treat. 2011;41(4):415-21. doi: 10.1016/j.jsat.2011.06.008. PMID: 21831559. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Kidorf M, Stitzer ML. Contingent access to methadone maintenance treatment: effects on cocaine use of mixed opiate/cocaine abusers. NIDA Res Monogr. 1994;141(361). Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Kidorf M, Stitzer ML. Contingent use of take-homes and split-dosing to reduce illicit drug use of methadone patients. Behav Ther. 1996;27(1):41-51. Excluded: Other wrong population (e.g., schizophrenia focus)

Kidorf M, Stitzer ML, Brooner RK, et al. Contingent methadone take-home doses reinforce adjunct therapy attendance of methadone maintenance patients. Drug Alcohol Depend. 1994;36(3):221-6. PMID: 7889813. Excluded: Wrong comparator

Killeen TK, McRae-Clark AL, Waldrop AE, et al. Contingency management in community programs treating adolescent substance abuse: a feasibility study. J Child Adolesc Psychiatr Nurs. 2012;25(1):33-41. doi: 10.1111/j.1744-6171.2011.00313.x. PMID: 22299805. Excluded: Wrong comparator

Killeen TK, Upadhyana H, McRae A, et al. Contingency management for community treatment-seeking adolescents with marijuana use disorders. Proceedings of the 70th Annual Scientific Meeting of the College on Problems of Drug Dependence. 2008. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Kim SJ, Marsch LA, Guarino H, et al. Predictors of outcome from computer-based treatment for substance use disorders: Results from a randomized clinical trial. Drug Alcohol Depend. 2015;157:174-8. doi: 10.1016/j.drugalcdep.2015.09.019. PMID: 26433562. Excluded: Wrong comparator

Kim TW, Bernstein J, Cheng DM, et al. Does screening and brief intervention for drug use in primary care increase receipt of substance use disorder treatment? Drug Alcohol Depend. 2015;156(13). Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Kimber J, Larney S, Hickman M, et al. Mortality risk of opioid substitution therapy with methadone versus buprenorphine: a retrospective cohort study. Lancet Psychiatry. 2015;2(10):901-8. doi: 10.1016/S2215-0366(15)00366-1. PMID: 26384619. Excluded: Wrong study design for key question

Appendix A5. List of Excluded Studies With Reasons For Exclusion

King VL, Brooner RK, Peirce JM, et al. A randomized trial of web-based videoconferencing for substance abuse counseling. J Subst Abuse Treat. 2014;46(1):36-42. doi: 10.1016/j.jsat.2013.08.009. PMID: 24035556. Excluded: Wrong comparator

King VL, Kidorf MS, Stoller KB, et al. A 12-month controlled trial of methadone medical maintenance integrated into an adaptive treatment model. J Subst Abuse Treat. 2006;31(4):385-93. PMID: 17084792. Excluded: Wrong comparator

King VL, Stoller KB, Hayes M, et al. A multicenter randomized evaluation of methadone medical maintenance. Drug Alcohol Depend. 2002;65(2):137-48. PMID: 11772475. Excluded: Wrong comparator

Kinlock TW, Battjes RJ, Schwartz RP, et al. A novel opioid maintenance program for prisoners: preliminary findings. J Subst Abuse Treat. 2002;22(3):141-7. PMID: 12039617. Excluded: Incarcerated population

Kinlock TW, Battjes RJ, Schwartz RP, et al. A novel opioid maintenance program for prisoners: report of post-release outcomes. Am J Drug Alcohol Abuse. 2005;31(3):433-54. PMID: 16161728. Excluded: Incarcerated population

Kinlock TW, Gordon MS, Schwartz RP, et al. A randomized clinical trial of methadone maintenance for prisoners: results at 12 months postrelease. J Subst Abuse Treat. 2009;37(3):277-85. doi: 10.1016/j.jsat.2009.03.002. PMID: 19339140. Excluded: Incarcerated population

Kinlock TW, Gordon MS, Schwartz RP, et al. A randomized clinical trial of methadone maintenance for prisoners: results at 1-month post-release. Drug Alcohol Depend. 2007;91(2-3):220-7. PMID: 17628351. Excluded: Incarcerated population

Kinlock TW, Gordon MS, Schwartz RP, et al. A study of methadone maintenance for male prisoners: 3-month postrelease outcomes. Crim Justice Behav. 2008;35(1):34-47. doi: 10.1177/0093854807309111. PMID: 18612373. Excluded: Incarcerated population

Kirby KC, Carpenedo CM, Dugosh KL, et al. Randomized clinical trial examining duration of voucher-based reinforcement therapy for cocaine abstinence. Drug Alcohol Depend. 2013;132(3):639-45. doi: 10.1016/j.drugalcdep.2013.04.015. PMID: 23680075. Excluded: Wrong comparator

Kirby KC, Kerwin ME, Carpenedo CM, et al. Interdependent group contingency management for cocaine-dependent methadone maintenance patients. J Appl Behav Anal. 2008;41(4):579-95. PMID: 19192861. Excluded: Wrong comparator

Kirby KC, Marlowe DB, Festinger DS, et al. Schedule of voucher delivery influences initiation of cocaine abstinence. J Consult Clin Psychol. 1998;66(5):761-7. PMID: 9803694. Excluded: Wrong comparator

Kirchmayer U, Davoli M, Verster A. Naltrexone maintenance treatment for opioid dependence. Cochrane Database Syst Rev. 2003 (2):CD001333. PMID: 12804405. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Kirchmayer U, Davoli M, Verster AD, et al. A systematic review on the efficacy of naltrexone maintenance treatment in opioid dependence. Addiction. 2002;97(10):1241-9. PMID: 12359026. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Kleber HK. The CASA multi-center trial of acupuncture for cocaine dependence. Acupunct Electrother Res. 1997;22(69). Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Klein NC, Alexander JF, Parsons BV. Impact of family systems intervention on recidivism and sibling delinquency: a model of primary prevention and program evaluation. J Consult Clin Psychol. 1977;45(3):469-74. PMID: 864062. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Knapp PW, Soares GOB, Farrell MF, et al. Psychosocial interventions for cocaine and psychostimulant amphetamines related disorders. Cochrane Database Syst Rev. 2015 (4) PMID: 17636713. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Knapp WP, Soares BG, Farrel M, et al. Psychosocial interventions for cocaine and psychostimulant amphetamines related disorders. Cochrane Database Syst Rev. 2007 (3):CD003023. PMID: 17636713. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Knealing TW, Wong CJ, Diemer KN, et al. A randomized controlled trial of the therapeutic workplace for community methadone patients: a partial failure to engage. Exp Clin Psychopharmacol. 2006;14(3):350-60. PMID: 16893278. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Korcha RA, Polcin DL, Evans K, et al. Intensive motivational interviewing for women with concurrent alcohol problems and methamphetamine dependence. J Subst Abuse Treat. 2014;46(2):113-9. doi: 10.1016/j.jsat.2013.08.013. PMID: 24074649. Excluded: Wrong comparator

Korthuis PT, Lum PJ, Vergara-Rodriguez P, et al. Feasibility and safety of extended-release naltrexone treatment of opioid and alcohol use disorder in HIV clinics: a pilot/feasibility randomized trial. Addiction. 2017;112(6):1036-44. doi: 10.1111/add.13753. PMID: 28061017. Excluded: Other wrong population (e.g., schizophrenia focus)

Kosten T, Oliveto A, Feingold A, et al. Desipramine and contingency management for cocaine and opiate dependence in buprenorphine maintained patients. Drug Alcohol Depend. 2003;70(3):315-25. PMID: 12757969. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Kosten T, Poling J, Oliveto A. Effects of reducing contingency management values on heroin and cocaine use for buprenorphine- and desipramine-treated patients. Addiction. 2003;98(5):665-71. PMID: 12751984. Excluded: Wrong comparator

Kosten TR, Kleber HD, Morgan C. Treatment of cocaine abuse with buprenorphine. Biol Psychiatry. 1989;26(6):637-9. Excluded: Non-FDA approved pharmacologic intervention

Kosten TR, Morgan C, Kleber HD. Phase II clinical trials of buprenorphine: detoxification and induction onto naltrexone. NIDA Res Monogr. 1992;121:101-19. PMID: 1406906. Excluded: Wrong comparator

Kosten TR, Morgan CH, Schottenfeld RS. Amantadine and desipramine in the treatment of cocaine abusing methadone maintained patients. NIDA Res Monogr. 1990;105:510-1. PMID: 1876103. Excluded: Non-FDA approved pharmacologic intervention

Kosten TR, Morgan CM, Falcione J, et al. Pharmacotherapy for cocaine-abusing methadone-maintained patients using amantadine or desipramine. Arch Gen Psychiatry. 1992;49(11):894-8. PMID: 1444728. Excluded: Non-FDA approved pharmacologic intervention

Kosten TR, Schottenfeld R, Ziedonis D, et al. Buprenorphine versus methadone maintenance for opioid dependence. J Nerv Ment Dis. 1993;181(6):358-64. PMID: 8501457. Excluded: Wrong comparator

Kosten TR, Schumann B, Wright D, et al. A preliminary study of desipramine in the treatment of cocaine abuse in methadone maintenance patients. J Clin Psychiatry. 1987;48(11):442-4. PMID: 3680185. Excluded: Non-FDA approved pharmacologic intervention

Kosten TR, Steinberg M, Diakogiannis IA. Crossover trial of mazindol for cocaine dependence. Am J Addict. 1993;2(2):161-4. doi: 10.3109/10550499309115955. Excluded: Non-FDA approved pharmacologic intervention

Kosten TR, Wu G, Huang W, et al. Pharmacogenetic randomized trial for cocaine abuse: disulfiram and dopamine beta-hydroxylase. Biol Psychiatry. 2013;73(3):219-24. doi: 10.1016/j.biopsych.2012.07.011. PMID: 22906516. Excluded: Non-FDA approved pharmacologic intervention

Kouimtsidis C, Reynolds M, Coulton S, et al. How does cognitive behaviour therapy work with opioid-dependent clients? Results of the UKCBTMM Study. Drugs Educ Prev Polic. 2012;19(3):253-8. doi: 10.3109/09687637.2011.579194. Excluded: Wrong comparator

Kourounis G, Richards BD, Kyprianou E, et al. Opioid substitution therapy: Lowering the treatment thresholds. Drug Alcohol Depend. 2016;161:1-8. doi: 10.1016/j.drugalcdep.2015.12.021. PMID: 26832931. Excluded: Wrong outcome

Kowalczyk WJ, Phillips KA, Jobes ML, et al. Clonidine maintenance prolongs opioid abstinence and decouples stress from craving in daily life: A randomized controlled trial with ecological momentary assessment. Am J Psychiatry. 2015;172(8):760-7. doi: 10.1176/appi.ajp.2014.14081014. PMID: 25783757. Excluded: Non-FDA approved pharmacologic intervention

Kraft MK, Rothbard AB, Hadley TR, et al. Are supplementary services provided during methadone maintenance really cost-effective? Am J Psychiatry. 1997;154(9):1214-9. PMID: 9286179. Excluded: Wrong comparator

Krupitsky E, Kibitov A, Zvartau E, et al. Pharmacogenetics of treatment of opioid dependence with oral naltrexone and long-acting sustained-release naltrexone implant. Drug Alcohol Depend. 2014;146(14). Excluded: Wrong outcome

Krupitsky E, Nunes EV, Ling W, et al. Injectable extended-release naltrexone (XR-NTX) for opioid dependence: long-term safety and effectiveness. Addiction. 2013;108(9):1628-37. doi: 10.1111/add.12208. PMID: 23701526. Excluded: Wrong study design for key question

Krupitsky E, Zvartau E, Blokhina E, et al. Pharmacogenetics of treatment of opioid dependence with oral naltrexone and long acting sustained release naltrexone implant. Eur Neuropsychopharmacol. 2013;23(5). Excluded: Wrong outcome

Krupitsky E, Zvartau E, Blokhina E, et al. Anhedonia, depression, anxiety, and craving for opiates in opiate addicts stabilized on oral naltrexone and long acting naltrexone implant. Drug Alcohol Depend. 2015;156(13). Excluded: Results reported elsewhere, duplicate results

Krupitsky E, Zvartau E, Blokhina E, et al. Anhedonia, depression, anxiety, and craving for opiates in opiate addicts stabilized on oral naltrexone and long acting naltrexone implant. Eur Neuropsychopharmacol. 2015;25(29). Excluded: Results reported elsewhere, duplicate results

Krupitsky E, Zvartau E, Blokhina E, et al. Anhedonia, depression, anxiety, and craving for opiates in opiate dependent patients stabilized on oral naltrexone or an extended release naltrexone implant. Neuropsychopharmacology. Conference: 55th annual meeting of the American College of Neuropsychopharmacology, ACNP. 2016;41:S205-S6. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Krupitsky E, Zvartau E, Masalov D, et al. Doubleblind placebo-controlled randomized clinical trial of naltrexone for heroin addiction and HIV risk reduction in Russia. Drug Alcohol Depend. 2002;66. Excluded: Results reported elsewhere, duplicate results

Krupitsky E, Zvartau EE, Woody G. Long acting naltrexone implants for heroin dependence. Eur Neuropsychopharmacol. 2009;19(12). Excluded: Results reported elsewhere, duplicate results

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Kumpfer KL, Alvarado R, Whiteside HO. Family-based interventions for substance use and misuse prevention. Subst Use Misuse. 2003;38(11-13):1759-87. PMID: 14582577. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Kunoe N, Lobmaier P, Vederhus JK, et al. Naltrexone implants after in-patient treatment for opioid dependence: randomised controlled trial. Br J Addict. 2009;194(6):541-6. doi: 10.1192/bjp.bp.108.055319. PMID: 19478295. Excluded: Wrong comparator

Kunoe N, Opheim A, Solli KK, et al. Design of a randomized controlled trial of extended-release naltrexone versus daily buprenorphine-naloxone for opioid dependence in Norway (NTX-SBX). BMC Pharmacol Toxicol. 2016;17(1):18. doi: 10.1186/s40360-016-0061-1. PMID: 27121539. Excluded: Wrong comparator

Kurland AA, McCabe L, Hanlon TE. Contingent naloxone (N-allylnoroxymorphone) treatment of the paroled narcotic addict. Int Pharmacopsychiatry. 1975;10(3):157-68. PMID: 1099047. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Kurti AN, Davis D, Redner R, et al. A review of the literature on remote monitoring technology in incentive-based interventions for health-related behavior change. Transl Issues Psychol Sci. 2016;2(2):128-52. doi: 10.1037/tps0000067. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Kurtz SP, Buttram ME, Pagano ME, et al. A randomized trial of brief assessment interventions for young adults who use drugs in the club scene. J Subst Abuse Treat. 2017;78:64-73. doi: 10.1016/j.jsat.2017.05.008. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Kurtz SP, Stall RD, Buttram ME, et al. A randomized trial of a behavioral intervention for high risk substance-using MSM. Aids Behav. 2013;17(9):2914-26. doi: 10.1007/s10461-013-0531-z. PMID: 23732957. Excluded: Other wrong population (e.g., schizophrenia focus)

LaCour F, Elk R, Grabowski J, et al. Contingency management interventions in the treatment of cocaine-dependent patients infected with tubercolosis. NIDA Res Monogr. 1997;174(76). Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Lagisetty P, Klasa K, Bush C, et al. Primary care models for treating opioid use disorders: What actually works? A systematic review. PLoS One. 2017;12(10):e0186315. doi: 10.1371/journal.pone.0186315. PMID: 29040331. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Lakshmana G. Efficacy of combination of motivational interviewing and cognitive behavior intervention with substance abuse street adolescents in India: A randomized control study. J Soc Work Pract Addict. 2016;16(4):337-57. doi: 10.1080/1533256X.2016.1235414. Excluded: Wrong country

Landabaso MA, Iraurgi I, Jimenez-Lerma JM, et al. A randomized trial of adding fluoxetine to a naltrexone treatment programme for heroin addicts. Addiction. 1998;93(5):739-44. PMID: 9692272. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Landovitz RJ, Fletcher JB, Shoptaw S, et al. Contingency management facilitates the use of postexposure prophylaxis among stimulant-using men who have sex with men. Open Forum Infect Dis. 2015;2(1) PMID: 25884003. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Laporte C, Vaillant-Roussel H, Pereira B, et al. Cannabis and young users-a brief intervention to reduce their consumption (CANABIC): A cluster randomized controlled trial in primary care. Ann Fam Med. 2017;15(2):131-9. doi: 10.1370/afm.2003. PMID: 28289112. Excluded: Poor quality

Laporte C, Vaillant-Roussel H, Pereira B, et al. CANABIC: CANnabis and adolescents: Effect of a brief intervention on their consumption - study protocol for a randomized controlled trial. Trials. 2014;15 PMID: 24479702. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Larney S. Does opioid substitution treatment in prisons reduce injecting-related HIV risk behaviours? A systematic review. Addiction. 2010;105(2):216-23. doi: 10.1111/j.1360-0443.2009.02826.x. PMID: 20078480. Excluded: Incarcerated population

Larochelle M, Bernson D, Land T, et al. Mortality after nonfatal opioid overdose: Medications for opioid use disorder are associated with lower risk. J Gen Intern Med. 2017;32(2):S250. Excluded: Wrong comparator

Lascaux M, Ionescu S, Phan O. Effectiveness of formalised therapy for adolescents with cannabis dependence: A randomised trial. Drugs Educ Prev Polic. 2016;23(5):404-9. doi: 10.3109/09687637.2016.1153603. Excluded: Wrong comparator

Lash SJ, Stephens RS, Burden JL, et al. Contracting, prompting, and reinforcing substance use disorder continuing care: a randomized clinical trial. Psychol Addict Behav. 2007;21(3):387-97. PMID: 17874889. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Latimer WW, Winters KC, D'Zurilla T, et al. Integrated family and cognitive-behavioral therapy for adolescent substance abusers: a stage I efficacy study. Drug Alcohol Depend. 2003;71(3):303-17. PMID: 12957348. Excluded: Wrong comparator

Laurer M, van der Vennet R. Effect of art production on negative mood and anxiety for adults in treatment for substance abuse. Art Therapy. 2015;32(4):177-83. doi: 10.1080/07421656.2015.1092731. Excluded: Wrong study design for key question

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Lavonas EJ, Severtson SG, Martinez EM, et al. Abuse and diversion of buprenorphine sublingual tablets and film. J Subst Abuse Treat. 2014;47(1):27-34. doi: 10.1016/j.jsat.2014.02.003. PMID: 24680219. Excluded: Wrong outcome

Law FD, Diaper AM, Melichar JK, et al. Buprenorphine/naloxone versus methadone and lofexidine in community stabilisation and detoxification: A randomised controlled trial of low dose short-term opiate-dependent individuals. J Psychopharmacol. 2017;31(8):1046-55. doi: 10.1177/0269881117711710. PMID: 28631527. Excluded: Wrong comparator

Law FD, Nutt DJ. Maintenance buprenorphine for opioid users. Lancet. 2003;361(9358):634-5. PMID: 12606172. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Ledberg A. Mortality related to methadone maintenance treatment in Stockholm, Sweden, during 2006-2013. J Subst Abuse Treat. 2017;74:35-41. doi: 10.1016/j.jsat.2016.12.005. PMID: 28132698. Excluded: Wrong study design for key question

Ledgerwood DM, Alessi SM, Hanson T, et al. Contingency management for attendance to group substance abuse treatment administered by clinicians in community clinics. J Appl Behav Anal. 2008;41(4):517-26. PMID: 19192856. Excluded: Wrong comparator

Ledgerwood DM, Petry NM. Does contingency management affect motivation to change substance use? Drug Alcohol Depend. 2006;83(1):65-72. PMID: 16310974. Excluded: Wrong comparator

Lee DC, Budney AJ, Brunette MF, et al. Outcomes from a computer-assisted intervention simultaneously targeting cannabis and tobacco use. Drug Alcohol Depend. 2015;155:134-40. doi: 10.1016/j.drugalcdep.2015.08.001. PMID: 26307942. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Lee EB, An W, Levin ME, et al. An initial meta-analysis of acceptance and commitment therapy for treating substance use disorders. Drug Alcohol Depend. 2015;155:1-7. doi: 10.1016/j.drugalcdep.2015.08.004. PMID: 26298552. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Lee J, Gourevitch MN, Joseph H, et al. Effectiveness of buprenorphine vs. methadone maintenance in jail and post-release: A pilot study. Subst Abus. 2009;30(2):204-5. doi: 10.1080/08897070902802133. Excluded: Incarcerated population

Lee JD, Friedmann PD, Boney TY, et al. Extended-release naltrexone to prevent relapse among opioid dependent, criminal justice system involved adults: rationale and design of a randomized controlled effectiveness trial. Contemp Clin Trials. 2015;41:110-7. doi: 10.1016/j.cct.2015.01.005. PMID: 25602580. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Lee JD, Friedmann PD, Kinlock TW, et al. Extended-release naltrexone to prevent opioid relapse in criminal justice offenders. N Engl J Med. 2016;374(13):1232-42. doi: 10.1056/NEJMoa1505409. PMID: 27028913. Excluded: Wrong comparator

Lee JD, Friedmann PD, Kinlock TW, et al. Extended-release naltrexone for opioid relapse prevention among opioid-dependent, criminal justice-involved adults. Drug Alcohol Depend. 2015;156(13). Excluded: Wrong comparator

Lee JD, Grossman E, Truncali A, et al. Buprenorphine-naloxone maintenance following release from jail. Subst Abus. 2012;33(1):40-7. doi: 10.1080/08897077.2011.620475. PMID: 22263712. Excluded: Wrong study design for key question

Lee JD, McDonald R, Grossman E, et al. Opioid treatment at release from jail using extended-release naltrexone: a pilot proof-of-concept randomized effectiveness trial. Addiction. 2015;110(6):1008-14. doi: 10.1111/add.12894. PMID: 25703440. Excluded: <3 month followup duration

Lee JD, Nunes EV, Mpa PN, et al. NIDA clinical trials network CTN-0051, extended-release naltrexone vs. buprenorphine for opioid treatment (X:BOT): Study design and rationale. Contemp Clin Trials. 2016;50:253-64. doi: 10.1016/j.cct.2016.08.004. PMID: 27521809. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Lee JD, Nunes EV, Jr., Novo P, et al. Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:bOT): a multicentre, open-label, randomised controlled trial. Lancet. 2018;27(391(10118)):309-19. doi: 10.1016/S0140-6736(17)32812-X. PMID: 29150198. Excluded: Wrong comparator

Lee NK, Rawson RA. A systematic review of cognitive and behavioural therapies for methamphetamine dependence. Drug Alcohol Rev. 2008;27(3):309-17. doi: 10.1080/09595230801919494. PMID: 18368613. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Lenz AS, Rosenbaum L, Sheperis D. Meta-analysis of randomized controlled trials of motivational enhancement therapy for reducing substance use. J Addict Offender Couns. 2016;37(2):66-86. doi: 10.1002/jaoc.12017. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Lerch J, Walters ST, Tang L, et al. Effectiveness of a computerized motivational intervention on treatment initiation and substance use: Results from a randomized trial. J Subst Abuse Treat. 2017;80:59-66. doi: 10.1016/j.jsat.2017.07.002. Excluded: <70% drug misuse or likely majority alcohol

Lester KM, Milby JB, Schumacher JE, et al. Impact of behavioral contingency management intervention on coping behaviors and PTSD symptom reduction in cocaine-addicted homeless. J Trauma Stress. 2007;20(4):565-75. PMID: 17721968. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Letourneau EJ, McCart MR, Sheidow AJ, et al. First evaluation of a contingency management intervention addressing adolescent substance use and sexual risk behaviors: Risk reduction therapy for adolescents. J Subst Abuse Treat. 2017;72:56-65. doi: 10.1016/j.jsat.2016.08.019. Excluded: Wrong comparator

Levin FR. Randomized controlled pharmacotherapy trials for cannabis use disorder in adults. J Am Acad Child Adolesc Psychiatry. 2016;Conference: 63rd annual meeting of the American Academy of Child and Adolescent Psychiatry. United States. Conference start:. 20161024. Conference end: 20161029 55(10 Supplement 1):S66-S7. Excluded: Non-FDA approved pharmacologic intervention

Levin FR, Mariani JJ, Chicurel M, et al. Utility of a contingency management strategy to improve retention in a pharmacologic treatment trial targeting cannabis dependence. Proceedings of the 69th Annual Scientific Meeting of the College on Problems of Drug Dependence. 2007. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Lewis MW, Petry NM. Contingency management treatments that reinforce completion of goal-related activities: participation in family activities and its association with outcomes. Drug Alcohol Depend. 2005;79(2):267-71. PMID: 16002037. Excluded: Wrong study design for key question

Lewis RA, Piercy FP, Sprenkle DH, et al. Family-based interventions for helping drug-abusing adolescents. J Adolesc Res. 1990;5(1):82-95. Excluded: Wrong comparator

Li L, Zhu S, Tse N, et al. Effectiveness of motivational interviewing to reduce illicit drug use in adolescents: a systematic review and meta-analysis. Addiction. 2016;111(5):795-805. doi: 10.1111/add.13285. PMID: 26687544. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Li W, Howard MO, Garland EL, et al. Mindfulness treatment for substance misuse: A systematic review and meta-analysis. J Subst Abuse Treat. 2017;75:62-96. doi: 10.1016/j.jsat.2017.01.008. PMID: 28153483. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Liang D, Han H, Du J, et al. A pilot study of a smartphone application supporting recovery from drug addiction. J Subst Abuse Treat. 2018;88:51-8. doi: 10.1016/j.jsat.2018.02.006. PMID: 29606226. Excluded: <3 month followup duration

Liddle H, Dakof G. A randomized controlled trial of intensive outpatient, family-based therapy vs. residential drug treatment for co-morbid adolescent substance abusers. Drug Alcohol Depend. 2002;66(1):S103. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Liddle HA. Family-based therapies for adolescent alcohol and drug use: research contributions and future research needs. Addiction. 2004;99 Suppl 2:76-92. PMID: 15488107. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Liddle HA. Multidimensional family therapy: A science-based treatment system for adolescent drug abuse. Sucht. 2010;56(1):43-50. doi: 10.1024/0939-5911/a000011. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Liddle HA. Multidimensional family therapy: Evidence base for transdiagnostic treatment outcomes, change mechanisms, and implementation in community settings. Fam Process. 2016;55(3):558-76. doi: 10.1111/famp.12243. PMID: 27565445. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Liddle HA, Dakof GA, Henderson C, et al. Implementation outcomes of multidimensional family therapy-detention to community: A reintegration program for drug-using juvenile detainees. Int J Offender Ther Comp Criminol. 2011;55(4):587-604. doi: 10.1177/0306624x10366960. PMID: 20427547. Excluded: Incarcerated population

Liddle HA, Dakof GA, Parker K, et al. Multidimensional family therapy for adolescent drug abuse: results of a randomized clinical trial. Am J Drug Alcohol Abuse. 2001;27(4):651-88. PMID: 11727882. Excluded: Wrong comparator

Liddle HA, Dakof GA, Turner RM, et al. Treating adolescent drug abuse: a randomized trial comparing multidimensional family therapy and cognitive behavior therapy. Addiction. 2008;103(10):1660-70. doi: 10.1111/j.1360-0443.2008.02274.x. PMID: 18705691. Excluded: Wrong comparator

Liddle HA, Rowe CL, Dakof GA, et al. Multidimensional family therapy for young adolescent substance abuse: twelve-month outcomes of a randomized controlled trial. J Consult Clin Psychol. 2009;77(1):12-25. doi: 10.1037/a0014160. PMID: 19170450. Excluded: Wrong comparator

Liddle HA, Rowe CL, Dakof GA, et al. Early intervention for adolescent substance abuse: pretreatment to posttreatment outcomes of a randomized clinical trial comparing multidimensional family therapy and peer group treatment. J Psychoactive Drugs. 2004;36(1):49-63. PMID: 15152709. Excluded: Wrong comparator

Liebschutz JM, Crooks D, Herman D, et al. Buprenorphine treatment for hospitalized, opioid-dependent patients: a randomized clinical trial. JAMA Intern Med. 2014;174(8):1369-76. doi: 10.1001/jamainternmed.2014.2556. PMID: 25090173. Excluded: Inpatient population

Liebschutz JM, Crooks D, Herman DS, et al. Initiating buprenorphine maintenance for opiate-dependent hospitalized patients: A randomized controlled trial. J Gen Intern Med. 2013;28(24). Excluded: Inpatient population

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Lincourt P, Kuettel TJ, Bombardier CH. Motivational interviewing in a group setting with mandated clients: a pilot study. Addict Behav. 2002;27(3):381-91. PMID: 12118626. Excluded: Wrong study design for key question

Lindeman CA. Adolescent substance abuse: The seven challenges treatment modality versus cognitive behavioral therapy: Walden University; 2009. Excluded: Wrong comparator

Lindstrom M, Filges T, Jorgensen A-MK. Brief strategic family therapy for young people in treatment for drug use. Res Soc Work Pract. 2015;25(1):61-80. doi: 10.1177/1049731514530003. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Linehan MM, Dimeff LA, Reynolds SK, et al. Dialectical behavior therapy versus comprehensive validation therapy plus 12-step for the treatment of opioid dependent women meeting criteria for borderline personality disorder. Drug Alcohol Depend. 2002;67(1):13-26. PMID: 12062776. Excluded: Other wrong population (e.g., schizophrenia focus)

Linehan MM, Schmidt H, 3rd, Dimeff LA, et al. Dialectical behavior therapy for patients with borderline personality disorder and drug-dependence. Am J Addict. 1999;8(4):279-92. PMID: 10598211. Excluded: Other wrong population (e.g., schizophrenia focus)

Ling Murtaugh K, Krishnamurti T, Davis AL, et al. Spend today, clean tomorrow: predicting methamphetamine abstinence in a randomized controlled trial. Health Psychol. 2013;32(9):958-66. doi: 10.1037/a0032922. PMID: 24001246. Excluded: Wrong comparator

Ling W, Amass L, Shoptaw S, et al. A multi-center randomized trial of buprenorphine-naloxone versus clonidine for opioid detoxification: findings from the National Institute on Drug Abuse Clinical Trials Network. Addiction. 2005;100(8):1090-100. PMID: 16042639. Excluded: Wrong comparator

Ling W, Charuvastra C, Collins JF, et al. Buprenorphine maintenance treatment of opiate dependence: a multicenter, randomized clinical trial. Addiction. 1998;93(4):475-86. PMID: 9684386. Excluded: <3 month followup duration

Ling W, Charuvastra C, Kaim SC, et al. Methadyl acetate and methadone as maintenance treatments for heroin addicts. A veterans administration cooperative study. Arch Gen Psychiatry. 1976;33(6):709-20. PMID: 779705. Excluded: Wrong comparator

Ling W, Dorus W, Hargreaves WA, et al. Alternative induction and crossover schedules for methadyl acetate. Arch Gen Psychiatry. 1984;41(2):193-9. PMID: 6365017. Excluded: Non-FDA approved pharmacologic intervention

Ling W, Hillhouse M, Ang A, et al. Comparison of behavioral treatment conditions in buprenorphine maintenance. Addiction. 2013;108(10):1788-98. doi: 10.1111/add.12266. PMID: 23734858. Excluded: Wrong comparator

Ling W, Klett CJ, Gillis RD. A cooperative clinical study of methadyl acetate. I. Three-times-a-week regimen. Arch Gen Psychiatry. 1978;35(3):345-53. PMID: 727887. Excluded: Non-FDA approved pharmacologic intervention

Ling W, Klett JC, Gillis RD. A cooperative clinical study of methadyl acetate. II. Friday-only regimen. Arch Gen Psychiatry. 1980;37(8):908-11. PMID: 7406654. Excluded: Non-FDA approved pharmacologic intervention

Ling W, Shoptaw S, Hillhouse M, et al. Double-blind placebo-controlled evaluation of the PROMETATM protocol for methamphetamine dependence. Addiction. 2012;107(2):361-9. doi: 10.1111/j.1360-0443.2011.03619.x. PMID: 22082089. Excluded: Non-FDA approved pharmacologic intervention

Ling W, Wesson DR, Charuvastra C, et al. A controlled trial comparing buprenorphine and methadone maintenance in opioid dependence. Arch Gen Psychiatry. 1996;53(5):401-7. PMID: 8624183. Excluded: Wrong comparator

Lintzeris N, Bammer G, Rushworth L, et al. Buprenorphine dosing regime for inpatient heroin withdrawal: a symptom-triggered dose titration study. Drug Alcohol Depend. 2003;70(3):287-94. PMID: 12757966. Excluded: <3 month followup duration

Lintzeris N, Bell J, Bammer G, et al. A randomized controlled trial of buprenorphine in the management of short-term ambulatory heroin withdrawal. Addiction. 2002;97(11):1395-404. PMID: 12410780. Excluded: Wrong comparator

Lintzeris N, Leung SY, Dunlop AJ, et al. A randomised controlled trial of sublingual buprenorphine-naloxone film versus tablets in the management of opioid dependence. Drug Alcohol Depend. 2013;131(1-2):119-26. doi: 10.1016/j.drugalcdep.2012.12.009. PMID: 23317685. Excluded: Wrong comparator

Lintzeris N, Strang J, Metrebian N, et al. Methodology for the randomised injecting opioid treatment trial (RIOTT): evaluating injectable methadone and injectable heroin treatment versus optimised oral methadone treatment in the UK. Harm Reduct J. 2006;3:28. PMID: 17002810. Excluded: Wrong comparator

Liu S, Li L, Shen W, et al. Scopolamine detoxification technique for heroin dependence: A randomized trial. CNS Drugs. 2013;27(12):1093-102. doi: 10.1007/s40263-013-0111-9. PMID: 24092568. Excluded: Wrong comparator

Lobmaier P, Kornor H, Kunoe N, et al. Sustained-release naltrexone for opioid dependence. Cochrane Database Syst Rev. 2008 (2):CD006140. doi: 10.1002/14651858.CD006140.pub2. PMID: 18425938. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Lobmaier PP, Kunoe N, Gossop M, et al. Naltrexone implants compared to methadone: outcomes six months after prison release. Eur Addict Res. 2010;16(3):139-45. doi: 10.1159/000313336. PMID: 20424458. Excluded: Wrong comparator

Lobmaier PP, Kunoe N, Gossop M, et al. Naltrexone depot formulations for opioid and alcohol dependence: a systematic review. CNS Neurosci Ther. 2011;17(6):629-36. doi: 10.1111/j.1755-5949.2010.00194.x. PMID: 21554565. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Lofwall MR, Stitzer ML, Bigelow GE, et al. Comparative safety and side effect profiles of buprenorphine and methadone in the outpatient treatment of opioid dependence. Addict Disord Their Treat. 2005;4(2):49-64. Excluded: Wrong comparator

Lofwall MR, Strain EC, Stitzer ML, et al. Comparative safety and side-effect profiles of buprenorphine vs. methadone in the outpatient treatment of opioid dependence. Proceedings of the 66th Annual Scientific Meeting of College on Problems of Drug Dependence. 2004. Excluded: Results reported elsewhere, duplicate results

Lones CE, Bond GR, McGovern MP, et al. Individual placement and support (IPS) for methadone maintenance therapy patients: A pilot randomized controlled trial. Adm Policy Ment Health. 2017;44(3):359-64. doi: 10.1007/s10488-017-0793-2. PMID: 28213673. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Longshore D, Annon J, Anglin MD, et al. Levo-alpha-acetylmethadol (LAAM) versus methadone: treatment retention and opiate use. Addiction. 2005;100(8):1131-9. PMID: 16042643. Excluded: Non-FDA approved pharmacologic intervention

Longshore D, Hsieh SC, Anglin MD. Reducing HIV risk behavior among injection drug users: effect of methadone maintenance treatment on number of sex partners. Int J Addict. 1994;29(6):741-57. PMID: 8034383. Excluded: Wrong study design for key question

Lott DC, Strain EC, Brooner RK, et al. HIV risk behaviors during pharmacologic treatment for opioid dependence: a comparison of levomethadyl acetate [corrected] buprenorphine, and methadone. J Subst Abuse Treat. 2006;31(2):187-94. PMID: 16919747. Excluded: Wrong comparator

Lott DC, Strain EC, Brooner RK, et al. HIV risk behaviors during pharmacologic treatment for opioid dependence: A comparison of levomethadyl acetate hydrochloride, buprenorphine, and methadone: "Erratum". J Subst Abuse Treat. 2006;31(3):317. doi: 10.1016/j.jsat.2006.09.001. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Lotts VA. Predicting treatment-related change in adolescent substance use from change in recovery environment: Sam Houston State University; 2013. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Lowe J, Liang H, Riggs C, et al. Community partnership to affect substance abuse among Native American adolescents. Am J Drug Alcohol Abuse. 2012;38(5):450-5. doi: 10.3109/00952990.2012.694534. PMID: 22931079. Excluded: Wrong comparator

Lua PL, Talib NS. Auricular acupuncture for drug dependence: an open-label randomized investigation on clinical outcomes, health-related quality of life, and patient acceptability. Altern Ther Health Med. 2013;19(4):28-42. PMID: 23981370. Excluded: Wrong comparator

Lucas GM, Beauchamp G, Aramrattana A, et al. Short-term safety of buprenorphine/naloxone in HIV-seronegative opioid-dependent Chinese and Thai drug injectors enrolled in HIV Prevention Trials Network 058. Int J Drug Policy. 2012;23(2):162-5. doi: 10.1016/j.drugpo.2011.06.005. PMID: 21852093. Excluded: Wrong study design for key question

Lucas GM, Chaudhry A, Hsu J, et al. Clinic-based treatment of opioid-dependent HIV-infected patients versus referral to an opioid treatment program: A randomized trial. Ann Intern Med. 2010;152(11):704-11. doi: 10.7326/0003-4819-152-11-201006010-00003. PMID: 20513828. Excluded: Wrong comparator

Lucas GM, Young A, Donnell D, et al. Hepatotoxicity in a 52-week randomized trial of short-term versus long-term treatment with buprenorphine/naloxone in HIV-negative injection opioid users in China and Thailand. Drug Alcohol Depend. 2014;142:139-45. doi: 10.1016/j.drugalcdep.2014.06.013. PMID: 24999060. Excluded: Wrong comparator

Ludwig AM, Levine J. A controlled comparison of five brief treatment techniques employing LSD, hypnosis, and psychotherapy. Am J Psychiatry. 1965;19:417-35. PMID: 14339608. Excluded: Wrong study design for key question

Lugoboni F, Mirijello A, Zamboni L, et al. High prevalence of constipation and reduced quality of life in opioid-dependent patients treated with opioid substitution treatments. Expert Opin Pharmacother. 2016;17(16):2135-41. doi: 10.1080/14656566.2016.1232391. PMID: 27603712. Excluded: Wrong study design for key question

Luoma JB, Kohlenberg BS, Hayes SC, et al. Slow and steady wins the race: a randomized clinical trial of acceptance and commitment therapy targeting shame in substance use disorders. J Consult Clin Psychol. 2012;80(1):43-53. doi: 10.1037/a0026070. PMID: 22040285. Excluded: Inpatient population

Lussier JP, Heil SH, Mongeon JA, et al. A meta-analysis of voucher-based reinforcement therapy for substance use disorders. Addiction. 2006;101(2):192-203. PMID: 16445548. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Luthar SS, Suchman NE, Altomare M. Relational psychotherapy mothers' group: A randomized clinical trial for substance abusing mothers. Dev Psychopathol. 2007;19(1):243-61. PMID: 17241493. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Ma J, Bao YP, Wang RJ, et al. Effects of medication-assisted treatment on mortality among opioids users: a systematic review and meta-analysis. Mol Psychiatry. 2018:1-16. doi: 10.1038/s41380-018-0094-5. PMID: 29934549. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

MacArthur GJ, Minozzi S, Martin N, et al. Opiate substitution treatment and HIV transmission in people who inject drugs: systematic review and meta-analysis. BMJ. 2012;345:e5945. doi: 10.1136/bmj.e5945. PMID: 23038795. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Macgowan MJ, Engle B. Evidence for optimism: behavior therapies and motivational interviewing in adolescent substance abuse treatment. Child Adolesc Psychiatr Clin N Am. 2010;19(3):527-45. doi: 10.1016/j.chc.2010.03.006. PMID: 20682219. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Maddux JF, Desmond DP, Vogtsberger KN. Patient-regulated methadone dose and optional counseling in methadone maintenance. Am J Addict. 1995;4(1):18-32. Excluded: Wrong comparator

Madigan K, Brennan D, Lawlor E, et al. A multi-center, randomized controlled trial of a group psychological intervention for psychosis with comorbid cannabis dependence over the early course of illness. Schizophr Res. 2013;143(1):138-42. doi: 10.1016/j.schres.2012.10.018. PMID: 23187069. Excluded: Other wrong population (e.g., schizophrenia focus)

Madlung-Kratzer E, Spitzer B, Brosch R, et al. A double-blind, randomized, parallel group study to compare the efficacy, safety and tolerability of slow-release oral morphine versus methadone in opioid-dependent in-patients willing to undergo detoxification. 2009;104(9):1549-57. doi: 10.1111/j.1360-0443.2009.02653.x. PMID: 19686525. Excluded: Wrong comparator

Madlung-Kratzer E, Spitzer B, Brosch R, et al. "A double-blind, randomized, parallel group study to compare the efficacy, safety and tolerability of slow-release oral morphine versus methadone in opioid dependent in-patients willing to undergo detoxification": Erratum. Addiction. 2009;104(11):1947. doi: 10.1111/j.1360-0443.2009.02818.x. Excluded: Inpatient population

Madras BK, Compton WM, Avula D, et al. Screening, brief interventions, referral to treatment (SBIRT) for illicit drug and alcohol use at multiple healthcare sites: Comparison at intake and 6 months later. Drug Alcohol Depend. 2009;99(1-3):280-95. doi: 10.1016/j.drugalcdep.2008.08.003. PMID: 18929451. Excluded: Wrong study design for key question

Magidson JF, Gorka SM, MacPherson L, et al. Examining the effect of the life enhancement treatment for substance use (LETS ACT) on residential substance abuse treatment retention. Addict Behav. 2011;36(6):615-23. doi: 10.1016/j.addbeh.2011.01.016. PMID: 21310539. Excluded: Inpatient population

Magill M. Cognitive-behavioral treatment with adult substance users: A meta-analysis. Dissertation Abstracts International Section A: Humanities and Social Sciences. 2008;68(10-A):4479. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Magill M, Apodaca TR, Borsari B, et al. A meta-analysis of motivational interviewing process: Technical, relational, and conditional process models of change. J Consult Clin Psychol. 2018;86(2):140-57. doi: 10.1037/ccp0000250. Excluded: Wrong outcome

Magill M, Ray LA. Cognitive-behavioral treatment with adult alcohol and illicit drug users: a meta-analysis of randomized controlled trials. J Stud Alcohol Drugs. 2009;70(4):516-27. PMID: 19515291. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Magura S, Blankertz L, Madison EM, et al. An innovative job placement model for unemployed methadone patients: a randomized clinical trial. Subst Use Misuse. 2007;42(5):811-28. PMID: 17613946. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Magura S, Lee JD, Hershberger J, et al. Buprenorphine and methadone maintenance in jail and post-release: a randomized clinical trial. Drug Alcohol Depend. 2009;99(1-3):222-30. doi: 10.1016/j.drugalcdep.2008.08.006. PMID: 18930603. Excluded: Wrong comparator

Malow RM, West JA, Corrigan SA, et al. Outcome of psychoeducation for HIV risk reduction. AIDS Educ Prev. 1994;6(2):113-25. PMID: 8018438. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Mandell W, Vlahov D, Latkin CA, et al. Changes in HIV risk behaviors among counseled injecting drug users. J Drug Issues. 1994;24(3):555-67. doi: 10.1177/002204269402400314. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Manganiello AJ. A comparative study of hypnotherapy and psychotherapy in the treatment of methadone addicts. Am J Clin Hypn. 1984;26(4):273-9. doi: 10.1080/00029157.1984.10402575. PMID: 6486078. Excluded: Wrong comparator

Mannaioni G, Lanzi C, Lotti M, et al. Methadone dose adjustments, plasma R-methadone levels and therapeutic outcome of heroin users: A randomized clinical trial. Eur Addict Res. 2018:9-18. doi: 10.1159/000485029. PMID: 29393208. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Mannelli P, Patkar AA, Peindl K, et al. Very low dose naltrexone addition in opioid detoxification: A randomized, controlled trial. Addict Biol. 2009;14(2):204-13. doi: 10.1111/j.1369-1600.2008.00119.x. PMID: 18715283. Excluded: <3 month followup duration

Mannelli P, Patkar AA, Peindl K, et al. Early outcomes following low dose naltrexone enhancement of opioid detoxification. Am J Addict. 2009;18(2):109-16. doi: 10.1080/10550490902772785. PMID: 19283561. Excluded: <3 month followup duration

Mannelli P, Patkar AA, Peindl K, et al. Effectiveness of low-dose naltrexone in the post-detoxification treatment of opioid dependence. J Clin Psychopharmacol. 2007;27(5):468-74. PMID: 17873678. Excluded: Wrong comparator

Mannelli P, Peindl K, Patkar AA, et al. Problem drinking and low-dose naltrexone-assisted opioid detoxification. J Stud Alcohol. 2011;72(3):507-13. PMID: 21513688. Excluded: <3 month followup duration

Mannelli P, Peindl K, Wu LT, et al. The combination very low-dose naltrexone-clonidine in the management of opioid withdrawal. Am J Drug Alcohol Abuse. 2012;38(3):200-5. doi: 10.3109/00952990.2011.644003. PMID: 22233189. Excluded: Non-FDA approved pharmacologic intervention

Mannelli P, Wu LT, Peindl KS, et al. Smoking and opioid detoxification: Behavioral changes and response to treatment. Nicotine Tob Res. 2013;15(10):1705-13. doi: 10.1093/ntr/ntt046. PMID: 23572466. Excluded: Wrong outcome

Manning V, Best D, Faulkner N, et al. Does active referral by a doctor or 12-Step peer improve 12-Step meeting attendance? Results from a pilot randomised control trial. Drug Alcohol Depend. 2012;126(1-2):131-7. doi: 10.1016/j.drugalcdep.2012.05.004. PMID: 22677458. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Mansergh G, Koblin BA, McKirnan DJ, et al. An intervention to reduce HIV risk behavior of substance-using men who have sex with men: a two-group randomized trial with a nonrandomized third group. PLoS Med. 2010;7(8):e1000329. doi: 10.1371/journal.pmed.1000329. PMID: 20811491. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Manuel JK, Hagedorn HJ, Finney JW. Implementing evidence-based psychosocial treatment in specialty substance use disorder care. Psychol Addict Behav. 2011;25(2):225-37. doi: 10.1037/a0022398. PMID: 21668085. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Marceau EM, Berry J, Lunn J, et al. Cognitive remediation improves executive functions, self-regulation and quality of life in residents of a substance use disorder therapeutic community. Drug Alcohol Depend. 2017;178:150-8. doi: 10.1016/j.drugalcdep.2017.04.023. PMID: 28651150. Excluded: Inpatient population

March JC, Oviedo-Joekes E, Perea-Milla E, et al. Controlled trial of prescribed heroin in the treatment of opioid addiction. J Subst Abuse Treat. 2006;31(2):203-11. PMID: 16919749. Excluded: Non-FDA approved pharmacologic intervention

Marchand KI, Oviedo-Joekes E, Guh D, et al. Client satisfaction among participants in a randomized trial comparing oral methadone and injectable diacetylmorphine for long-term opioid-dependency. BMC Health Serv Res. 2011;11:174. doi: 10.1186/1472-6963-11-174. PMID: 21791093. Excluded: Wrong comparator

Margolin A. Acupuncture for the treatment of cocaine addiction: a randomized controlled trial. Survey of Anesthesiology. 2002;47(2):118. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Margolin A, Avants S, Change P, et al. Acupuncture for the treatment of cocaine dependence in methadone-maintained patients. Am J Addict. 1993;2(3):194-201. doi: 10.3109/10550499309113938. Excluded: Wrong study design for key question

Margolin A, Avants S, Malison RT, et al. High- and low-dose mazindol for cocaine dependence in methadone-maintained patients: A preliminary evaluation. Subst Abus. 1997;18(3):125-31. doi: 10.1080/08897079709511358. Excluded: Non-FDA approved pharmacologic intervention

Margolin A, Avants SK, Arnold R. Acupuncture and spirituality-focused group therapy for the treatment of HIV-positive drug users: a preliminary study. J Psychoactive Drugs. 2005;37(4):385-90. PMID: 16480165. Excluded: Wrong comparator

Margolin A, Avants SK, Holford TR. Interpreting conflicting findings from clinical trials of auricular acupuncture for cocaine addiction: does treatment context influence outcome? J Altern Complement Med. 2002;8(2):111-21. PMID: 12006119. Excluded: <3 month followup duration

Margolin A, Avants SK, Kleber HD. Rationale and design of the cocaine alternative treatments study (CATS): a randomized, controlled trial of acupuncture. J Altern Complement Med. 1998;4(4):405-18. PMID: 9884178. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Margolin A, Avants SK, Kosten TR. Mazindol for relapse prevention to cocaine abuse in methadone-maintained patients. Am J Drug Alcohol Abuse. 1995;21(4):469-81. PMID: 8561098. Excluded: Non-FDA approved pharmacologic intervention

Margolin A, Avants SK, Kosten TR, et al. A double-blind study of mazindol for treatment of cocaine abuse in newly abstinent cocaine abusing methadone-maintained patients: a prelliminary report. NIDA Res Monogr. 1994;141:446. Excluded: Non-FDA approved pharmacologic intervention

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Margolin A, Avants SK, Warburton LA, et al. A randomized clinical trial of a manual-guided risk reduction intervention for HIV-positive injection drug users. Health Psychol. 2003;22(2):223-8. PMID: 12683743. Excluded: Wrong comparator

Marijuana Treatment Project Research Group, Vendetti J, McRee B, et al. Correlates of pre-treatment drop-out among persons with marijuana dependence. Addiction. 2002;97 Suppl 1:125-34. PMID: 12460134. Excluded: Wrong study design for key question

Marinković M, Djordjević-Jovanović L, Miljković S, et al. Quality of life of treated opiate addicts in the methadone maintenance program and those treated with buprenorphine. Vojnosanit Pregl. 2017;74(5):435-44. doi: 10.2298/VSP150710227M. Excluded: Wrong study design for key question

Marin-Navarrete R, Horigian VE, Medina-Mora ME, et al. Motivational enhancement treatment in outpatient addiction centers: A multisite randomized trial. Int J Clin Health Psychol. 2017;17(1):9-19. doi: 10.1016/j.ijchp.2016.05.001. Excluded: <70% drug misuse or likely majority alcohol

Marques AC, Formigoni ML. Comparison of individual and group cognitive-behavioral therapy for alcohol and/or drug-dependent patients. Addiction. 2001;96(6):835-46. PMID: 11399215. Excluded: Other wrong population (e.g., schizophrenia focus)

Marsch LA. The efficacy of methadone maintenance interventions in reducing illicit opiate use, HIV risk behavior and criminality: a meta-analysis. Addiction. 1998;93(4):515-32. PMID: 9684390. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Marsch LA, Bickel WK, Badger GJ, et al. Buprenorphine treatment for opioid dependence: the relative efficacy of daily, twice and thrice weekly dosing. Drug Alcohol Depend. 2005;77(2):195-204. PMID: 15664721. Excluded: Wrong comparator

Marsch LA, Bickel WK, Badger GJ, et al. Comparison of pharmacological treatments for opioid-dependent adolescents: a randomized controlled trial. Arch Gen Psychiatry. 2005;62(10):1157-64. PMID: 16203961. Excluded: Wrong comparator

Marsch LA, Guarino H, Acosta M, et al. Web-based behavioral treatment for substance use disorders as a partial replacement of standard methadone maintenance treatment. J Subst Abuse Treat. 2014;46(1):43-51. doi: 10.1016/j.jsat.2013.08.012. PMID: 24060350. Excluded: Wrong comparator

Marsch LA, Moore SK, Borodovsky JT, et al. A randomized controlled trial of buprenorphine taper duration among opioid-dependent adolescents and young adults. Addiction. 2016;111(8):1406-15. doi: 10.1111/add.13363. PMID: 26918564. Excluded: Wrong comparator

Marsch LA, Stephens MA, Mudric T, et al. Predictors of outcome in LAAM, buprenorphine, and methadone treatment for opioid dependence. Exp Clin Psychopharmacol. 2005;13(4):293-302. PMID: 16366759. Excluded: Wrong comparator

Marsden J, Goetz C, Meynen T, et al. Memory-focused cognitive therapy for cocaine use disorder: theory, procedures and preliminary evidence from an external pilot randomised controlled trial. EBioMedicine. 2018;29:177-89. doi: 10.1016/j.ebiom.2018.01.039. PMID: 29478874. Excluded: Wrong comparator

Marshall K, Gowing L, Ali R, et al. Pharmacotherapies for cannabis dependence. Cochrane Database Syst Rev. 2014 (12) PMID: 25515775. Excluded: Non-FDA approved pharmacologic intervention

Martell BA, Orson FM, Poling J, et al. Cocaine vaccine for the treatment of cocaine dependence in methadone-maintained patients: a randomized, double-blind, placebo-controlled efficacy trial. Arch Gen Psychiatry. 2009;66(10):1116-23. doi: 10.1001/archgenpsychiatry.2009.128. PMID: 19805702. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Martin G, Copeland J, Allsop S, et al. The adolescent cannabis check-up. Sixty Eight Annual Scientific Meeting of the College on Problems of Drug Dependence. 2005. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Martin WR, Jasinski DR, Mansky PA. Naltrexone, an antagonist for the treatment of heroin dependence. Effects in man. Arch Gen Psychiatry. 1973;28(6):784-91. PMID: 4707988. Excluded: Incarcerated population

Mason WA, Kosterman R, Hawkins JD, et al. Reducing adolescents' growth in substance use and delinquency: randomized trial effects of a parent-training prevention intervention. Prev Sci. 2003;4(3):203-12. PMID: 12940470. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Matheson C, Jaffray M, Bond C, et al. Improving outcomes and quality of life for people on methadone maintenance therapy (MMT): The enhanced pharmacy services (EPS) randomised controlled trial. Int J Pharm Pract. 2010;18:75-6. doi: 10.1111/j.2042-7174.2010.tb00512.x. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Mattick RP, Ali R, White JM, et al. Buprenorphine versus methadone maintenance therapy: a randomized double-blind trial with 405 opioid-dependent patients. Addiction. 2003;98(4):441-52. PMID: 12653814. Excluded: Wrong comparator

Mattick RP, Breen C, Kimber J, et al. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. Cochrane Database Syst Rev. 2009 (3):CD002209. doi: 10.1002/14651858.CD002209.pub2. PMID: 19588333. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Mattick RP, Breen C, Kimber J, et al. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database Syst Rev. 2014 (2):CD002207. doi: 10.1002/14651858.CD002207.pub4. PMID: 24500948. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Mattick RP, Kimber J, Breen C, et al. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database Syst Rev. 2008 (2):CD002207. doi: 10.1002/14651858.CD002207.pub3. PMID: 18425880. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Matz J, Graff C, Vainio PJ, et al. Effect of nalmefene 20 and 80 mg on the corrected QT interval and T-wave morphology: a randomized, double-blind, parallel-group, placebo- and moxifloxacin-controlled, single-centre study. Clin Drug Invest. 2011;31(11):799-811. doi: 10.2165/11592950-000000000-00000. PMID: 21967071. Excluded: Non-FDA approved pharmacologic intervention

Mauger S, Fraser R, Gill K. Utilizing buprenorphine-naloxone to treat illicit and prescription-opioid dependence. Neuropsychiatr Dis Treat. 2014;10:587-98. doi: 10.2147/NDT.S39692. PMID: 24741316. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Mausbach BT, Semple SJ, Strathdee SA, et al. Efficacy of a behavioral intervention for increasing safer sex behaviors in HIV-negative, heterosexual methamphetamine users: results from the Fast-Lane Study. Ann Behav Med. 2007;34(3):263-74. PMID: 18020936. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Mayer AR, Wilcox CE, Dodd AB, et al. The efficacy of attention bias modification therapy in cocaine use disorders. Am J Drug Alcohol Abuse. 2016;42(4):459-68. doi: 10.3109/00952990.2016.1151523. PMID: 27184297. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Mayet S, Farrell M, Ferri M, et al. Psychosocial treatment for opiate abuse and dependence. Cochrane Database Syst Rev. 2005 (1):CD004330. PMID: 15744796. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Mayet S, Farrell MF, Ferri M, et al. Psychosocial treatment for opiate abuse and dependence. Cochrane Database Syst Rev. 2014 (4) PMID: 15744796. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Mays KL, Clark DL, Gordon AJ. Treating addiction with tunes: a systematic review of music therapy for the treatment of patients with addictions. Substance Abuse. 2008;29(4):51-9. doi: 10.1080/08897070802418485. PMID: 19042198. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

McAuley A, Aucott L, Matheson C. Exploring the life-saving potential of naloxone: A systematic review and descriptive meta-analysis of take home naloxone (THN) programmes for opioid users. Int J Drug Policy. 2015;26(12):1183-8. doi: 10.1016/j.drugpo.2015.09.011. PMID: 26508033. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

McAuliffe WE. A randomized controlled trial of recovery training and self-help for opioid addicts in New England and Hong Kong. J Psychoactive Drugs. 1990;22(2):197-209. doi: 10.1080/02791072.1990.10472544. PMID: 2197394. Excluded: Other wrong population (e.g., schizophrenia focus)

McCambridge J, Gossop M, Beswick T, et al. In-patient detoxification procedures, treatment retention, and post-treatment opiate use: comparison of lofexidine + naloxone, lofexidine + placebo, and methadone. Drug Alcohol Depend. 2007;88(1):91-5. PMID: 17064857. Excluded: Wrong outcome

McCaul ME, Stitzer ML, Bigelow GE, et al. Contingency management interventions: effects on treatment outcome during methadone detoxification. J Appl Behav Anal. 1984;17(1):35-43. PMID: 6725168. Excluded: <3 month followup duration

McDermott KA, Griffin ML, Connery HS, et al. Initial response as a predictor of 12-week buprenorphine-naloxone treatment response in a prescription opioid-dependent population. J Clin Psychiatry. 2015;76(2):189-94. doi: 10.4088/JCP.14m09096. PMID: 25562462. Excluded: Wrong comparator

McDonald R, Strang J. Are take-home naloxone programmes effective? Systematic review utilizing application of the Bradford Hill criteria. Addiction. 2016;111(7):1177-87. doi: 10.1111/add.13326. PMID: 27028542. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

McDonald RD, Tofighi B, Laska E, et al. Extended-release naltrexone opioid treatment at jail reentry (XOR). Contemp Clin Trials. 2016;49:57-64. doi: 10.1016/j.cct.2016.05.002. PMID: 27178765. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

McGillicuddy NB, Rychtarik RG, Duquette JA, et al. Development of a skill training program for parents of substance-abusing adolescents. J Subst Abuse Treat. 2001;20(1):59-68. PMID: 11239729. Excluded: <3 month followup duration

McGillicuddy NB, Rychtarik RG, Papandonatos GD. Skill training versus 12-step facilitation for parents of substance-abusing teens. J Subst Abuse Treat. 2015;50:11-7. doi: 10.1016/j.jsat.2014.09.006. PMID: 25306932. Excluded: Wrong outcome

McGlone L, Mactier H. Infants of opioid-dependent mothers: neurodevelopment at six months. Early Hum Dev. 2015;91(1):19-21. doi: 10.1016/j.earlhumdev.2014.10.006. PMID: 25460252. Excluded: Wrong study design for key question

McGovern MP, Lambert-Harris C, Xie H, et al. A randomized controlled trial of treatments for co-occurring substance use disorders and post-traumatic stress disorder. Addiction. 2015;110(7):1194-204. doi: 10.1111/add.12943. PMID: 25846251. Excluded: Other wrong population (e.g., schizophrenia focus)

McGregor C, Ali R, White JM, et al. A comparison of antagonist-precipitated withdrawal under anesthesia to standard inpatient withdrawal as a precursor to maintenance naltrexone treatment in heroin users: outcomes at 6 and 12 months. Drug Alcohol Depend. 2002;68(1):5-14. PMID: 12167548. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

McKay JR, Alterman AI, Cacciola JS, et al. Group counseling versus individualized relapse prevention aftercare following intensive outpatient treatment for cocaine dependence: initial results. J Consult Clin Psychol. 1997;65(5):778-88. PMID: 9337497. Excluded: Wrong comparator

McKay JR, Lynch KG, Shepard DS, et al. The effectiveness of telephone-based continuing care for alcohol and cocaine dependence: 24-month outcomes. Arch Gen Psychiatry. 2005;62(2):199-207. Excluded: Wrong comparator

McKay JR, van Horn D, Ivey M, et al. Enhanced continuing care provided in parallel to intensive outpatient treatment does not improve outcomes for patients with cocaine dependence. J Stud Alcohol Drugs. 2013;74(4):642-51. PMID: 23739030. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

McKay JR, Van Horn DH, Lynch KG, et al. An adaptive approach for identifying cocaine dependent patients who benefit from extended continuing care. J Consult Clin Psychol. 2013;81(6):1063-73. doi: 10.1037/a0034265. PMID: 24041231. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

McKeganey N, Russell C, Cockayne L. Medically assisted recovery from opiate dependence within the context of the UK drug strategy: methadone and Suboxone (buprenorphine-naloxone) patients compared. J Subst Abuse Treat. 2013;44(1):97-102. doi: 10.1016/j.jsat.2012.04.003. PMID: 22703715. Excluded: Wrong comparator

McKellar J, Wagner T, Harris A, et al. One-year outcomes of telephone case monitoring for patients with substance use disorder. Addict Behav. 2012;37(10):1069-74. doi: 10.1016/j.addbeh.2012.03.009. PMID: 22651986. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

McKenzie M, Zaller N, Dickman SL, et al. A randomized trial of methadone initiation prior to release from incarceration. Subst Abus. 2012;33(1):19-29. doi: 10.1080/08897077.2011.609446. PMID: 22263710. Excluded: Incarcerated population

McLachlan C, Crofts N, Wodak A, et al. The effects of methadone on immune function among injecting drug users: a review. Addiction. 1993;88(2):257-63. PMID: 8220063. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

McLellan AT, Arndt IO, Metzger DS, et al. The effects of psychosocial services in substance abuse treatment. JAMA. 1993;269(15):1953-9. PMID: 8385230. Excluded: Wrong comparator

McLellan AT, Grossman DS, Blaine JD, et al. Acupuncture treatment for drug abuse: a technical review. J Subst Abuse Treat. 1993;10(6):569-76. PMID: 8308942. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

McLoughlin BC, PushpaRajah JA, Gillies D, et al. Cannabis and schizophrenia. Cochrane Database Syst Rev. 2014 (10)doi: 10.1002/14651858.CD004837.pub3. PMID: 25314586. Excluded: Other wrong population (e.g., schizophrenia focus)

McMillan GP, Lapham S, Lackey M. The effect of a jail methadone maintenance therapy (MMT) program on inmate recidivism. Addiction. 2008;103(12):2017-23. doi: 10.1111/j.1360-0443.2008.02361.x. PMID: 19469745. Excluded: Incarcerated population

McNicholas LF, Holbrook AM, O'Grady KE, et al. Effect of hepatitis C virus status on liver enzymes in opioid-dependent pregnant women maintained on opioid-agonist medication. Addiction. 2012;107 Suppl 1:91-7. doi: 10.1111/j.1360-0443.2012.04043.x. PMID: 23106931. Excluded: Wrong comparator

McRae AL, Budney AJ, Brady KT. Treatment of marijuana dependence: a review of the literature. J Subst Abuse Treat. 2003;24(4):369-76. PMID: 12867212. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Meade CS, Weiss RD, Fitzmaurice GM, et al. HIV risk behavior in treatment-seeking opioid-dependent youth: Results from a NIDA clinical trials network multisite study. J Acquir Immune Defic Syndr. 2010;55(1):65-72. doi: 10.1097/QAI.0b013e3181d916db. PMID: 20393347. Excluded: Wrong comparator

Meader N. A comparison of methadone, buprenorphine and alpha(2) adrenergic agonists for opioid detoxification: a mixed treatment comparison meta-analysis. Drug Alcohol Depend. 2010;108(1-2):110-4. doi: 10.1016/j.drugalcdep.2009.12.008. PMID: 20074867. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Meader N, Li R, Des Jarlais CD, et al. Psychosocial interventions for reducing injection and sexual risk behaviour for preventing HIV in drug users. Cochrane Database Syst Rev. 2010 (1)doi: 10.1002/14651858.CD007192.pub2. PMID: 20091623. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Meandzija B, O'Connor PG, Fitzgerald B, et al. HIV infection and cocaine use in methadone maintained and untreated intravenous drug users. Drug Alcohol Depend. 1994;36(2):109-13. PMID: 7851277. Excluded: Wrong study design for key question

Medvin RB, Brooks AC, Carpenedo CM, et al. Expanded brief intervention in primary care results in reduced self-reported substance use at six-month follow-up: Preliminary results. Drug Alcohol Depend. 2015;156(13). Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Meier A, McGovern MP, Lambert-Harris C, et al. Adherence and competence in two manual-guided therapies for co-occurring substance use and posttraumatic stress disorders: clinician factors and patient outcomes. Am J Drug Alcohol Abuse. 2015;41(6):527-34. doi: 10.3109/00952990.2015.1062894. PMID: 26286351. Excluded: Other wrong population (e.g., schizophrenia focus)

Melendez-Torres GJ, Bonell C. Systematic review of cognitive behavioural interventions for HIV risk reduction in substance-using men who have sex with men. Int J STD AIDS. 2014;25(9):627-35. doi: 10.1177/0956462413515638. PMID: 24352122. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Mello NK, Mendelson JH, Kuehnle JC, et al. Operant analysis of human heroin self-administration and the effects of naltrexone. J Pharmacol Exp Ther. 1981;216(1):45-54. PMID: 7452507. Excluded: <3 month followup duration

Mendelson J, Jones RT, Welm S, et al. Buprenorphine and naloxone combinations: the effects of three dose ratios in morphine-stabilized, opiate-dependent volunteers. Psychopharmacology (Berl). 1999;141(1):37-46. PMID: 9952063. Excluded: <3 month followup duration

Mendelson J, Jones RT, Welm S, et al. Buprenorphine and naloxone interactions in methadone maintenance patients. Biol Psychiatry. 1997;41(11):1095-101. PMID: 9146820. Excluded: <3 month followup duration

Menza TW, Jameson DR, Hughes JP, et al. Contingency management to reduce methamphetamine use and sexual risk among men who have sex with men: a randomized controlled trial. BMC Public Health. 2010;10:774. doi: 10.1186/1471-2458-10-774. PMID: 21172026. Excluded: Wrong comparator

Merchant RC, Baird JR, Liu T. Short-term efficacy of a brief intervention to reduce drug misuse and increase drug treatment utilization among adult emergency department patients. Acad Emerg Med. 2015;22(10):1172-80. doi: 10.1111/acem.12767. PMID: 26375468. Excluded: Poor quality

Merchant RC, Baird JR, Liu T, et al. Brief intervention to increase emergency department uptake of combined rapid human immunodeficiency virus and hepatitis C screening among a drug misusing population. Acad Emerg Med. 2014;21(7):752-67. doi: 10.1111/acem.12419. PMID: 25125271. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Merchant RC, Zhang Z, Liu T, et al. Does a brief intervention reduce drug use and increase drug treatment utilization among adult emergency department patients over a one-year period? Acad Emerg Med. 2016;23(10). Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Messina N, Farabee D, Rawson R. Treatment responsivity of cocaine-dependent patients with antisocial personality disorder to cognitive-behavioral and contingency management interventions. J Consult Clin Psychol. 2003;71(2):320-9. PMID: 12699026. Excluded: Wrong comparator

Metz V, Jagsch R, Ebner N, et al. Impact of treatment approach on maternal and neonatal outcome in pregnant opioid-maintained women. Hum Psychopharmacol. 2011;26(6):412-21. doi: 10.1002/hup.1224. PMID: 21823171. Excluded: Wrong comparator

Metzger DS, Donnell D, Celentano DD, et al. Expanding substance use treatment options for HIV prevention with buprenorphine-naloxone: HIV prevention trials network 058. J Acquir Immune Defic Syndr. 2015;68(5):554-61. doi: 10.1097/QAI.0000000000000510. PMID: 25564105. Excluded: Wrong comparator

Meyer MC, Johnston AM, Crocker AM, et al. Methadone and buprenorphine for opioid dependence during pregnancy: a retrospective cohort study. J Addict Med. 2015;9(2):81-6. doi: 10.1097/ADM.0000000000000092. PMID: 25622120. Excluded: Wrong comparator

Michel L, Lions C, Maradan G, et al. Suicidal risk among patients enrolled in methadone maintenance treatment: HCV status and implications for suicide prevention (ANRS Methaville). Compr Psychiatry. 2015;62:123-31. doi: 10.1016/j.comppsych.2015.07.004. PMID: 26343476. Excluded: Wrong study design for key question

Milburn NG, Iribarren FJ, Rice E, et al. A family intervention to reduce sexual risk behavior, substance use, and delinquency among newly homeless youth. J Adolesc Health. 2012;50(4):358-64. doi: 10.1016/j.jadohealth.2011.08.009. PMID: 22443839. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Milby JB, Clarke C, Toro C, et al. Effectiveness of urine surveillance as an adjunct to outpatient psychotherapy for drug abusers. Int J Addict. 1980;15(7):993-1001. PMID: 7450954. Excluded: Wrong comparator

Milby JB, Garrett C, English C, et al. Take-home methadone: contingency effects on drug-seeking and productivity of narcotic addicts. Addict Behav. 1978;3(3-4):215-20. PMID: 735908. Excluded: Wrong comparator

Milby JB, Schumacher JE, Raczynski JM, et al. Sufficient conditions for effective treatment of substance abusing homeless persons. Drug Alcohol Depend. 1996;43(1-2):39-47. doi: 10.1016/S0376-8716%2896%2901286-0. Excluded: Other wrong population (e.g., schizophrenia focus)

Miller WR, Yahne CE, Tonigan JS. Motivational interviewing in drug abuse services: a randomized trial. J Consult Clin Psychol. 2003;71(4):754-63. PMID: 12924680. Excluded: Wrong comparator

Mills EJ, Wu P, Gagnier J, et al. Efficacy of acupuncture for cocaine dependence: A systematic review & meta-analysis. Harm Reduct J. 2005;2. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Min Z, Xu L, Chen H, et al. A pilot assessment of relapse prevention for heroin addicts in a Chinese rehabilitation center. Am J Drug Alcohol Abuse. 2011;37(3):141-7. doi: 10.3109/00952990.2010.538943. PMID: 21438799. Excluded: Wrong study design for key question

Minozzi S, Amato L, Bellisario C, et al. Maintenance treatments for opiate -dependent adolescents. Cochrane Database Syst Rev. 2014 (6):CD007210. doi: 10.1002/14651858.CD007210.pub3. PMID: 24957634. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Minozzi S, Amato L, Bellisario C, et al. Detoxification treatments for opiate dependent adolescents. Cochrane Database Syst Rev. 2014 (4):CD006749. doi: 10.1002/14651858.CD006749.pub3. PMID: 24777492. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Minozzi S, Amato L, Bellisario C, et al. Maintenance agonist treatments for opiate-dependent pregnant women. Cochrane Database Syst Rev. 2013 (12):CD006318. doi: 10.1002/14651858.CD006318.pub3. PMID: 24366859. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Minozzi S, Amato L, Davoli M. Maintenance treatments for opiate dependent adolescent. Cochrane Database Syst Rev. 2009 (2):CD007210. doi: 10.1002/14651858.CD007210.pub2. PMID: 19370679. Excluded: Wrong comparator

Minozzi S, Amato L, Davoli M. Detoxification treatments for opiate dependent adolescents. Cochrane Database Syst Rev. 2009 (2):CD006749. doi: 10.1002/14651858.CD006749.pub2. PMID: 19370651. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Minozzi S, Amato L, Pani PP, et al. Dopamine agonists for the treatment of cocaine dependence. Cochrane Database Syst Rev. 2015 (5) PMID: 26014366. Excluded: Non-FDA approved pharmacologic intervention

Minozzi S, Amato L, Vecchi S, et al. Oral naltrexone maintenance treatment for opioid dependence. Cochrane Database Syst Rev. 2011 (4):CD001333. doi: 10.1002/14651858.CD001333.pub4. PMID: 21491383. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Minozzi S, Cinquini M, Amato L, et al. Anticonvulsants for cocaine dependence. Cochrane Database Syst Rev. 2015 (6) PMID: 25882271. Excluded: Non-FDA approved pharmacologic intervention

Mintz J, O'Brien CP, O'Hare K, et al. Double-blind detoxification of methadone maintenance patients. Int J Addict. 1975;10(5):815-24. PMID: 1176233. Excluded: Wrong comparator

Mintzer MZ, Correia CJ, Strain EC. A dose-effect study of repeated administration of buprenorphine/naloxone on performance in opioid-dependent volunteers. Drug Alcohol Depend. 2004;74(2):205-9. PMID: 15099664. Excluded: <3 month followup duration

Miranda R, Ray L, Blanchard A, et al. Effects of naltrexone on adolescent alcohol cue reactivity and sensitivity: an initial randomized trial. Addict Biol. 2014;19(5):941-54. doi: 10.1111/adb.12050. PMID: 23489253. Excluded: Other wrong population (e.g., schizophrenia focus)

Mitchell SG, Gryczynski J, Schwartz RP, et al. Changes in quality of life following buprenorphine treatment: Relationship with treatment retention and illicit opioid use. J Psychoactive Drugs. 2015;47(2):149-57. doi: 10.1080/02791072.2015.1014948. PMID: 25950595. Excluded: Wrong study design for key question

Mitchell SG, Gryczynski J, Schwartz RP, et al. A randomized trial of intensive outpatient (IOP) vs. standard outpatient (OP) buprenorphine treatment for African Americans. Drug Alcohol Depend. 2013;128(3):222-9. doi: 10.1016/j.drugalcdep.2012.08.027. PMID: 22999817. Excluded: Wrong comparator

Mitchell TB, White JM, Somogyi AA, et al. Comparative pharmacodynamics and pharmacokinetics of methadone and slow-release oral morphine for maintenance treatment of opioid dependence. Drug Alcohol Depend. 2003;72(1):85-94. PMID: 14563546. Excluded: <3 month followup duration

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Mitchell TB, White JM, Somogyi AA, et al. Slow-release oral morphine versus methadone: a crossover comparison of patient outcomes and acceptability as maintenance pharmacotherapies for opioid dependence. Addiction. 2004;99(8):940-5. PMID: 15265090. Excluded: Wrong comparator

Mitcheson L, McCambridge J, Byrne S. Pilot cluster-randomised trial of adjunctive motivational interviewing to reduce crack cocaine use in clients on methadone maintenance. Eur Addict Res. 2007;13(1):6-10. PMID: 17172773. Excluded: <3 month followup duration

Mogro-Wilson C, Letendre J, Toi H, et al. Utilizing mutual aid in reducing adolescent substance use and developing group engagement. Res Soc Work Pract. 2015;25(1):129-38. doi: 10.1177/1049731513518080. Excluded: <3 month followup duration

Mojtabai R, Zivin JG. Effectiveness and cost-effectiveness of four treatment modalities for substance disorders: a propensity score analysis. Health Serv Res. 2003;38(1 Pt 1):233-59. PMID: 12650390. Excluded: Wrong study design for key question

Mok MS, Lippmann M, Steen SN. Multidose/observational, comparative clinical analgetic evaluation of buprenorphine. J Clin Pharmacol. 1981;21(7):323-9. PMID: 7263931. Excluded: Wrong comparator

Monico LB, Gryczynski J, Schwartz RP, et al. Treatment outcomes among a cohort of African American buprenorphine patients: follow-up at 12 months. Am J Drug Alcohol Abuse. 2018;44(6):604-10. doi: 10.1080/00952990.2018.1461877. PMID: 29718715. Excluded: Wrong comparator

Montgomery L, Burlew AK, Kosinski AS, et al. Motivational enhancement therapy for African American substance users: a randomized clinical trial. Cultur Divers Ethnic Minor Psychol. 2011;17(4):357-65. doi: 10.1037/a0025437. PMID: 21988576. Excluded: Wrong outcome

Montgomery L, Carroll KM, Petry NM. Initial abstinence status and contingency management treatment outcomes: does race matter? J Consult Clin Psychol. 2015;83(3):473-81. doi: 10.1037/a0039021. PMID: 25798729. Excluded: Wrong outcome

Montgomery L, Robinson C, Seaman EL, et al. A scoping review and meta-analysis of psychosocial and pharmacological treatments for cannabis and tobacco use among African Americans. Psychol Addict Behav. 2017;31(8):922-43. doi: 10.1037/adb0000326. PMID: 29199844. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Monti PM, Abrams DB, Binkoff JA, et al. Communication skills training, communication skills training with family and cognitive behavioral mood management training for alcoholics. J Stud Alcohol. 1990;51(3):263-70. PMID: 2342366. Excluded: Other wrong population (e.g., schizophrenia focus)

Monti PM, Rohsenow DJ, Michalec E, et al. Brief coping skills treatment for cocaine abuse: substance use outcomes at three months. Addiction. 1997;92(12):1717-28. PMID: 9581004. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Monti PM, Rohsenow DJ, Rubonis AV, et al. Cue exposure with coping skills treatment for male alcoholics: a preliminary investigation. J Consult Clin Psychol. 1993;61(6):1011-9. PMID: 7906700. Excluded: Other wrong population (e.g., schizophrenia focus)

Monti PM, Rohsenow DJ, Swift RM, et al. Naltrexone and cue exposure with coping and communication skills training for alcoholics: treatment process and 1-year outcomes. Alcohol Clin Exp Res. 2001;25(11):1634-47. PMID: 11707638. Excluded: Other wrong population (e.g., schizophrenia focus)

Montoya ID, Gorelick DA, Preston KL, et al. Randomized trial of buprenorphine for treatment of concurrent opiate and cocaine dependence. Clin Pharmacol Ther. 2004;75(1):34-48. PMID: 14749690. Excluded: Wrong comparator

Montoya ID, Schroeder JR, Preston KL, et al. Influence of psychotherapy attendance on buprenorphine treatment outcome. J Subst Abuse Treat. 2005;28(3):247-54. PMID: 15857725. Excluded: Wrong comparator

Montoya ID, Svikis D, Marcus SC, et al. Psychiatric care of patients with depression and comorbid substance use disorders. J Clin Psychiatry. 2000;61(9):698-705; quiz 6. PMID: 11030495. Excluded: Wrong study design for key question

Mooney L, Hillhouse MP, Thomas C, et al. Psychiatric symptoms and treatment outcomes in cocaine-dependent adults treated with buprenorphine and long-acting naltrexone. Drug Alcohol Depend. 2015;156(13). Excluded: <3 month followup duration

Mooney LJ, Nielsen S, Saxon A, et al. Cocaine use reduction with buprenorphine (CURB): rationale, design, and methodology. Contemp Clin Trials. 2013;34(2):196-204. doi: 10.1016/j.cct.2012.11.002. PMID: 23159524. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Mooney ME, Poling J, Gonzalez G, et al. Preliminary study of buprenorphine and bupropion for opioid-dependent smokers. Am J Addict. 2008;17(4):287-92. doi: 10.1080/10550490802138814. PMID: 18612883. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Moore BA, Barry DT, Sullivan LE, et al. Counseling and directly observed medication for primary care buprenorphine maintenance: a pilot study. J Addict Med. 2012;6(3):205-11. doi: 10.1097/ADM.0b013e3182596492. PMID: 22614936. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Moore BA, Fiellin DA, Cutter CJ, et al. Cognitive behavioral therapy improves treatment outcomes for prescription opioid users in primary care buprenorphine treatment. J Subst Abuse Treat. 2016;71:54-7. doi: 10.1016/j.jsat.2016.08.016. PMID: 27776678. Excluded: Wrong comparator

Moore SK, Marsch LA, Badger GJ, et al. Improvement in psychopathology among opioid-dependent adolescents during behavioral-pharmacological treatment. J Addict Med. 2011;5(4):264-71. doi: 10.1097/ADM.0b013e3182191099. PMID: 22107875. Excluded: Wrong comparator

Morgan JR, Schackman BR, Leff JA, et al. Injectable naltrexone, oral naltrexone, and buprenorphine utilization and discontinuation among individuals treated for opioid use disorder in a United States commercially insured population. J Subst Abuse Treat. 2018;85:90-6. doi: 10.1016/j.jsat.2017.07.001. Excluded: Wrong study design for key question

Morgenstern J, Blanchard KA, Kahler C, et al. Testing mechanisms of action for intensive case management. Addiction. 2008;103(3):469-77. doi: 10.1111/j.1360-0443.2007.02100.x. PMID: 18269366. Excluded: Wrong outcome

Morgenstern J, Blanchard KA, McCrady BS, et al. Effectiveness of intensive case management for substance-dependent women receiving temporary assistance for needy families. Am J Public Health. 2006;96(11):2016-23. doi: 10.2105/ajph.2005.076380. PMID: 17018819. Excluded: Wrong comparator

Morgenstern J, Blanchard KA, Morgan TJ, et al. Testing the effectiveness of cognitive-behavioral treatment for substance abuse in a community setting: within treatment and posttreatment findings. J Consult Clin Psychol. 2001;69(6):1007-17. PMID: 11777104. Excluded: <70% drug misuse or likely majority alcohol

Morgenstern J, Bux DA, Parsons J, et al. Randomized trial to reduce club drug use and HIV risk behaviors among men who have sex with men. J Consult Clin Psychol. 2009;77(4):645-56. doi: 10.1037/a0015588. PMID: 19634958. Excluded: Other wrong population (e.g., schizophrenia focus)

Morgenstern J, Hogue A, Dauber S, et al. A practical clinical trial of coordinated care management to treat substance use disorders among public assistance beneficiaries. J Consult Clin Psychol. 2009;77(2):257-69. doi: 10.1037/a0014489. PMID: 19309185. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Morie KP, Nich C, Hunkele K, et al. Alexithymia level and response to computer-based training in cognitive behavioral therapy among cocaine-dependent methadone maintained individuals. Drug Alcohol Depend. 2015;152:157-63. doi: 10.1016/j.drugalcdep.2015.04.004. PMID: 25982006. Excluded: <3 month followup duration

Morley KC, Sitharthan G, Haber PS, et al. The efficacy of an opportunistic cognitive behavioral intervention package (OCB) on substance use and comorbid suicide risk: a multisite randomized controlled trial. J Consult Clin Psychol. 2014;82(1):130-40. doi: 10.1037/a0035310. PMID: 24364795. Excluded: Other wrong population (e.g., schizophrenia focus)

Morley KC, Teesson M, Reid SC, et al. Naltrexone versus acamprosate in the treatment of alcohol dependence: A multi-centre, randomized, double-blind, placebo-controlled trial. Addiction. 2006;101(10):1451-62. doi: 10.1111/j.1360-0443.2006.01555.x. PMID: 16968347. Excluded: Other wrong population (e.g., schizophrenia focus)

Morral AR, McCaffrey DF, Ridgeway G. Effectiveness of community-based treatment for substance-abusing adolescents: 12-month outcomes of youths entering phoenix academy or alternative probation dispositions. Psychol Addict Behav. 2004;18(3):257-68. doi: 10.1037/0893-164x.18.3.257. PMID: 15482081. Excluded: Wrong comparator

Motamed M, Marsch LA, Solhkhah R, et al. Differences in treatment outcomes between prescription opioid-dependent and heroin-dependent adolescents. J Addict Med. 2008;2(3):158-64. doi: 10.1097/ADM.0b013e31816b2f84. PMID: 21768987. Excluded: <3 month followup duration

Msekela S, Krupitsky E, Zvartau E, et al. Stabilization of remission from opioid dependence with long-acting naltrexone implant. Eur Neuropsychopharmacol. 2014;24(6). Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Mullins SM, Suarez M, Ondersma SJ, et al. The impact of motivational interviewing on substance abuse treatment retention: a randomized control trial of women involved with child welfare. J Subst Abuse Treat. 2004;27(1):51-8. doi: 10.1016/j.jsat.2004.03.010. PMID: 15223094. Excluded: Wrong comparator

Murphy KM. Music therapy in addictions treatment: A systematic review of the literature and recommendations for future research. Music and Medicine. 2017;9(1):15-23. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Mysels DJ, Cheng WY, Nunes EV, et al. The association between naltrexone treatment and symptoms of depression in opioid-dependent patients. Am J Drug Alcohol Abuse. 2011;37(1):22-6. doi: 10.3109/00952990.2010.540281. PMID: 21192125. Excluded: <3 month followup duration

Najavits LM, Gallop RJ, Weiss RD. Seeking safety therapy for adolescent girls with PTSD and substance use disorder: a randomized controlled trial. J Behav Health Serv Res. 2006;33(4):453-63. doi: 10.1007/s11414-006-9034-2. PMID: 16858633. Excluded: Other wrong population (e.g., schizophrenia focus)

Najavits LM, Johnson KM. Pilot study of Creating Change, a new past-focused model for PTSD and substance abuse. Am J Addict. 2014;23(5):415-22. doi: 10.1111/j.1521-0391.2014.12127.x. PMID: 24628840. Excluded: Other wrong population (e.g., schizophrenia focus)

Neufeld KJ, Kidorf MS, Kolodner K, et al. A behavioral treatment for opioid-dependent patients with antisocial personality. J Subst Abuse Treat. 2008;34(1):101-11. PMID: 17574801. Excluded: Wrong study design for key question

Newman RG, Gevertz SG. Efficacy versus effectiveness of buprenorphine and methadone maintenance in pregnancy. J Addict Dis. 2011;30(4):318-22. doi: 10.1080/10550887.2011.609806. PMID: 22026523. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Newman RG, Whitehill WB. Double-blind comparison of methadone and placebo maintenance treatments of narcotic addicts in Hong Kong. Lancet. 1979;2(8141):485-8. PMID: 90214. Excluded: Inpatient population

Newton AS, Dong K, Mabood N, et al. Brief emergency department interventions for youth who use alcohol and other drugs: a systematic review. Pediatr Emerg Care. 2013;29(5):673-84. doi: 10.1097/PEC.0b013e31828ed325. PMID: 23640153. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Nich C, McCance-Katz EF, Petrakis IL, et al. Sex differences in cocaine-dependent individuals' response to disulfiram treatment. Addict Behav. 2004;29(6):1123-8. PMID: 15236812. Excluded: Non-FDA approved pharmacologic intervention

Nielsen S, Larance B, Degenhardt L, et al. Opioid agonist treatment for pharmaceutical opioid dependent people. Cochrane Database Syst Rev. 2016 (5):CD011117. doi: 10.1002/14651858.CD011117.pub2. PMID: 27157143. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Nissen L. Strength-based approaches to juvenile justice: Assessment and programming. . Joint Meeting on Adolescent Treatment Effectiveness (JMATE); 2005 Washington, DC. Excluded: Results reported elsewhere, duplicate results

Nolan S, Dias Lima V, Fairbairn N, et al. The impact of methadone maintenance therapy on hepatitis C incidence among illicit drug users. Addiction. 2014;109(12):2053-9. doi: 10.1111/add.12682. PMID: 25041346. Excluded: Wrong study design for key question

Noormohammadi A, Forinash A, Yancey A, et al. Buprenorphine versus methadone for opioid dependence in pregnancy. Ann Pharmacother. 2016;50(8):666-72. doi: 10.1177/1060028016648367. PMID: 27199497. Excluded: Wrong comparator

Norberg MM, Hides L, Olivier J, et al. Brief interventions to reduce ecstasy use: a multi-site randomized controlled trial. Behav Ther. 2014;45(6):745-59. Excluded: Wrong comparator

Nunes EV, Gordon M, Friedmann PD, et al. Relapse to opioid use disorder after inpatient treatment: Protective effect of injection naltrexone. J Subst Abuse Treat. 2018;85:49-55. doi: 10.1016/j.jsat.2017.04.016. PMID: 28473233. Excluded: Wrong comparator

Nunes EV, Rothenberg JL, Sullivan MA, et al. Behavioral therapy to augment oral naltrexone for opioid dependence: a ceiling on effectiveness? Am J Drug Alcohol Abuse. 2006;32(4):503-17. PMID: 17127538. Excluded: Wrong comparator

Nyamathi AM, Nandy K, Greengold B, et al. Effectiveness of intervention on improvement of drug use among methadone maintained adults. J Addict Dis. 2011;30(1):6-16. doi: 10.1080/10550887.2010.531669. PMID: 21218306. Excluded: Wrong comparator

O'Brien CP, Childress AR, Arndt IO, et al. Pharmacological and behavioral treatments of cocaine dependence: controlled studies. J Clin Psychiatry. 1988;49 Suppl:17-22. PMID: 3276670. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

O'Brien CP, Friedmann PD, Nunes E, et al. Depot naltrexone as relapse prevention for opioid-dependent parolees. Drug Alcohol Depend. 2014;146(14). Excluded: Wrong comparator

Ochoa E, Madoz-Gurpide A, Salvador E. Gender differences in the treatment of the opiate dependence with naltrexone. Actas Esp Psiquiatr. 2008;36(4):197-204. PMID: 18461494. Excluded: Wrong study design for key question

O'Connell MJ, Kasprow WJ, Rosenheck RA. Differential impact of supported housing on selected subgroups of homeless veterans with substance abuse histories. Psychiatric Services. 2012;63(12):1195-205. PMID: 23117205. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

O'Connor PG, Oliveto AH, Shi JM, et al. A randomized trial of buprenorphine maintenance for heroin dependence in a primary care clinic for substance users versus a methadone clinic. Am J Med. 1998;105(2):100-5. PMID: 9727815. Excluded: Wrong comparator

O'Connor PG, Waugh ME, Carroll KM, et al. Primary care-based ambulatory opioid detoxification: the results of a clinical trial. J Gen Intern Med. 1995;10(5):255-60. PMID: 7616334. Excluded: <3 month followup duration

O'Farrell TJ, Murphy M, Alter J, et al. Behavioral family counseling for substance abuse: a treatment development pilot study. Addict Behav. 2010;35(1):1-6. PMID: 19717243. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

O'Farrell TJ, Schumm JA, Murphy MM, et al. A randomized clinical trial of behavioral couples therapy versus individually-based treatment for drug-abusing women. J Consult Clin Psychol. 2017;85(4):309-22. doi: 10.1037/ccp0000185. PMID: 28333533. Excluded: Wrong comparator

Ogel K, Coskun S. Cognitive behavioral therapy-based brief intervention for volatile substance misusers during adolescence: a follow-up study. Subst Use Misuse. 2011;46 Suppl 1:128-33. doi: 10.3109/10826084.2011.580233. PMID: 21609157. Excluded: Other wrong population (e.g., schizophrenia focus)

Oldham NS, Wright NM, Adams CE, et al. The Leeds evaluation of efficacy of detoxification study (LEEDS) project: an open-label pragmatic randomised control trial comparing the efficacy of differing therapeutic agents for primary care detoxification from either street heroin or methadone [ISRCTN07752728]. BMC Fam Pract. 2004;5:9. PMID: 15117415. Excluded: Wrong comparator

Oliveto A, Poling J, Mancino MJ, et al. Randomized, double blind, placebo-controlled trial of disulfiram for the treatment of cocaine dependence in methadone-stabilized patients. Drug Alcohol Depend. 2011;113(2-3):184-91. doi: 10.1016/j.drugalcdep.2010.07.022. PMID: 20828943. Excluded: Non-FDA approved pharmacologic intervention

Oliveto A, Poling J, Sevarino KA, et al. Efficacy of dose and contingency management procedures in LAAM-maintained cocaine-dependent patients. Drug Alcohol Depend. 2005;79(2):157-65. PMID: 16002025. Excluded: Wrong comparator

Olmstead TA, Cohen JP, Petry NM. Health-care service utilization in substance abusers receiving contingency management and standard care treatments. Addiction. 2012;107(8):1462-70. doi: 10.1111/j.1360-0443.2012.03831.x. PMID: 22296262. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Ondersma SJ, Winhusen T, Lewis DF. Pre-treatment change in a randomized trial with pregnant substance-abusing women in community-based outpatient treatment. Contemp Clin Trials. 2012;33(5):1074-9. doi: 10.1016/j.cct.2012.06.002. PMID: 22710564. Excluded: Wrong study design for key question

O'Neill K, Baker A, Cooke M, et al. Evaluation of a cognitive-behavioural intervention for pregnant injecting drug users at risk of HIV infection. Addiction. 1996;91(8):1115-25. PMID: 8828240. Excluded: Wrong comparator

Ong T-h. The effectiveness of an indigenised group counselling programme in aftercare service for drug supervisees: A one-year follow-up study. Int J Adv Couns. 1991;14(4):285-300. doi: 10.1007/BF00116538. Excluded: Wrong study design for key question

Ordean A, Kahan M, Graves L, et al. Integrated care for pregnant women on methadone maintenance treatment: Canadian primary care cohort study. Can Fam Physician. 2013;59(10):e462-9. PMID: 24130301. Excluded: Wrong study design for key question

Oreskovich MR, Saxon AJ, Ellis ML, et al. A double-blind, double-dummy, randomized, prospective pilot study of the partial mu opiate agonist, buprenorphine, for acute detoxification from heroin. Drug Alcohol Depend. 2005;77(1):71-9. PMID: 15607843. Excluded: Wrong comparator

Oslin DW. Evidence-based treatment of geriatric substance abuse. Psychiatr Clin North Am. 2005;28(4):897-911, ix. PMID: 16325734. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Oslin DW, Pettinati HM, Volpicelli JR, et al. The effects of naltrexone on alcohol and cocaine use in dually addicted patients. J Subst Abuse Treat. 1999;16(2):163-7. PMID: 10023615. Excluded: Non-FDA approved pharmacologic intervention

Osterman R, Lewis D, Winhusen T. Efficacy of motivational enhancement therapy to decrease alcohol and illicit-drug use in pregnant substance users reporting baseline alcohol use. J Subst Abuse Treat. 2017;77:150-5. doi: 10.1016/j.jsat.2017.02.003. PMID: 28254158. Excluded: Wrong outcome

Otiashvili D, Piralishvili G, Sikharulidze Z, et al. Methadone and buprenorphine-naloxone are effective in reducing illicit buprenorphine and other opioid use, and reducing HIV risk behavior--outcomes of a randomized trial. Drug Alcohol Depend. 2013;133(2):376-82. doi: 10.1016/j.drugalcdep.2013.06.024. PMID: 23916321. Excluded: Wrong comparator

Otto KC, Quinn C, Sung YF. Auricular acupuncture as an adjunctive treatment for cocaine addiction. A pilot study. Am J Addict. 1998;7(2):164-70. PMID: 9598220. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Otto MW, Hearon BA, McHugh RK, et al. A randomized, controlled trial of the efficacy of an interoceptive exposure-based CBT for treatment-refractory outpatients with opioid dependence. J Psychoactive Drugs. 2014;46(5):402-11. doi: 10.1080/02791072.2014.960110. PMID: 25364993. Excluded: Other wrong population (e.g., schizophrenia focus)

Ouimette PC, Finney JW, Moos RH. Twelve-step and cognitive--behavioral treatment for substance abuse: a comparison of treatment effectiveness. J Consult Clin Psychol. 1997;65(2):230-40. PMID: 9086686. Excluded: Wrong comparator

Oviedo-Joekes E, Brissette S, MacDonald S, et al. Safety profile of injectable hydromorphone and diacetylmorphine for long-term severe opioid use disorder. Drug Alcohol Depend. 2017;176:55-62. doi: 10.1016/j.drugalcdep.2017.02.021. PMID: 28521199. Excluded: Non-FDA approved pharmacologic intervention

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Ozechowski TJ, Liddle HA. Family-based therapy for adolescent drug abuse: knowns and unknowns. Clin Child Fam Psychol Rev. 2000;3(4):269-98. PMID: 11225740. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Paddock SM, Hepner KA, Hudson T, et al. Association between process-based quality indicators and mortality for patients with substance use disorders. J Stud Alcohol Drugs. 2017;78(4):588-96. PMID: 28728641. Excluded: Wrong study design for key question

Pani PP, Maremmani I, Pirastu R, et al. Buprenorphine: a controlled clinical trial in the treatment of opioid dependence. Drug Alcohol Depend. 2000;60(1):39-50. PMID: 10821988. Excluded: Wrong comparator

Pani PP, Pirastu R, Ricci A, et al. Prohibition of take-home dosages: negative consequences on methadone maintenance treatment. Drug Alcohol Depend. 1996;41(1):81-4. PMID: 8793314. Excluded: Wrong comparator

Pani PP, Trogu E, Contu P, et al. Psychiatric severity and treatment response in a comprehensive methadone maintenance treatment program. Drug Alcohol Depend. 1997;48(2):119-26. doi: 10.1016/S0376-8716%2897%2900115-4. Excluded: Wrong study design for key question

Pani PP, Trogu E, Vacca R, et al. Disulfiram for the treatment of cocaine dependence. Cochrane Database Syst Rev. 2010 (1):CD007024. doi: 10.1002/14651858.CD007024.pub2. PMID: 20091613. Excluded: Non-FDA approved pharmacologic intervention

Pani PP, Trogu E, Vecchi S, et al. Antidepressants for cocaine dependence and problematic cocaine use. Cochrane Database Syst Rev. 2011 (12) PMID: 22161371. Excluded: Non-FDA approved pharmacologic intervention

Paris M, Silva M, Anez-Nava L, et al. Culturally adapted, web-based cognitive behavioral therapy for Spanish-speaking individuals with substance use disorders: a randomized clinical trial. Am J Public Health. 2018;108(11):1535-42. doi: 10.2105/ajph.2018.304571. PMID: 30252519. Excluded: Wrong comparator

Parmar A, Sarkar S. Brief interventions for cannabis use disorders: A review. Addict Disord Their Treat. 2017;16(2):80-93. doi: 10.1097/ADT.0000000000000100. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Parsons BV, Jr., Alexander JF. Short-term family intervention: A therapy outcome study. J Consult Clin Psychol. 1973;41(2):195-201. PMID: 4747932. Excluded: Wrong outcome

Parsons JT, Lelutiu-Weinberger C, Botsko M, et al. A randomized controlled trial utilizing motivational interviewing to reduce HIV risk and drug use in young gay and bisexual men. J Consult Clin Psychol. 2014;82(1):9-18. doi: 10.1037/a0035311. PMID: 24364800. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Parwatikar SD, Knowles RR. Methadone-naloxone in combination for the treatment of heroin addicts. Clin Pharmacol Ther. 1973;14(6):941-8. PMID: 4584151. Excluded: Wrong comparator

Passetti LL, Godley MD, Kaminer Y. Continuing care for adolescents in treatment for substance use disorders. Child Adolesc Psychiatr Clin N Am. 2016;25(4):669-84. doi: 10.1016/j.chc.2016.06.003. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Passos SR, Camacho LA, Lopes CS, et al. Nefazodone in out-patient treatment of inhaled cocaine dependence: a randomized double-blind placebo-controlled trial. Addiction. 2005;100(4):489-94. doi: 10.1111/j.1360-0443.2005.01041.x. PMID: 15784063. Excluded: Non-FDA approved pharmacologic intervention

Patients more likely to engage in treatment at 30 days when given buprenorphine in the ED, referred for follow-up. ED Management. 2015;27(8):92-5. PMID: 26258203. Excluded: <3 month followup duration

Paulozzi LJ, Logan JE, Hall AJ, et al. A comparison of drug overdose deaths involving methadone and other opioid analgesics in West Virginia. Addiction. 2009;104(9):1541-8. doi: 10.1111/j.1360-0443.2009.02650.x. PMID: 19686524. Excluded: Wrong study design for key question

Peck JA, Reback CJ, Yang X, et al. Sustained reductions in drug use and depression symptoms from treatment for drug abuse in methamphetamine-dependent gay and bisexual men. J Urban Health. 2005;82(1 Suppl 1):i100-8. PMID: 15738315. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Peirce JM, Petry NM, Stitzer ML, et al. Effects of lower-cost incentives on stimulant abstinence in methadone maintenance treatment: a National Drug Abuse Treatment Clinical Trials Network study. Arch Gen Psychiatry. 2006;63(2):201-8. PMID: 16461864. Excluded: Wrong comparator

Peirce JM, Schacht RL, Brooner RK, et al. Incentivizing attendance to prolonged exposure in methadone maintenance. Drug Alcohol Depend. 2015;156(13). Excluded: Other wrong population (e.g., schizophrenia focus)

Peles E, Sason A, Schreiber S, et al. Newborn birth-weight of pregnant women on methadone or buprenorphine maintenance treatment: A national contingency management approach trial. Am J Addict. 2017;26(2):167-75. doi: 10.1111/ajad.12508. PMID: 28191917. Excluded: Wrong comparator

Perez-Mana C, Castells X, Torrens M, et al. Efficacy of psychostimulant drugs for amphetamine abuse or dependence. Cochrane Database Syst Rev. 2013 (9)doi: 10.1002/14651858.CD009695.pub2. PMID: 23996457. Excluded: Non-FDA approved pharmacologic intervention

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Perry AE, Neilson M, Martyn-St James M, et al. Pharmacological interventions for drug-using offenders. Cochrane Database Syst Rev. 2015 (6):CD010862. doi: 10.1002/14651858.CD010862.pub2. PMID: 26035084. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Perry AE, Neilson M, Martyn-St James M, et al. Interventions for female drug-using offenders. Cochrane Database Syst Rev. 2015 (6):CD010910. doi: 10.1002/14651858.CD010910.pub2. PMID: 26035085. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Peters EN, Nich C, Carroll KM. Primary outcomes in two randomized controlled trials of treatments for cannabis use disorders. Drug Alcohol Depend. 2011;118(2-3):408-16. doi: 10.1016/j.drugalcdep.2011.04.021. PMID: 21620591. Excluded: Wrong outcome

Peterson PL, Baer JS, Wells EA, et al. Short-term effects of a brief motivational intervention to reduce alcohol and drug risk among homeless adolescents. Psychol Addict Behav. 2006;20(3):254-64. Excluded: Other wrong population (e.g., schizophrenia focus)

Petitjean S, Stohler R, Deglon JJ, et al. Double-blind randomized trial of buprenorphine and methadone in opiate dependence. Drug Alcohol Depend. 2001;62(1):97-104. PMID: 11173173. Excluded: Wrong comparator

Petrakis IL, Carroll KM, Nich C, et al. Disulfiram treatment for cocaine dependence in methadone-maintained opioid addicts. Addiction. 2000;95(2):219-28. PMID: 10723850. Excluded: Non-FDA approved pharmacologic intervention

Petry NM, Alessi SM. Prize-based contingency management is efficacious in cocaine-abusing patients with and without recent gambling participation. J Subst Abuse Treat. 2010;39(3):282-8. doi: 10.1016/j.jsat.2010.06.011. PMID: 20667679. Excluded: Wrong outcome

Petry NM, Alessi SM, Carroll KM, et al. Contingency management treatments: Reinforcing abstinence versus adherence with goal-related activities. J Consult Clin Psychol. 2006;74(3):592-601. Excluded: Wrong comparator

Petry NM, Alessi SM, Hanson T. Contingency management improves abstinence and quality of life in cocaine abusers. J Consult Clin Psychol. 2007;75(2):307-15. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Petry NM, Alessi SM, Hanson T, et al. Randomized trial of contingent prizes versus vouchers in cocaine-using methadone patients. J Consult Clin Psychol. 2007;75(6):983-91. PMID: 18085914. Excluded: Wrong comparator

Petry NM, Alessi SM, Marx J, et al. Vouchers versus prizes: contingency management treatment of substance abusers in community settings. J Consult Clin Psychol. 2005;73(6):1005-14. PMID: 16392974. Excluded: Wrong comparator

Petry NM, Barry D, Alessi SM, et al. A randomized trial adapting contingency management targets based on initial abstinence status of cocaine-dependent patients. J Consult Clin Psychol. 2012;80(2):276-85. doi: 10.1037/a0026883. PMID: 22229758. Excluded: Wrong comparator

Petry NM, Ford JD, Barry D. Contingency management is especially efficacious in engendering long durations of abstinence in patients with sexual abuse histories. Psychol Addict Behav. 2011;25(2):293-300. doi: 10.1037/a0022632. PMID: 21443305. Excluded: Other wrong population (e.g., schizophrenia focus)

Petry NM, Kolodner KB, Li R, et al. Prize-based contingency management does not increase gambling. Drug Alcohol Depend. 2006;83(3):269-73. PMID: 16377101. Excluded: Wrong outcome

Petry NM, Martin B. Low-cost contingency management for treating cocaine- and opioid-abusing methadone patients. J Consult Clin Psychol. 2002;70(2):398-405. PMID: 11952198. Excluded: Wrong comparator

Petry NM, Martin B, Simcic F, Jr. Prize reinforcement contingency management for cocaine dependence: integration with group therapy in a methadone clinic. J Consult Clin Psychol. 2005;73(2):354-9. PMID: 15796645. Excluded: Wrong comparator

Petry NM, Peirce JM, Stitzer ML, et al. Effect of prize-based incentives on outcomes in stimulant abusers in outpatient psychosocial treatment programs: a national drug abuse treatment clinical trials network study. Arch Gen Psychiatry. 2005;62(10):1148-56. doi: 10.1001/archpsyc.62.10.1148. PMID: 16203960. Excluded: Wrong comparator

Petry NM, Roll JM, Rounsaville BJ, et al. Serious adverse events in randomized psychosocial treatment studies: safety or arbitrary edicts? J Consult Clin Psychol. 2008;76(6):1076-82. doi: 10.1037/a0013679. PMID: 19045975. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Petry NM, Tedford J, Austin M, et al. Prize reinforcement contingency management for treating cocaine users: how low can we go, and with whom? Addiction. 2004;99(3):349-60. PMID: 14982548. Excluded: Wrong comparator

Petry NM, Weinstock J, Alessi SM. A randomized trial of contingency management delivered in the context of group counseling. J Consult Clin Psychol. 2011;79(5):686-96. doi: 10.1037/a0024813. PMID: 21806297. Excluded: Wrong comparator

Pettinati HM, Kampman KM, Lynch KG, et al. A pilot trial of injectable, extended-release naltrexone for the treatment of co-occurring cocaine and alcohol dependence. Am J Addict. 2014;23(6):591-7. doi: 10.1111/j.1521-0391.2014.12146.x. PMID: 25251201. Excluded: Non-FDA approved pharmacologic intervention

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Pettinati HM, Kampman KM, Lynch KG, et al. Gender differences with high-dose naltrexone in patients with co-occurring cocaine and alcohol dependence. J Subst Abuse Treat. 2008;34(4):378-90. PMID: 17664051. Excluded: Non-FDA approved pharmacologic intervention

Pettinati HM, Kampman KM, Lynch KG, et al. A double blind, placebo-controlled trial that combines disulfiram and naltrexone for treating co-occurring cocaine and alcohol dependence. Addict Behav. 2008;33(5):651-67. PMID: 18079068. Excluded: Non-FDA approved pharmacologic intervention

Phan O, Henderson CE, Angelidis T, et al. European youth care sites serve different populations of adolescents with cannabis use disorder. Baseline and referral data from the INCANT trial. BMC Psychiatry. 2011;11doi: 10.1186/1471-244X-11-110. PMID: 21749677. Excluded: Wrong outcome

Piehler TF, Winters KC. Parental involvement in brief interventions for adolescent marijuana use. Psychol Addict Behav. 2015;29(3):512-21. doi: 10.1037/adb0000106. PMID: 26415058. Excluded: School setting

Pilowsky DJ, Wu LT. Screening instruments for substance use and brief interventions targeting adolescents in primary care: a literature review. Addict Behav. 2013;38(5):2146-53. doi: 10.1016/j.addbeh.2013.01.015. PMID: 23454877. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Pinto H, Maskrey V, Swift L, et al. The SUMMIT trial: a field comparison of buprenorphine versus methadone maintenance treatment. J Subst Abuse Treat. 2010;39(4):340-52. doi: 10.1016/j.jsat.2010.07.009. PMID: 20817384. Excluded: Wrong comparator

Pinto H, Rumball D, Maskrey V, et al. A pilot study for a randomized controlled and patient preference trial of buprenorphine versus methadone maintenance treatment in the management of opiate dependent patients. J Subst Use. 2008;13(2):73-82. Excluded: Wrong comparator

Piotrowski NA, Hall S. Treatment of multiple drug abuse in the methadone clinic. Motivating behavior change among illicit drug abusers. 1999. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Piotrowski NA, Tusel DJ, Sees KL, et al. Contingency contracting with monetary reinforcers for abstinence from multiple drugs in a methadone program. Exp Clin Psychopharmacol. 1999;7(4):399-411. PMID: 10609975. Excluded: Wrong comparator

Piralishvili G, Otiashvili D, Sikharulidze Z, et al. Opioid addicted buprenorphine injectors: drug use during and after 12-weeks of buprenorphine-naloxone or methadone in the Republic of Georgia. J Subst Abuse Treat. 2015;50:32-7. doi: 10.1016/j.jsat.2014.10.003. PMID: 25456093. Excluded: Wrong comparator

Polcin DL, Bond J, Korcha R, et al. Randomized trial of intensive motivational interviewing for methamphetamine dependence. J Addict Dis. 2014;33(3):253-65. doi: 10.1080/10550887.2014.950029. PMID: 25115166. Excluded: Wrong comparator

Pollack MH, Otto MW, Kaufman MJ, et al. Renshaw cognitive-behavioral therapy for illicit drug use during methadone maintenance: treatment outcomes and MR spectroscopy findings. Drug Alcohol Depend. 2001;63(1). Excluded: Other wrong population (e.g., schizophrenia focus)

Pollack MH, Penava SA, Bolton E, et al. A novel cognitive-behavioral approach for treatment-resistant drug dependence. J Subst Abuse Treat. 2002;23(4):335-42. PMID: 12495795. Excluded: Other wrong population (e.g., schizophrenia focus)

Pompili M, Venturini P, Lamis DA, et al. Rehabilitation of the adolescent with a substance use disorder: Overview of treatment efficacy. Int J Emerg Ment Health. 2015;17(3):617-23. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Posadzki P, Choi J, Lee MS, et al. Yoga for addictions: A systematic review of randomised clinical trials. Focus Altern Complement Ther. 2014;19(1):1-8. doi: 10.1111/fct.12080. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Prendergast ML, Podus D, Chang E. Program factors and treatment outcomes in drug dependence treatment: an examination using meta-analysis. Subst Use Misuse. 2000;35(12-14):1931-65. PMID: 11138713. Excluded: Wrong outcome

Preston KL, Umbricht A, Epstein DH. Methadone dose increase and abstinence reinforcement for treatment of continued heroin use during methadone maintenance. Arch Gen Psychiatry. 2000;57(4):395-404. PMID: 10768702. Excluded: Wrong comparator

Preston KL, Umbricht A, Epstein DH. Abstinence reinforcement maintenance contingency and one-year follow-up. Drug Alcohol Depend. 2002;67(2):125-37. PMID: 12095662. Excluded: Wrong comparator

Printz DMB, Buono FD, Lloyd DP, et al. Gender differences in timing of reminder messages for automated, CBT-based treatment for methadone. Drug Alcohol Depend. 2016;171. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Raby WN, Carpenter KM, Rothenberg J, et al. Intermittent marijuana use is associated with improved retention in naltrexone treatment for opiate-dependence. Am J Addict. 2009;18(4):301-8. doi: 10.1080/10550490902927785. PMID: 19444734. Excluded: Wrong outcome

Rahimi-Movaghar A, Amin-Esmaeili M, Hefazi M, et al. Pharmacological therapies for maintenance treatments of opium dependence. Cochrane Database Syst Rev. 2013 (1):CD007775. doi: 10.1002/14651858.CD007775.pub2. PMID: 23440817. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Rahimi-Movaghar A, Hefazi M, Davoli M, et al. Pharmacological therapies for management of opium withdrawal. Cochrane Database Syst Rev. 2009 (1)doi: 10.1002/14651858.CD007522. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Raisch DW, Fye CL, Boardman KD, et al. Opioid dependence treatment, including buprenorphine/naloxone. Ann Pharmacother. 2002;36(2):312-21. PMID: 11847954. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Raistrick D, West D, Finnegan O, et al. A comparison of buprenorphine and lofexidine for community opiate detoxification: results from a randomized controlled trial. Addiction. 2005;100(12):1860-7. PMID: 16367987. Excluded: Wrong comparator

Rash CJ, Alessi SM, Petry NM. Contingency management is efficacious for cocaine abusers with prior treatment attempts. Exp Clin Psychopharmacol. 2008;16(6):547-54. doi: 10.1037/a0014042. PMID: 19086775. Excluded: Wrong outcome

Rash CJ, Stitzer M, Weinstock J. Contingency management: New directions and remaining challenges for an evidence-based intervention. J Subst Abuse Treat. 2017;72:10-8. doi: 10.1016/j.jsat.2016.09.008. PMID: 27746057. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Rawson RA, Glazer M, Callahan EJ, et al. Naltrexone and behavior therapy for heroin addiction. NIDA Res Monogr. 1979 (25):26-43. PMID: 117373. Excluded: Wrong comparator

Rawson RA, Huber A, McCann M, et al. A comparison of contingency management and cognitive-behavioral approaches during methadone maintenance treatment for cocaine dependence. Arch Gen Psychiatry. 2002;59(9):817-24. PMID: 12215081. Excluded: Wrong comparator

Rawson RA, Marinelli-Casey P, Anglin MD, et al. A multi-site comparison of psychosocial approaches for the treatment of methamphetamine dependence. Addiction. 2004;99(6):708-17. doi: 10.1111/j.1360-0443.2004.00707.x. PMID: 15139869. Excluded: Wrong comparator

Rawson RA, McCann MJ, Shoptaw SJ, et al. Naltrexone for opioid dependence: evaluation of a manualized psychosocial protocol to enhance treatment response. Drug Alcohol Rev. 2001;20(1):67-78. Excluded: Wrong comparator

Rawson RA, Tennant FS, Jr. Five-year follow-up of opiate addicts with naltrexone and behavior therapy. NIDA Res Monogr. 1984;49:289-95. PMID: 6434974. Excluded: Wrong study design for key question

Rees V, Copeland J, Swift W, et al. Brief cognitive behavioral interventions for cannabis dependence. NIDA Res Monogr. 1999;179(79). Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Reimer J, Verthein U, Karow A, et al. Physical and mental health in severe opioid-dependent patients within a randomized controlled maintenance treatment trial. Addiction. 2011;106(9):1647-55. doi: 10.1111/j.1360-0443.2011.03463.x. PMID: 21489005. Excluded: Wrong comparator

Rezapour T, Hatami J, Farhoudian A, et al. Cognitive rehabilitation for individuals with opioid use disorder: a randomized controlled trial. Neuropsychol Rehabil. 2017. Excluded: Wrong comparator

Riggs PD, Hall SK, Mikulich-Gilbertson SK, et al. A randomized controlled trial of pemoline for attention-deficit/hyperactivity disorder in substance-abusing adolescents. J Am Acad Child Adolesc Psychiatry. 2004;43(4):420-9. doi: 10.1097/00004583-200404000-00008. PMID: 15187802. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Rigter H. The European INCANT (international cannabis need of treatment) study. Neuropsychiatr Enfance Adolesc. 2012;60(5 SUPPL. 1):S26. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Rigter H, Henderson CE, Pelc I, et al. Multidimensional family therapy lowers the rate of cannabis dependence in adolescents: A randomised controlled trial in Western European outpatient settings. Drug Alcohol Depend. 2013;130(1-3):85-93. Excluded: Wrong comparator

Rigter H, Pelc I, Tossmann P, et al. INCANT: a transnational randomized trial of multidimensional family therapy versus treatment as usual for adolescents with cannabis use disorder. BMC Psychiatry. 2010;10:28. doi: 10.1186/1471-244X-10-28. PMID: 20380718. Excluded: Wrong comparator

Robbins MS, Feaster DJ, Horigian VE, et al. Therapist adherence in brief strategic family therapy for adolescent drug abusers. J Consult Clin Psychol. 2011;79(1):43-53. doi: 10.1037/a0022146. PMID: 21261433. Excluded: Wrong outcome

Robbins MS, Feaster DJ, Horigian VE, et al. Brief strategic family therapy versus treatment as usual: results of a multisite randomized trial for substance using adolescents. J Consult Clin Psychol. 2011;79(6):713-27. doi: 10.1037/a0025477. PMID: 21967492. Excluded: Wrong comparator

Robbins MS, Szapocznik J, Dillon FR, et al. The efficacy of structural ecosystems therapy with drug-abusing/dependent African American and Hispanic American adolescents. J Fam Psychol. 2008;22(1):51-61. doi: 10.1037/0893-3200.22.1.51. PMID: 18266532. Excluded: Other wrong population (e.g., schizophrenia focus)

Robbins MS, Szapocznik J, Horigian VE, et al. Brief strategic family therapy for adolescent drug abusers: a multi-site effectiveness study. Contemp Clin Trials. 2009;30(3):269-78. doi: 10.1016/j.cct.2009.01.004. PMID: 19470315. Excluded: Wrong comparator

Robles E, Stitzer ML, Strain EC, et al. Voucher-based reinforcement of opiate abstinence during methadone detoxification. Drug Alcohol Depend. 2002;65(2):179-89. PMID: 11772479. Excluded: Wrong comparator

Roffman RA, Stephens RS, Simpson EE, et al. Treatment of marijuana dependence: preliminary results. J Psychoactive Drugs. 1988;20(1):129-37. doi: 10.1080/02791072.1988.10524382. PMID: 3392627. Excluded: <3 month followup duration

Rogers RE, Higgins ST, Silverman K, et al. Abstinence-contingent reinforcement and engagement in non-drug-related activities among illicit drug abusers. Psychol Addict Behav. 2008;22(4):544-50. doi: 10.1037/0893-164X.22.4.544. PMID: 19071979. Excluded: Wrong comparator

Rohsenow DJ, Monti PM, Martin RA, et al. Motivational enhancement and coping skills training for cocaine abusers: effects on substance use outcomes. Addiction. 2004;99(7):862-74. doi: 10.1111/j.1360-0443.2004.00743.x. PMID: 15200582. Excluded: Wrong comparator

Rohsenow DJ, Monti PM, Martin RA, et al. Brief coping skills treatment for cocaine abuse: 12-month substance use outcomes. J Consult Clin Psychol. 2000;68(3):515-20. PMID: 10883569. Excluded: Wrong comparator

Rohsenow DJ, Monti PM, Rubonis AV, et al. Cue exposure with coping skills training and communication skills training for alcohol dependence: 6- and 12-month outcomes. Addiction. 2001;96(8):1161-74. doi: 10.1080/09652140120060752. PMID: 11487422. Excluded: Other wrong population (e.g., schizophrenia focus)

Roll JM, Chudzynski J, Cameron JM, et al. Duration effects in contingency management treatment of methamphetamine disorders. Addict Behav. 2013;38(9):2455-62. doi: 10.1016/j.addbeh.2013.03.018. PMID: 23708468. Excluded: Wrong comparator

Roll JM, Petry NM, Stitzer ML, et al. Contingency management for the treatment of methamphetamine use disorders. Am J Psychiatry. 2006;163(11):1993-9. Excluded: Wrong comparator

Romo L, Le Strat Y, Aubry C, et al. The role of brief motivational intervention on self-efficacy and abstinence in a cohort of patients with alcohol dependence. Int J Psychiatry Med. 2009;39(3):313-23. doi: 10.2190/PM.39.3.g. PMID: 19967902. Excluded: Other wrong population (e.g., schizophrenia focus)

Roozen HG, Boulogne JJ, van Tulder MW, et al. A systematic review of the effectiveness of the community reinforcement approach in alcohol, cocaine and opioid addiction. Drug Alcohol Depend. 2004;74(1):1-13. PMID: 15072802. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Roozen HG, de Waart R, van der Windt DA, et al. A systematic review of the effectiveness of naltrexone in the maintenance treatment of opioid and alcohol dependence. Eur Neuropsychopharmacol. 2006;16(5):311-23. PMID: 16361086. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Rosen MI, Dieckhaus K, McMahon TJ, et al. Improved adherence with contingency management. AIDS Patient Care STDS. 2007;21(1):30-40. PMID: 17263651. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Rosenblum A, Magura S, Kayman DJ, et al. Motivationally enhanced group counseling for substance users in a soup kitchen: a randomized clinical trial. Drug Alcohol Depend. 2005;80(1):91-103. doi: 10.1016/j.drugalcdep.2005.03.012. PMID: 16157232. Excluded: Wrong comparator

Rosenthal R, Kim S, Lofwall M, et al. A randomized trial of buprenorphine implants in adults stabilized on sublingual buprenorphine. Am J Addict. 2017;Conference: 27th annual meeting and symposium of the american academy of addiction psychiatry, AAAP. 2017. United states 26(3):265-6. Excluded: Results reported elsewhere, duplicate results

Rosenthal RN, Lofwall MR, Kim S, et al. Effect of buprenorphine implants on illicit opioid use among abstinent adults with opioid dependence treated with sublingual buprenorphine: A randomized clinical trial. JAMA. 2016;316(3):282-90. doi: 10.1001/jama.2016.9382. PMID: 27434441. Excluded: Wrong comparator

Rostami R, Dehghani-Arani F. Neurofeedback training as a new method in treatment of crystal methamphetamine dependent patients: A preliminary study. Appl Psychophysiol Biofeed. 2015;40(3):151-61. doi: 10.1007/s10484-015-9281-1. PMID: 25894106. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Rothenberg JL, Sullivan MA, Bornstein G, et al. Behavioral naltrexone therapy: Efficacy of a new behavioral treatment for heroin dependence and future directions. Drug Alcohol Depend. 2002;66(1). Excluded: Wrong study design for key question

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Rothenberg JL, Sullivan MA, Church SH, et al. Behavioral naltrexone therapy: an integrated treatment for opiate dependence. J Subst Abuse Treat. 2002;23(4):351-60. PMID: 12495797. Excluded: Wrong study design for key question

Rounsaville BJ, Glazer W, Wilber CH, et al. Short-term interpersonal psychotherapy in methadone-maintained opiate addicts. Arch Gen Psychiatry. 1983;40(6):629-36. PMID: 6342563. Excluded: Wrong comparator

Rowan-Szal G, Joe GW, Chatham LR, et al. A simple reinforcement system for methadone clients in a community-based treatment program. J Subst Abuse Treat. 1994;11(3):217-23. PMID: 8072049. Excluded: Wrong comparator

Rowan-Szal GA, Bartholomew NG, Chatham LR, et al. A combined cognitive and behavioral intervention for cocaine-using methadone clients. J Psychoactive Drugs. 2005;37(1):75-84. PMID: 15916253. Excluded: Wrong comparator

Rowe CL. Family therapy for drug abuse: review and updates 2003-2010. J Marital Fam Ther. 2012;38(1):59-81. doi: 10.1111/j.1752-0606.2011.00280.x. PMID: 22283381. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Runarsdottir V, Hansdottir I, Tyrfingsson T, et al. Extended-release injectable naltrexone (xr-ntx) with intensive psychosocial therapy for amphetamine-dependent persons seeking treatment: A placebo-controlled trial. J Addict Med. 2017;11(3):197-204. doi: 10.1097/ADM.0000000000000297. PMID: 28379861. Excluded: Non-FDA approved pharmacologic intervention

Sabioni P, Le Foll B. Psychosocial and pharmacological interventions for the treatment of cannabis use disorder. F1000Res. 2018;7:173. doi: 10.12688/f1000research.11191.1. PMID: 29497498. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Saitz R, Palfai TP, Cheng DM, et al. Screening and brief intervention for drug use in primary care: The aspire randomized trial. J Gen Intern Med. 2013;28(24). Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Salehi M, Emadossadat A, Kheirabadi GR, et al. The effect of buprenorphine on methamphetamine cravings. J Clin Psychopharmacol. 2015;35(6):724-7. doi: 10.1097/JCP.0000000000000408. PMID: 26468683. Excluded: Non-FDA approved pharmacologic intervention

Salisbury AL, Coyle MG, O'Grady KE, et al. Fetal assessment before and after dosing with buprenorphine or methadone. Addiction. 2012;107 Suppl 1:36-44. doi: 10.1111/j.1360-0443.2012.04037.x. PMID: 23106925. Excluded: Wrong comparator

Salisbury-Afshar E. Buprenorphine maintenance vs. methadone maintenance or placebo for opioid use disorder. Am Fam Physician. 2015;91(3):165-6. PMID: 25822268. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Salloum IM, Jones YO. Efficacy of pharmacotherapy for comorbid major depression and substance use disorders: A review. Curr Psychiatry Rev. 2008;4(1):14-27. doi: 10.2174/157340008783743785. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Samet JH, Krupitsky EM, Cheng DM, et al. Mitigating risky sexual behaviors among Russian narcology hospital patients: the PREVENT (partnership to reduce the epidemic via engagement in narcology treatment) randomized controlled trial. Addiction. 2008;103(9):1474-83. doi: 10.1111/j.1360-0443.2008.02251.x. PMID: 18636998. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Santa Ana EJ, Wulfert E, Nietert PJ. Efficacy of group motivational interviewing (GMI) for psychiatric inpatients with chemical dependence. J Consult Clin Psychol. 2007;75(5):816-22. PMID: 17907864. Excluded: Other wrong population (e.g., schizophrenia focus)

Santisteban DA, Coatsworth JD, Perez-Vidal A, et al. Efficacy of brief strategic family therapy in modifying Hispanic adolescent behavior problems and substance use. J Fam Psychol. 2003;17(1):121-33. PMID: 12666468. Excluded: <70% drug misuse or likely majority alcohol

Santisteban DA, Mena MP, Muir J, et al. The efficacy of two adolescent substance abuse treatments and the impact of comorbid depression: results of a small randomized controlled trial. Psychiatr Rehabil J. 2015;38(1):55-64. doi: 10.1037/prj0000106. PMID: 25799306. Excluded: Other wrong population (e.g., schizophrenia focus)

Santisteban DA, Szapocznik J, Perez-Vidal A, et al. Efficacy of intervention for engaging youth and families into treatment and some variables that may contribute to differential effectiveness. J Fam Psychol. 1996;10(1):35. Excluded: Wrong comparator

Satre DD, Leibowitz A, Sterling SA, et al. A randomized clinical trial of motivational interviewing to reduce alcohol and drug use among patients with depression. J Consult Clin Psychol. 2016;84(7):571-9. doi: 10.1037/ccp0000096. PMID: 26985728. Excluded: Other wrong population (e.g., schizophrenia focus)

Saulle R, Vecchi S, Gowing L. Supervised dosing with a long-acting opioid medication in the management of opioid dependence. Cochrane Database Syst Rev. 2017;4:CD011983. doi: 10.1002/14651858.CD011983.pub2. PMID: 28447766. Excluded: Wrong comparator

Saunders B, Wilkinson C, Phillips M. The impact of a brief motivational intervention with opiate users attending a methadone programme. Addiction. 1995;90(3):415-24. PMID: 7735025. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Saunders E, McGovern MP, Lambert-Harris C, et al. The impact of addiction medications on outcomes for persons with co-occurring PTSD and opioid use disorders. Drug Alcohol Depend. 2016;171. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Saunders EC, McGovern MP, Lambert-Harris C, et al. The impact of addiction medications on treatment outcomes for persons with co-occurring PTSD and opioid use disorders. Am J Addict. 2015;24(8):722-31. doi: 10.1111/ajad.12292. PMID: 26388539. Excluded: Other wrong population (e.g., schizophrenia focus)

Saunders JB, Jones R, Dean A, et al. Comparison of rapid opiate detoxification and naltrexone with methadone maintenance in the treatment of opiate dependence: A randomized controlled trial. Drug Alcohol Depend. 2002;66(1). Excluded: Wrong comparator

Saxon AJ, Hser YI, Woody G, et al. Medication-assisted treatment for opioid addiction: Methadone and buprenorphine. J Food Drug Anal. 2013;21(4 SUPPL.):S69-S72. doi: 10.1016/j.jfda.2013.09.037. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Saxon AJ, Ling W, Hillhouse M, et al. Buprenorphine/naloxone and methadone effects on laboratory indices of liver health: a randomized trial. Drug Alcohol Depend. 2013;128(1-2):71-6. doi: 10.1016/j.drugalcdep.2012.08.002. PMID: 22921476. Excluded: Wrong comparator

Sayegh CS, Huey SJ, Zara EJ, et al. Follow-up treatment effects of contingency management and motivational interviewing on substance use: A meta-analysis. Psychol Addict Behav. 2017;31(4):403-14. doi: 10.1037/adb0000277. PMID: 28437121. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Schaeffer CM, Henggeler SW, Ford JD, et al. RCT of a promising vocational/employment program for high-risk juvenile offenders. J Subst Abuse Treat. 2014;46(2):134-43. doi: 10.1016/j.jsat.2013.06.012. PMID: 23958035. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Schaub M, Sullivan R, Haug S, et al. Web-based cognitive behavioral self-help intervention to reduce cocaine consumption in problematic cocaine users: Randomized controlled trial. J Med Internet Res. 2012;14(6):e166. doi: 10.2196/jmir.2244. PMID: 23192752. Excluded: Poor quality

Scherbaum N, Kluwig J, Specka M, et al. Group psychotherapy for opiate addicts in methadone maintenance treatment--a controlled trial. Eur Addict Res. 2005;11(4):163-71. PMID: 16110222. Excluded: Wrong comparator

Schinke SP, Schilling RF, Gilchrist LD. Prevention of drug and alcohol abuse in American Indian youths. Soc Work Res Abstr. 1986;22(4):18-9. doi: 10.1093/swra/22.4.18. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Schmitt JM, Stotts AL, Rhoades HM, et al. Naltrexone combined with relapse prevention for the treatment of cocaine dependence. NIDA Res Monogr. 1999;180(112). Excluded: Results reported elsewhere, duplicate results

Schmitz JM, Averill P, Sayre S, et al. Cognitive–behavioral treatment of bipolar disorder and substance abuse: A preliminary randomized study. Addict Disord Their Treat. 2002;1(1):17-24. Excluded: Other wrong population (e.g., schizophrenia focus)

Schmitz JM, Lindsay JA, Green CE, et al. High-dose naltrexone therapy for cocaine-alcohol dependence. Am J Addict. 2009;18(5):356-62. doi: 10.3109/10550490903077929. PMID: 19874153. Excluded: Non-FDA approved pharmacologic intervention

Schmitz JM, Stotts AL, Rhoades HM, et al. Naltrexone and relapse prevention treatment for cocaine-dependent patients. Addict Behav. 2001;26(2):167-80. PMID: 11316375. Excluded: <3 month followup duration

Schmitz JM, Stotts AL, Sayre SL, et al. Treatment of cocaine-alcohol dependence with naltrexone and relapse prevention therapy. Am J Addict. 2004;13(4):333-41. PMID: 15370932. Excluded: Wrong comparator

Schmitz JM, Stotts AL, Sayre SL, et al. Naltrexone and relapse prevention treatment for cocaine-alcohol-dependent patients. Drug Alcohol Depend. 2002;66(1). Excluded: <3 month followup duration

Schmitz JM, Stotts AL, Vujanovic AA, et al. A sequential multiple assignment randomized trial for cocaine cessation and relapse prevention: Tailoring treatment to the individual. Contemp Clin Trials. 2018;65:109-15. doi: 10.1016/j.cct.2017.12.015. PMID: 29287664. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Schottenfeld RS, Chawarski MC, Pakes JR, et al. Methadone versus buprenorphine with contingency management or performance feedback for cocaine and opioid dependence. Am J Psychiatry. 2005;162(2):340-9. PMID: 15677600. Excluded: Wrong comparator

Schottenfeld RS, Mokri A, Taheri Nakhost H, et al. Buprenorphine vs naltrexone maintenance treatment for opium- or heroin-dependent individuals in Iran: Preliminary findings of a pilot randomized clinical trial. Proceedings of the 69th Annual Scientific Meeting of the College on Problems of Drug Dependence. 2007. Excluded: Results reported elsewhere, duplicate results

Schottenfeld RS, Pakes JR, Kosten TR. Prognostic factors in buprenorphine- versus methadone-maintained patients. J Nerv Ment Dis. 1998;186(1):35-43. PMID: 9457145. Excluded: Wrong comparator

Schottenfeld RS, Pakes JR, Oliveto A, et al. Buprenorphine vs methadone maintenance treatment for concurrent opioid dependence and cocaine abuse. Arch Gen Psychiatry. 1997;54(8):713-20. PMID: 9283506. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Schroeder JR, Epstein DH, Umbricht A, et al. Changes in HIV risk behaviors among patients receiving combined pharmacological and behavioral interventions for heroin and cocaine dependence. Addict Behav. 2006;31(5):868-79. PMID: 16085366. Excluded: Wrong comparator

Schroeder JR, Schmittner JP, Epstein DH, et al. Adverse events among patients in a behavioral treatment trial for heroin and cocaine dependence: effects of age, race, and gender. Drug Alcohol Depend. 2005;80(1):45-51. PMID: 16157230. Excluded: Wrong comparator

Schuler ME, Nair P, Black MM. Ongoing maternal drug use, parenting attitudes, and a home intervention: effects on mother-child interaction at 18 months. J Dev Behav Pediatr. 2002;23(2):87-94. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Schwartz RP, Kelly SM, Mitchell SG, et al. Interim methadone and patient navigation in jail: Rationale and design of a randomized clinical trial. Contemp Clin Trials. 2016;49:21-8. doi: 10.1016/j.cct.2016.06.002. PMID: 27282117. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Schwartz RP, Kelly SM, Mitchell SG, et al. Patient-centered methadone treatment: a randomized clinical trial. Addiction. 2017;112(3):454-64. doi: 10.1111/add.13622. PMID: 27661788. Excluded: Wrong comparator

Schwartz RP, Kelly SM, O'Grady KE, et al. Randomized trial of standard methadone treatment compared to initiating methadone without counseling: 12-month findings. Addiction. 2012;107(5):943-52. doi: 10.1111/j.1360-0443.2011.03700.x. PMID: 22029398. Excluded: Wrong comparator

Scott WC, Kaiser D, Othmer S, et al. Effects of an EEG biofeedback protocol on a mixed substance abusing population. Am J Drug Alcohol Abuse. 2005;31(3):455-69. PMID: 16161729. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Sealock MD, Gottfredson DC, Gallagher CA. Drug treatment for juvenile offenders: Some good and bad news. J Res Crime Delinq. 1997;34(2):210-36. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Secades-Villa R, Garcia-Rodriguez O, Garcia-Fernandez G, et al. Community reinforcement approach plus vouchers among cocaine-dependent outpatients: twelve-month outcomes. Psychol Addict Behav. 2011;25(1):174-9. doi: 10.1037/a0021451. PMID: 21261406. Excluded: Wrong comparator

Secades-Villa R, Garcia-Rodriguez O, Higgins ST, et al. Community reinforcement approach plus vouchers for cocaine dependence in a community setting in Spain: six-month outcomes. J Subst Abuse Treat. 2008;34(2):202-7. PMID: 17512158. Excluded: Wrong comparator

Secades-Villa R, Sanchez-Hervas E, Zacares-Romaguera F, et al. Community reinforcement approach (CRA) for cocaine dependence in the Spanish public health system: 1 year outcome. Drug Alcohol Rev. 2011;30(6):606-12. doi: 10.1111/j.1465-3362.2010.00250.x. PMID: 21355914. Excluded: Wrong comparator

Sees KL, Delucchi KL, Masson C, et al. Methadone maintenance vs 180-day psychosocially enriched detoxification for treatment of opioid dependence: a randomized controlled trial. JAMA. 2000;283(10):1303-10. PMID: 10714729. Excluded: Wrong comparator

Senay EC, Dorus W, Goldberg F, et al. Withdrawal from methadone maintenance. Rate of withdrawal and expectation. Arch Gen Psychiatry. 1977;34(3):361-7. PMID: 843188. Excluded: Wrong comparator

Sexton T, Turner CW. The effectiveness of functional family therapy for youth with behavioral problems in a community practice setting. J Fam Psychol. 2010;24(3):339-48. doi: 10.1037/a0019406. PMID: 20545407. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Sharma A, O'Grady KE, Kelly SM, et al. Pharmacotherapy for opioid dependence in jails and prisons: research review update and future directions. Subst Abuse Rehabil. 2016;7:27-40. doi: 10.2147/SAR.S81602. PMID: 27217808. Excluded: Incarcerated population

Shaul L, Koeter MW, Schippers GM. Brief motivation enhancing intervention to prevent criminal recidivism in substance-abusing offenders under supervision: A randomized trial. Psychology, Crime & Law. 2016;22(9):903-14. doi: 10.1080/1068316X.2016.1202248. Excluded: <70% drug misuse or likely majority alcohol

Shetty V, Murphy DA, Zigler C, et al. Randomized controlled trial of personalized motivational interventions in substance using patients with facial injuries. J Oral Maxillofac Surg. 2011;69(9):2396-411. doi: 10.1016/j.joms.2010.12.040. PMID: 21496991. Excluded: <70% drug misuse or likely majority alcohol

Shoptaw S, Huber A, Peck J, et al. Randomized, placebo-controlled trial of sertraline and contingency management for the treatment of methamphetamine dependence. Drug Alcohol Depend. 2006;85(1):12-8. doi: 10.1016/j.drugalcdep.2006.03.005. PMID: 16621339. Excluded: Wrong comparator

Sigmon SC. Interim treatment: Bridging delays to opioid treatment access. Prev Med. 2015;80:32-6. doi: 10.1016/j.ypmed.2015.04.017. PMID: 25937593. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Sigmon SC, Correia CJ, Stitzer ML. Cocaine abstinence during methadone maintenance: effects of repeated brief exposure to voucher-based reinforcement. Exp Clin Psychopharmacol. 2004;12(4):269-75. PMID: 15571444. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Sigmon SC, Ochalek TA, Meyer AC, et al. Interim buprenorphine vs. waiting list for opioid dependence. N Engl J Med. 2016;375(25):2504-5. doi: 10.1056/NEJMc1610047. PMID: 28002704. Excluded: <3 month followup duration

Silverman K, Higgins ST, Brooner RK, et al. Sustained cocaine abstinence in methadone maintenance patients through voucher-based reinforcement therapy. Arch Gen Psychiatry. 1996;53(5):409-15. PMID: 8624184. Excluded: Wrong comparator

Silverman K, Robles E, Mudric T, et al. A randomized trial of long-term reinforcement of cocaine abstinence in methadone-maintained patients who inject drugs. J Consult Clin Psychol. 2004;72(5):839-54. PMID: 15482042. Excluded: Wrong comparator

Silverman K, Svikis D, Robles E, et al. A reinforcement-based therapeutic workplace for the treatment of drug abuse: Six-month abstinence outcomes. Exp Clin Psychopharmacol. 2001;9(1):14-23. PMID: 11519628. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Silverman K, Wong CJ, Needham M, et al. A randomized trial of employment-based reinforcement of cocaine abstinence in injection drug users. J Appl Behav Anal. 2007;40(3):387-410. PMID: 17970256. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Simpson DD, Joe GW, Rowan-Szal GA, et al. Drug abuse treatment process components that improve retention. J Subst Abuse Treat. 1997;14(6):565-72. PMID: 9437628. Excluded: Wrong comparator

Sinadinovic K, Wennberg P, Berman AH. Targeting problematic users of illicit drugs with internet-based screening and brief intervention: a randomized controlled trial. Drug Alcohol Depend. 2012;126(1-2):42-50. doi: 10.1016/j.drugalcdep.2012.04.016. PMID: 22613182. Excluded: Other wrong population (e.g., schizophrenia focus)

Sinadinovic K, Wennberg P, Berman AH. Internet-based screening and brief intervention for illicit drug users: a randomized controlled trial with 12-month follow-up. J Stud Alcohol Drugs. 2014;75(2):313-8. PMID: 24650825. Excluded: Other wrong population (e.g., schizophrenia focus)

Sinha R, Easton C, Renee-Aubin L, et al. Engaging young probation-referred marijuana-abusing individuals in treatment: a pilot trial. Am J Addict. 2003;12(4):314-23. PMID: 14504024. Excluded: Wrong comparator

Slesnick N, Erdem G. Efficacy of ecologically-based treatment with substance-abusing homeless mothers: substance use and housing outcomes. J Subst Abuse Treat. 2013;45(5):416-25. doi: 10.1016/j.jsat.2013.05.008. PMID: 23890686. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Slesnick N, Erdem G, Bartle-Haring S, et al. Intervention with substance-abusing runaway adolescents and their families: results of a randomized clinical trial. J Consult Clin Psychol. 2013;81(4):600-14. doi: 10.1037/a0033463. PMID: 23895088. Excluded: Wrong comparator

Slesnick N, Prestopnik JL. Ecologically based family therapy outcome with substance abusing runaway adolescents. J Adolesc. 2005;28(2):277-98. doi: 10.1016/j.adolescence.2005.02.008. PMID: 15878048. Excluded: Wrong comparator

Slesnick N, Prestopnik JL. Comparison of family therapy outcome with alcohol-abusing, runaway adolescents. J Marital Fam Ther. 2009;35(3):255-77. doi: 10.1111/j.1752-0606.2009.00121.x. PMID: 19522781. Excluded: Other wrong population (e.g., schizophrenia focus)

Smelson D, Kalman D, Losonczy MF, et al. A brief treatment engagement intervention for individuals with co-occurring mental illness and substance use disorders: results of a randomized clinical trial. Community Ment Health J. 2012;48(2):127-32. doi: 10.1007/s10597-010-9346-9. PMID: 20859765. Excluded: Other wrong population (e.g., schizophrenia focus)

Smith DC, Hall JA, Williams JK, et al. Comparative efficacy of family and group treatment for adolescent substance abuse. Am J Addict. 2006;15 Suppl 1:131-6. doi: 10.1080/10550490601006253. PMID: 17182429. Excluded: Wrong comparator

Smith L, Mosley J, Johnson J, et al. Probuphine (Buprenorphine) subdermal implants for the treatment of opioid-dependent patients. P T. 2017;42(8):505-8. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Smith TE. Reducing adolescents' marihuana abuse. Soc Work Health Care. 1983;9(1):33-44. doi: 10.1300/J010v09n01_03. PMID: 6605586. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Sokol R, LaVertu AE, Morrill D, et al. Group-based treatment of opioid use disorder with buprenorphine: A systematic review. J Subst Abuse Treat. 2018;84:78-87. doi: 10.1016/j.jsat.2017.11.003. PMID: 29195596. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Somoza E, Carter J, Upadhyaya H, et al. A double-blind, placebo controlled clinical trial of naltrexone as a treatment for cocaine dependence. NIDA Res Monogr. 1998;179(138). Excluded: Non-FDA approved pharmacologic intervention

Sordo L, Barrio G, Bravo MJ, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. BMJ. 2017;357:j1550. doi: 10.1136/bmj.j1550. PMID: 28446428. Excluded: Wrong study design for key question

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Sorensen JL, Masson CL, Delucchi K, et al. Randomized trial of drug abuse treatment-linkage strategies. J Consult Clin Psychol. 2005;73(6):1026-35. PMID: 16392976. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Sorsdahl K, Stein DJ, Corrigall J, et al. The efficacy of a blended motivational interviewing and problem solving therapy intervention to reduce substance use among patients presenting for emergency services in South Africa: A randomized controlled trial. Subst Abuse Treat Prev Policy. 2015;10:46. doi: 10.1186/s13011-015-0042-1. PMID: 26576946. Excluded: Wrong country

Soyka M. Buprenorphine use in pregnant opioid users: a critical review. CNS Drugs. 2013;27(8):653-62. doi: 10.1007/s40263-013-0072-z. PMID: 23775478. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Soyka M, Trader A, Klotsche J, et al. Six-year mortality rates of patients in methadone and buprenorphine maintenance therapy: Results from a nationally representative cohort study. J Clin Psychopharmacol. 2011;31(5):678-80. doi: 10.1097/JCP.0b013e31822cd446. PMID: 21881461. Excluded: Wrong study design for key question

Spirito A, Hernandez L, Marceau K, et al. Effects of a brief, parent-focused intervention for substance using adolescents and their sibling. J Subst Abuse Treat. 2017;77:156-65. doi: 10.1016/j.jsat.2017.02.002. PMID: 28259500. Excluded: Wrong comparator

Spoth R, Redmond C, Clair S, et al. Preventing substance misuse through community-university partnerships: randomized controlled trial outcomes 41/2 years past baseline. Am J Prev Med. 2011;40(4):440-7. doi: 10.1016/j.amepre.2010.12.012. PMID: 21406278. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Spoth R, Redmond C, Shin C, et al. Brief family intervention effects on adolescent substance initiation: school-level growth curve analyses 6 years following baseline. J Consult Clin Psychol. 2004;72(3):535-42. PMID: 15279537. Excluded: School setting

Spoth R, Redmond C, Shin C, et al. Substance-use outcomes at 18 months past baseline: the PROSPER community-university partnership trial. Am J Prev Med. 2007;32(5):395-402. PMID: 17478265. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Spoth R, Redmond C, Shin C, et al. PROSPER community-university partnership delivery system effects on substance misuse through 6 1/2 years past baseline from a cluster randomized controlled intervention trial. Prev Med. 2013;56(3-4):190-6. doi: 10.1016/j.ypmed.2012.12.013. PMID: 23276777. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Spoth R, Redmond C, Shin C, et al. PROSPER delivery of universal preventive interventions with young adolescents: long-term effects on emerging adult substance misuse and associated risk behaviors. Psychol Med. 2017;47(13):2246-59. doi: 10.1017/S0033291717000691. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Spoth R, Trudeau L, Guyll M, et al. Universal intervention effects on substance use among young adults mediated by delayed adolescent substance initiation. J Consult Clin Psychol. 2009;77(4):620-32. doi: 10.1037/a0016029. PMID: 19634956. Excluded: Wrong study design for key question

Spoth RL, Randall GK, Trudeau L, et al. Substance use outcomes 51/2 years past baseline for partnership-based, family-school preventive interventions. Drug Alcohol Depend. 2008;96(1-2):57-68. doi: 10.1016/j.drugalcdep.2008.01.023. PMID: 18434045. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Spoth RL, Redmond C, Shin C. Randomized trial of brief family interventions for general populations: adolescent substance use outcomes 4 years following baseline. J Consult Clin Psychol. 2001;69(4):627-42. PMID: 11550729. Excluded: School setting

Spoth RL, Trudeau LS, Guyll M, et al. Benefits of universal intervention effects on a youth protective shield 10 years after baseline. J Adolesc Health. 2012;50(4):414-7. doi: 10.1016/j.jadohealth.2011.06.010. PMID: 22443848. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Spruit IP. The effectiveness of the medical prescription of heroin studied by randomized trials in The Netherlands, watched suspiciously by parliament and neighborhoods. Subst Use Misuse. 2002;37(4):555-63. PMID: 12064437. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Srisurapanont M, Sombatmai S, Boripuntakul T. Brief intervention for students with methamphetamine use disorders: a randomized controlled trial. Am J Addict. 2007;16(2):111-6. PMID: 17453612. Excluded: <3 month followup duration

Srivastava A, Kahan M, Nader M. Primary care management of opioid use disorders: Abstinence, methadone, or buprenorphine-naloxone? Can Fam Physician. 2017;63(3):200-5. PMID: 28292795. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Staiger PK, Kyrios M, Williams JS, et al. Improving the retention rate for residential treatment of substance abuse by sequential intervention for social anxiety. BMC Psychiatry. 2014;14:43. doi: 10.1186/1471-244X-14-43. PMID: 24533512. Excluded: Inpatient population

Stanger C, Budney AJ, Kamon JL, et al. A randomized trial of contingency management for adolescent marijuana abuse and dependence. Drug Alcohol Depend. 2009;105(3):240-7. doi: 10.1016/j.drugalcdep.2009.07.009. PMID: 19717250. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Stein MD, Caviness CM, Morse EF, et al. A developmental-based motivational intervention to reduce alcohol and marijuana use among non-treatment-seeking young adults: a randomized controlled trial. Addiction. 2017;113(3):440-53. doi: 10.1111/add.14026. PMID: 28865169. Excluded: Other wrong population (e.g., schizophrenia focus)

Steinka-Fry KT, Tanner-Smith EE, Dakof GA, et al. Culturally sensitive substance use treatment for racial/ethnic minority youth: A meta-analytic review. J Subst Abuse Treat. 2017;75:22-37. doi: 10.1016/j.jsat.2017.01.006. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Stephens RS, Roffman RA, Simpson EE. Treating adult marijuana dependence: a test of the relapse prevention model. J Consult Clin Psychol. 1994;62(1):92-9. PMID: 8034835. Excluded: Wrong comparator

Stewart DG, Siebert EC, Arlt VK, et al. READY or not: Findings from a school-based MI intervention for adolescent substance use. J Subst Abuse Treat. 2016;71:23-9. doi: 10.1016/j.jsat.2016.08.007. PMID: 27776673. Excluded: School setting

Stitzer M, Calsyn D, Matheson T, et al. Development of a multi-target contingency management intervention for HIV positive substance users. J Subst Abuse Treat. 2017;72:66-71. doi: 10.1016/j.jsat.2016.08.018. PMID: 27624618. Excluded: Other wrong population (e.g., schizophrenia focus)

Stitzer ML, Iguchi MY, Felch LJ. Contingent take-home incentive: effects on drug use of methadone maintenance patients. J Consult Clin Psychol. 1992;60(6):927-34. PMID: 1460154. Excluded: Wrong comparator

Stoermer R, Drewe J, Dursteler-Mac Farland KM, et al. Safety of injectable opioid maintenance treatment for heroin dependence. Biol Psychiatry. 2003;54(8):854-61. PMID: 14550686. Excluded: <3 month followup duration

Stoller KB, Bigelow GE, Walsh SL, et al. Effects of buprenorphine/naloxone in opioid-dependent humans. Psychopharmacology (Berl). 2001;154(3):230-42. PMID: 11351930. Excluded: Inpatient population

Stotts AL, Green C, Masuda A, et al. A stage I pilot study of acceptance and commitment therapy for methadone detoxification. Drug Alcohol Depend. 2012;125(3):215-22. doi: 10.1016/j.drugalcdep.2012.02.015. PMID: 22425411. Excluded: Wrong outcome

Stotts AL, Northrup TF. The promise of third-wave behavioral therapies in the treatment of substance use disorders. Curr Opin Psychol. 2015;2:75-81. PMID: 26693170. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Stotts AL, Schmitz JM, Rhoades HM, et al. Motivational interviewing with cocaine-dependent patients: A pilot study. J Consult Clin Psychol. 2001;69(5):858-62. doi: 10.1037/0022-006X.69.5.858. Excluded: Wrong comparator

Strain EC, Stitzer ML, Liebson IA, et al. Dose-response effects of methadone in the treatment of opioid dependence. Ann Intern Med. 1993;119(1):23-7. PMID: 8498759. Excluded: Wrong comparator

Strain EC, Stitzer ML, Liebson IA, et al. Comparison of buprenorphine and methadone in the treatment of opioid dependence. Am J Psychiatry. 1994;151(7):1025-30. PMID: 8010359. Excluded: Wrong comparator

Strain EC, Stitzer ML, Liebson IA, et al. Buprenorphine versus methadone in the treatment of opioid-dependent cocaine users. Psychopharmacology (Berl). 1994;116(4):401-6. PMID: 7701040. Excluded: Wrong comparator

Strang J, Best D, Ridge G, et al. Randomised clinical trial of the effects of time on a waiting list on clinical outcomes in opiate addicts awaiting outpatient treatment. Drugs Educ Prev Polic. 2005;12(Suppl1):115-8. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Streck JM, Ochalek TA, Hruska B, et al. Improvement in psychiatric symptoms during interim buprenorphine treatment. Drug Alcohol Depend. 2017;171. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Suchman NE, DeCoste CL, McMahon TJ, et al. Mothering from the inside out: Results of a second randomized clinical trial testing a mentalization-based intervention for mothers in addiction treatment. Dev Psychopathol. 2017;29(2):617-36. doi: 10.1017/S0954579417000220. PMID: 28401850. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Sullivan LE, Barry D, Moore BA, et al. A trial of integrated buprenorphine/naloxone and HIV clinical care. Clin Infect Dis. 2006;43 Suppl 4:S184-90. PMID: 17109305. Excluded: Wrong comparator

Sullivan LE, Bruce RD, Haltiwanger D, et al. Initial strategies for integrating buprenorphine into HIV care settings in the United States. Clin Infect Dis. 2006;43 Suppl 4:S191-6. PMID: 17109306. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Sullivan LE, Moore BA, Chawarski MC, et al. Buprenorphine/naloxone treatment in primary care is associated with decreased human immunodeficiency virus risk behaviors. J Subst Abuse Treat. 2008;35(1):87-92. PMID: 17933486. Excluded: Wrong study design for key question

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Sullivan MA, Bisaga A, Glass A, et al. Opioid use and dropout in patients receiving oral naltrexone with or without single administration of injection naltrexone. Drug Alcohol Depend. 2015;147:122-9. doi: 10.1016/j.drugalcdep.2014.11.028. PMID: 25555621. Excluded: Wrong comparator

Sullivan MA, Bisaga A, Mariani JJ, et al. Naltrexone treatment for opioid dependence: does its effectiveness depend on testing the blockade? Drug Alcohol Depend. 2013;133(1):80-5. doi: 10.1016/j.drugalcdep.2013.05.030. PMID: 23827259. Excluded: <3 month followup duration

Sun HM, Li XY, Chow EP, et al. Methadone maintenance treatment programme reduces criminal activity and improves social well-being of drug users in China: a systematic review and meta-analysis. BMJ Open. 2015;5(1):e005997. doi: 10.1136/bmjopen-2014-005997. PMID: 25573521. Excluded: Wrong comparator

Surratt HL, Inciardi JA. An effective HIV risk-reduction protocol for drug-using female sex workers. J Prev Interv Community. 2010;38(2):118-31. doi: 10.1080/10852351003640732. PMID: 20391059. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Sussman S, Sun P, Rohrbach LA, et al. One-year outcomes of a drug abuse prevention program for older teens and emerging adults: evaluating a motivational interviewing booster component. Health Psychol. 2012;31(4):476-85. doi: 10.1037/a0025756. PMID: 21988096. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Svikis DS, Keyser-Marcus L, Stitzer M, et al. Randomized multi-site trial of the job seekers' workshop in patients with substance use disorders. Drug Alcohol Depend. 2012;120(1-3):55-64. doi: 10.1016/j.drugalcdep.2011.06.024. PMID: 21802222. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Sweeney LP, Samet JH, Larson MJ, et al. Establishment of a multidisciplinary health evaluation and linkage to primary care (HELP) clinic in a detoxification unit. J Addict Dis. 2004;23(2):33-45. PMID: 15132341. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Swisher JD, Warner RW, Herr EL. Experimental comparison of four approaches to drug abuse prevention among ninth and eleventh graders. J Couns Psychol. 1972;19(4):328-32. doi: 10.1037/h0033084. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Szapocznik J, Kurtines WM, Foote F, et al. Conjoint versus one-person family therapy: further evidence for the effectiveness of conducting family therapy through one person with drug-abusing adolescents. J Consult Clin Psychol. 1986;54(3):395-7. PMID: 3722570. Excluded: Wrong comparator

Szapocznik J, Kurtines WM, Foote FH, et al. Conjoint versus one-person family therapy: some evidence for the effectiveness of conducting family therapy through one person. J Consult Clin Psychol. 1983;51(6):889-99. PMID: 6655103. Excluded: Wrong comparator

Szapocznik J, Muir JA, Duff JH, et al. Brief strategic family therapy: implementing evidence-based models in community settings. Psychotherapy Research. 2015;25(1):121-33. doi: 10.1080/10503307.2013.856044. PMID: 24274187. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Szapocznik J, Williams RA. Brief strategic family therapy: twenty-five years of interplay among theory, research and practice in adolescent behavior problems and drug abuse. Clin Child Fam Psychol Rev. 2000;3(2):117-34. PMID: 11227062. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Tait RJ, Hulse GK. A systematic review of the effectiveness of brief interventions with substance using adolescents by type of drug. Drug Alcohol Rev. 2003;22(3):337-46. PMID: 15385228. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Tait RJ, Hulse GK. Adolescent substance use and hospital presentations: a record linkage assessment of 12-month outcomes. Drug Alcohol Depend. 2005;79(3):365-71. PMID: 15896928. Excluded: Wrong study design for key question

Tait RJ, Hulse GK, Robertson SI. Effectiveness of a brief-intervention and continuity of care in enhancing attendance for treatment by adolescent substance users. Drug Alcohol Depend. 2004;74(3):289-96. PMID: 15194207. Excluded: Other wrong population (e.g., schizophrenia focus)

Tait RJ, Hulse GK, Robertson SI, et al. Emergency department-based intervention with adolescent substance users: 12-month outcomes. Drug Alcohol Depend. 2005;79(3):359-63. PMID: 16102378. Excluded: Other wrong population (e.g., schizophrenia focus)

Tait RJ, McKetin R, Kay-Lambkin F, et al. Breakingtheice: a protocol for a randomised controlled trial of an internet-based intervention addressing amphetamine-type stimulant use. BMC Psychiatry. 2012;12:67. doi: 10.1186/1471-244X-12-67. PMID: 22731926. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Tang YY, Tang R, Posner MI. Mindfulness meditation improves emotion regulation and reduces drug abuse. Drug Alcohol Depend. 2016;163 Suppl 1:S13-8. doi: 10.1016/j.drugalcdep.2015.11.041. PMID: 27306725. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Tanner-Smith EE, Steinka-Fry KT, Hennessy EA, et al. Can brief alcohol interventions for youth also address concurrent illicit drug use? results from a meta-analysis. J Youth Adolesc. 2015;44(5):1011-23. doi: 10.1007/s10964-015-0252-x. PMID: 25600491. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Tanner-Smith EE, Steinka-Fry KT, Hensman Kettrey H, et al. Adolescent substance use treatment effectiveness: A systematic review and meta-analysis. Nashville, TN: Peabody Research Institute, Vanderbilt University; 2016. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Tanner-Smith EE, Wilson SJ, Lipsey MW. The comparative effectiveness of outpatient treatment for adolescent substance abuse: A meta-analysis. J Subst Abuse Treat. 2013;44(2):145-58. doi: 10.1016/j.jsat.2012.05.006. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Tarantino N, Lamis DA, Ballard ED, et al. Parent-child conflict and drug use in college women: A moderated mediation model of self-control and mindfulness. J Couns Psychol. 2015;62(2):303-13. doi: 10.1037/cou0000013. PMID: 24660687. Excluded: Wrong study design for key question

Taxman FS, Walters ST, Sloas LB, et al. Motivational tools to improve probationer treatment outcomes. Contemp Clin Trials. 2015;43:120-8. doi: 10.1016/j.cct.2015.05.016. PMID: 26009023. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Ter Riet G, Kleijnen J, Knipschild P. A meta-analysis of studies into the effect of acupuncture on addiction. Br J Gen Pract. 1990;40(338):379-82. PMID: 2148263. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Terplan M, Lui S. Psychosocial interventions for pregnant women in outpatient illicit drug treatment programs compared to other interventions. Cochrane Database Syst Rev. 2007 (4):CD006037. PMID: 17943878. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Terplan M, Ramanadhan S, Locke A, et al. Psychosocial interventions for pregnant women in outpatient illicit drug treatment programs compared to other interventions. Cochrane Database Syst Rev. 2015 (4):CD006037. doi: 10.1002/14651858.CD006037.pub3. PMID: 25835053. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Tetrault JM, Moore BA, Barry DT, et al. Brief versus extended counseling along with buprenorphine/naloxone for HIV-infected opioid dependent patients. J Subst Abuse Treat. 2012;43(4):433-9. doi: 10.1016/j.jsat.2012.07.011. PMID: 22938914. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

The Marijuana Treatment Project Research Group. Brief treatments for cannabis dependence: Findings from a randomized multisite trial. Addictive behaviors: New readings on etiology, prevention, and treatment. Washington, DC: American Psychological Association; US; 2009:429-57. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Thomas CP, Fullerton CA, Kim M, et al. Medication-assisted treatment with buprenorphine: assessing the evidence. Psychiatr Serv. 2014;65(2):158-70. doi: 10.1176/appi.ps.201300256. PMID: 24247147. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Thornton PI, Igleheart HC, Silverman LH. Subliminal stimulation of symbiotic fantasies as an aid in the treatment of drug abusers. Int J Addict. 1987;22(8):751-65. PMID: 3316063. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Throckmorton DC, Temple R, Rappaport BA, et al. Injectable extended-release naltrexone for opioid dependence. Lancet. 2011;378(9792):665-6. doi: 10.1016/S0140-6736%2811%2961332-9. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Thylstrup B, Hesse M. Impulsive lifestyle counseling to prevent dropout from treatment for substance use disorders in people with antisocial personality disorder: A randomized study. Addict Behav. 2016;57:48-54. doi: 10.1016/j.addbeh.2016.02.001. PMID: 26882500. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Thylstrup B, Schroder S, Hesse M. Psycho-education for substance use and antisocial personality disorder: a randomized trial. BMC Psychiatry. 2015;15:283. doi: 10.1186/s12888-015-0661-0. PMID: 26573140. Excluded: Other wrong population (e.g., schizophrenia focus)

Tiihonen J, Krupitsky E, Verbitskaya E, et al. Naltrexone implant for the treatment of polydrug dependence: a randomized controlled trial. Am J Psychiatry. 2012;169(5):531-6. PMID: 22764364. Excluded: <3 month followup duration

Timko C, DeBenedetti A. A randomized controlled trial of intensive referral to 12-step self-help groups: one-year outcomes. Drug Alcohol Depend. 2007;90(2-3):270-9. PMID: 17524574. Excluded: Wrong comparator

Timko C, Debenedetti A, Billow R. Intensive referral to 12-Step self-help groups and 6-month substance use disorder outcomes. Addiction. 2006;101(5):678-88. Excluded: Wrong comparator

Timko C, Kong C, Vittorio L, et al. Screening and brief intervention for unhealthy substance use in patients with chronic medical conditions: A systematic review. J Clin Nurs. 2016;25(21-22):3131-43. doi: 10.1111/jocn.13244. PMID: 27140392. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Timko C, Schultz NR, Cucciare MA, et al. Retention in medication-assisted treatment for opiate dependence: A systematic review. J Addict Dis. 2016;35(1):22-35. doi: 10.1080/10550887.2016.1100960. PMID: 26467975. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Timko C, Sempel JM. Intensity of acute services, self-help attendance and one-year outcomes among dual diagnosis patients. J Stud Alcohol Drugs. 2004;65(2):274-82. doi: 10.15288/jsa.2004.65.274. Excluded: Other wrong population (e.g., schizophrenia focus)

Tjagvad C, Skurtveit S, Linnet K, et al. Methadone-related overdose deaths in a liberal opioid maintenance treatment programme. Eur Addict Res. 2016;22(5):249-58. doi: 10.1159/000446429. PMID: 27246839. Excluded: Wrong study design for key question

Tolou-Shams M, Dauria E, Conrad SM, et al. Outcomes of a family-based HIV prevention intervention for substance using juvenile offenders. J Subst Abuse Treat. 2017;77:115-25. doi: 10.1016/j.jsat.2017.03.013. PMID: 28476263. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Tossmann HP, Jonas B, Tensil MD, et al. A controlled trial of an internet-based intervention program for cannabis users. Cyberpsychol Behav Soc Netw. 2011;14(11):673-9. doi: 10.1089/cyber.2010.0506. PMID: 21651419. Excluded: Poor quality

Tsai LC, Doan TJ. Breastfeeding among mothers on opioid maintenance treatment: A literature review. J Hum Lact. 2016;32(3):521-9. doi: 10.1177/0890334416641909. PMID: 27053175. Excluded: Wrong study design for key question

Tsui JI, Evans JL, Lum PJ, et al. Association of opioid agonist therapy with lower incidence of hepatitis C virus infection in young adult injection drug users. JAMA Intern Med. 2014;174(12):1974-81. doi: 10.1001/jamainternmed.2014.5416. PMID: 25347412. Excluded: Wrong study design for key question

Tuchman E, Gregory C, Simson M, et al. Safety, efficacy, and feasibility of office-based prescribing and community pharmacy dispensing of methadone: Results of a pilot study in New Mexico. Addict Disord Their Treat. 2006;5(2):43-51. Excluded: Wrong comparator

Tucker T, Ritter A, Maher C, et al. A randomized control trial of group counseling in a naltrexone treatment program. J Subst Abuse Treat. 2004;27(4):277-88. PMID: 15610829. Excluded: Wrong comparator

Turner KM, Hutchinson S, Vickerman P, et al. The impact of needle and syringe provision and opiate substitution therapy on the incidence of hepatitis C virus in injecting drug users: pooling of UK evidence. Addiction. 2011;106(11):1978-88. doi: 10.1111/j.1360-0443.2011.03515.x. PMID: 21615585. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Tusel DJ, Piotrowski NA, Sees KL, et al. Contingency contracting for illicit drug use wit opioid addicts in methadone treatment. NIDA Res Monogr. 1994;153(155). Excluded: Wrong comparator

Tuten M, DeFulio A, Jones HE, et al. Abstinence-contingent recovery housing and reinforcement-based treatment following opioid detoxification. Addiction. 2012;107(5):973-82. doi: 10.1111/j.1360-0443.2011.03750.x. PMID: 22151478. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Tuten M, Svikis DS, Keyser-Marcus L, et al. Lessons learned from a randomized trial of fixed and escalating contingency management schedules in opioid-dependent pregnant women. Am J Drug Alcohol Abuse. 2012;38(4):286-92. doi: 10.3109/00952990.2011.643977. PMID: 22352784. Excluded: Wrong comparator

Unger A, Jagsch R, Bawert A, et al. Are male neonates more vulnerable to neonatal abstinence syndrome than female neonates? Gend Med. 2011;8(6):355-64. doi: 10.1016/j.genm.2011.10.001. PMID: 22088886. Excluded: Wrong comparator

Unger AS, Martin PR, Kaltenbach K, et al. Clinical characteristics of Central European and North American samples of pregnant women screened for opioid agonist treatment. Eur Addict Res. 2010;16(2):99-107. doi: 10.1159/000284683. PMID: 20160444. Excluded: Wrong outcome

Valls-Serrano C, Caracuel A, Verdejo-Garcia A. Goal management training and mindfulness meditation improve executive functions and transfer to ecological tasks of daily life in polysubstance users enrolled in therapeutic community treatment. Drug Alcohol Depend. 2016;165:9-14. doi: 10.1016/j.drugalcdep.2016.04.040. PMID: 27246405. Excluded: Wrong outcome

van Dam D, Ehring T, Vedel E, et al. Trauma-focused treatment for posttraumatic stress disorder combined with CBT for severe substance use disorder: a randomized controlled trial. BMC Psychiatry. 2013;13:172. doi: 10.1186/1471-244X-13-172. PMID: 23782590. Excluded: Other wrong population (e.g., schizophrenia focus)

van Dam D, Vedel E, Ehring T, et al. Psychological treatments for concurrent posttraumatic stress disorder and substance use disorder: a systematic review. Clin Psychol Rev. 2012;32(3):202-14. doi: 10.1016/j.cpr.2012.01.004. PMID: 22406920. Excluded: Other wrong population (e.g., schizophrenia focus)

Van den Brink W, Haasen C. Evidenced-based treatment of opioid-dependent patients. Can J Psychiatry. 2006;51(10):635-46. PMID: 17052031. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

van Emmerik-van Oortmerssen K, Vedel E, Koeter MW, et al. Investigating the efficacy of integrated cognitive behavioral therapy for adult treatment seeking substance use disorder patients with comorbid ADHD: study protocol of a randomized controlled trial. BMC Psychiatry. 2013;13:132. doi: 10.1186/1471-244X-13-132. PMID: 23663651. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Van Ryzin MJ, Roseth CJ, Fosco GM, et al. A component-centered meta-analysis of family-based prevention programs for adolescent substance use. Clin Psychol Rev. 2016;45:72-80. doi: 10.1016/j.cpr.2016.03.007. Excluded: Wrong study design for key question

Vaughn MG, Howard MO. Adolescent substance abuse treatment: A synthesis of controlled evaluations. Res Soc Work Pract. 2004;14(5):325-35. doi: 10.1177/1049731504265834. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Vederhus JK, Timko C, Kristensen O, et al. Motivational intervention to enhance post-detoxification 12-Step group affiliation: a randomized controlled trial. Addiction. 2014;109(5):766-73. doi: 10.1111/add.12471. PMID: 24400937. Excluded: Wrong outcome

Veilleux JC, Colvin PJ, Anderson J, et al. A review of opioid dependence treatment: pharmacological and psychosocial interventions to treat opioid addiction. Clin Psychol Rev. 2010;30(2):155-66. doi: 10.1016/j.cpr.2009.10.006. PMID: 19926374. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Verthein U, Haasen C, Krausz M. Auricular acupuncture as a treatment of cocaine, heroin, and alcohol addiction: A pilot study. Addict Disord Their Treat. 2002;1(1):11-6. doi: 10.1097/00132576-200205000-00003. Excluded: Wrong study design for key question

Vigna-Taglianti F, Vadrucci S, Faggiano F, et al. Is universal prevention against youths' substance misuse really universal? Gender-specific effects in the EU-Dap school-based prevention trial. J Epidemiol Community Health. 2009;63(9):722-8. doi: 10.1136/jech.2008.081513. PMID: 19395396. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Vocci FJ. Cognitive remediation in the treatment of stimulant abuse disorders: a research agenda. Exp Clin Psychopharmacol. 2008;16(6):484-97. doi: 10.1037/a0014101. PMID: 19086769. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Vorma H, Naukkarinen H, Sarna S, et al. Treatment of out-patients with complicated benzodiazepine dependence: comparison of two approaches. Addiction. 2002;97(7):851-9. PMID: 12133124. Excluded: Other wrong population (e.g., schizophrenia focus)

Vorma H, Naukkarinen H, Sarna S, et al. Long-term outcome after benzodiazepine withdrawal treatment in subjects with complicated dependence. Drug Alcohol Depend. 2003;70(3):309-14. PMID: 12757968. Excluded: Other wrong population (e.g., schizophrenia focus)

Wagoner JL, Piazza NJ. Group therapy for adult substance abusers on probation. J Offender Rehabil. 1993;19(3-4):41-56. doi: 10.1300/J076v19n03_02. Excluded: Wrong comparator

Wain R, Wilbourne PL, Harris KW, et al. Motivational interview improves treatment entry in homeless veterans. Drug Alcohol Depend. 2011;115(1-2):113-9. doi: 10.1016/j.drugalcdep.2010.11.006. Excluded: Wrong outcome

Waldron HB, Kaminer Y. On the learning curve: the emerging evidence supporting cognitive-behavioral therapies for adolescent substance abuse. Addiction. 2004;99 Suppl 2:93-105. PMID: 15488108. Excluded: Not a peer-reviewed study, wrong publication type, nonsystematic review, etc.

Waldron HB, Slesnick N, Brody JL, et al. Treatment outcomes for adolescent substance abuse at 4- and 7-month assessments. J Consult Clin Psychol. 2001;69(5):802-13. PMID: 11680557. Excluded: Wrong comparator

Waldron HB, Turner CW. Evidence-based psychosocial treatments for adolescent substance abuse. J Clin Child Adolesc Psychol. 2008;37(1):238-61. doi: 10.1080/15374410701820133. PMID: 18444060. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Walker DD, Roffman RA, Stephens RS, et al. Motivational enhancement therapy for adolescent marijuana users: a preliminary randomized controlled trial. J Consult Clin Psychol. 2006;74(3):628-32. doi: 10.1037/0022-006x.74.3.628. PMID: 16822119. Excluded: School setting

Walker DD, Stephens R, Roffman R, et al. Randomized controlled trial of motivational enhancement therapy with nontreatment-seeking adolescent cannabis users: a further test of the teen marijuana check-up. Psychol Addict Behav. 2011;25(3):474-84. doi: 10.1037/a0024076. PMID: 21688877. Excluded: School setting

Walter L, Hillhouse M, Saxon A, et al. The cocaine use reduction with buprenorphine study: Cocaine use findings. Drug Alcohol Depend. 2015;156(13). Excluded: Non-FDA approved pharmacologic intervention

Wang LJ, Lu SF, Chong MY, et al. A family-oriented therapy program for youths with substance abuse: Long-term outcomes related to relapse and academic or social status. Neuropsychiatr Dis Treat. 2016;12:699-706. doi: 10.2147/NDT.S105199. PMID: 27099500. Excluded: Wrong country

Wang X, Tan L, Li Y, et al. HCV and HIV infection among heroin addicts in methadone maintenance treatment (MMT) and not in MMT in Changsha and Wuhan, China. PLoS One. 2012;7(9):e45632. doi: 10.1371/journal.pone.0045632. PMID: 23029149. Excluded: Wrong outcome

Warden D, Subramaniam GA, Carmody T, et al. Predictors of attrition with buprenorphine/naloxone treatment in opioid dependent youth. Addict Behav. 2012;37(9):1046-53. doi: 10.1016/j.addbeh.2012.04.011. PMID: 22626890. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Washburn AM, Fullilove RE, Fullilove MT, et al. Acupuncture heroin detoxification: a single-blind clinical trial. J Subst Abuse Treat. 1993;10(4):345-51. PMID: 8411294. Excluded: <3 month followup duration

Watson J, Toner P, Day E, et al. Youth social behaviour and network therapy (Y-SBNT): adaptation of a family and social network intervention for young people who misuse alcohol and drugs - a randomised controlled feasibility trial. Health Technol Assess. 2017;21(15):1-260. doi: 10.3310/hta21150. PMID: 28399988. Excluded: Wrong comparator

Wechsberg WM, Zule WA, Riehman KS, et al. African-American crack abusers and drug treatment initiation: barriers and effects of a pretreatment intervention. Subst Abuse Treat Prev Policy. 2007;2:10. PMID: 17394653. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Weinstock J, Rash CJ, Petry NM. Contingency management for cocaine use in methadone maintenance patients: when does abstinence happen? Psychol Addict Behav. 2010;24(2):282-91. doi: 10.1037/a0017542. PMID: 20565154. Excluded: Wrong comparator

Weiss L, Petry NM. Older methadone patients achieve greater durations of cocaine abstinence with contingency management than younger patients. Am J Addict. 2013;22(2):119-26. doi: 10.1111/j.1521-0391.2013.00306.x. PMID: 23414496. Excluded: Wrong comparator

Weiss R, Potter JS, Griffin ML, et al. Long-term outcomes from the national drug abuse treatment clinical trials network prescription opioid addiction treatment study. Drug Alcohol Depend. 2015;156(13). Excluded: Results reported elsewhere, duplicate results

Weiss RD, Potter JS, Griffin ML, et al. Long-term outcomes from the national drug abuse treatment clinical trials network prescription opioid addiction treatment study. Drug Alcohol Depend. 2015;150:112-9. doi: 10.1016/j.drugalcdep.2015.02.030. PMID: 25818060. Excluded: Wrong study design for key question

Weiss RD, Rao V. The prescription opioid addiction treatment study: What have we learned. Drug Alcohol Depend. 2017;173 Suppl 1:S48-S54. doi: 10.1016/j.drugalcdep.2016.12.001. PMID: 28363320. Excluded: Wrong study design for key question

Welle-Strand GK, Skurtveit S, Jones HE, et al. Neonatal outcomes following in utero exposure to methadone or buprenorphine: A national cohort study of opioid-agonist treatment of pregnant women in Norway from 1996 to 2009. Drug Alcohol Depend. 2013;127(1-3):200-6. doi: 10.1016/j.drugalcdep.2012.07.001. Excluded: Wrong comparator

Wetzel H, Szegedi A, Scheurich A, et al. Combination treatment with nefazodone and cognitive-behavioral therapy for relapse prevention in alcohol-dependent men: a randomized controlled study. J Clin Psychiatry. 2004;65(10):1406-13. PMID: 15491246. Excluded: Other wrong population (e.g., schizophrenia focus)

White A. Trials of acupuncture for drug dependence: a recommendation for hypotheses based on the literature. Acupunct Med. 2013;31(3):297-304. doi: 10.1136/acupmed-2012-010277. PMID: 23665887. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Wikner BN, Ohman I, Selden T, et al. Opioid-related mortality and filled prescriptions for buprenorphine and methadone. Drug Alcohol Rev. 2014;33(5):491-8. doi: 10.1111/dar.12143. PMID: 24735085. Excluded: Wrong study design for key question

Winhusen T, Kropp F, Babcock D, et al. Motivational enhancement therapy to improve treatment utilization and outcome in pregnant substance users. J Subst Abuse Treat. 2008;35(2):161-73. PMID: 18083322. Excluded: Wrong comparator

Winklbaur-Hausknost B, Jagsch R, Graf-Rohrmeister K, et al. Lessons learned from a comparison of evidence-based research in pregnant opioid-dependent women. Hum Psychopharmacol. 2013;28(1):15-24. doi: 10.1002/hup.2275. PMID: 23161599. Excluded: Wrong comparator

Winters KC, Fahnhorst T, Botzet A, et al. Brief intervention for drug-abusing adolescents in a school setting: outcomes and mediating factors. J Subst Abuse Treat. 2012;42(3):279-88. doi: 10.1016/j.jsat.2011.08.005. PMID: 22000326. Excluded: School setting

Winters KC, Leitten W. Brief intervention for drug-abusing adolescents in a school setting. Psychol Addict Behav. 2007;21(2):249-54. Excluded: School setting

Winters KC, Stinchfield R, Latimer WW, et al. Long-term outcome of substance-dependent youth following 12-step treatment. J Subst Abuse Treat. 2007;33(1):61-9. PMID: 17588490. Excluded: Inpatient population

Winters KC, Stinchfield RD, Opland E, et al. The effectiveness of the Minnesota model approach in the treatment of adolescent drug abusers. Addiction. 2000;95(4):601-12. PMID: 10829335. Excluded: Inpatient population

Witkiewitz K, Bowen S. Depression, craving, and substance use following a randomized trial of mindfulness-based relapse prevention. J Consult Clin Psychol. 2010;78(3):362-74. doi: 10.1037/a0019172. PMID: 20515211. Excluded: <70% drug misuse or likely majority alcohol

Witkiewitz K, Bowen S, Douglas H, et al. Mindfulness-based relapse prevention for substance craving. Addict Behav. 2013;38(2):1563-71. doi: 10.1016/j.addbeh.2012.04.001. PMID: 22534451. Excluded: Wrong outcome

Witkiewitz K, Greenfield BL, Bowen S. Mindfulness-based relapse prevention with racial and ethnic minority women. Addict Behav. 2013;38(12):2821-4. doi: 10.1016/j.addbeh.2013.08.018. PMID: 24018224. Excluded: Wrong comparator

Appendix A5. List of Excluded Studies With Reasons For Exclusion

Wood SK, Eckley L, Hughes K, et al. Computer-based programmes for the prevention and management of illicit recreational drug use: a systematic review. Addict Behav. 2014;39(1):30-8. doi: 10.1016/j.addbeh.2013.09.010. PMID: 24144590. Excluded: Systematic review or meta-analysis used as a source document only to identify individual studies

Woodruff SI, Clapp JD, Eisenberg K, et al. Randomized clinical trial of the effects of screening and brief intervention for illicit drug use: the life shift/shift gears study. Addict Sci Clin Pract. 2014;9:8. doi: 10.1186/1940-0640-9-8. PMID: 24886786. Excluded: Poor quality

Woody GE, McLellan AT, Luborsky L, et al. Twelve-month follow-up of psychotherapy for opiate dependence. Am J Psychiatry. 1987;144(5):590-6. PMID: 3578568. Excluded: Wrong comparator

Woody GE, Poole SA, Subramaniam G, et al. Extended vs short-term buprenorphine-naloxone for treatment of opioid-addicted youth: a randomized trial. JAMA. 2008;300(17):2003-11. doi: 10.1001/jama.2008.574. PMID: 18984887. Excluded: Wrong comparator

Yancovitz SR, Des Jarlais DC, Peyser NP, et al. A randomized trial of an interim methadone maintenance clinic. Am J Public Health. 1991;81(9):1185-91. PMID: 1659236. Excluded: Wrong comparator

Yazdanbakhsh K, Dehghan F, Mirzaei S, et al. The effectiveness of levinson-based cognitive-behavioral therapy on psychological well-being of methamphetamine-dependent patients. Acta medica Mediterranea. 2016;32(Specialue5):2001-4. Excluded: <3 month followup duration

Yen CF, Wu HY, Yen JY, et al. Effects of brief cognitive-behavioral interventions on confidence to resist the urges to use heroin and methamphetamine in relapse-related situations. J Nerv Ment Dis. 2004;192(11):788-91. PMID: 15505525. Excluded: Wrong outcome

Yonkers KA, Howell HB, Allen AE, et al. A treatment for substance abusing pregnant women. Arch Women Ment Health. 2009;12(4):221-7. doi: 10.1007/s00737-009-0069-2. PMID: 19350369. Excluded: Wrong study design for key question

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Ziaee SS, Fadardi JS, Cox WM, et al. Effects of attention control training on drug abusers' attentional bias and treatment outcome. J Consult Clin Psychol. 2016;84(10):861-73. doi: 10.1037/a0040290. PMID: 27281374. Excluded: Wrong psychosocial intervention (e.g. prevention, housing, etc.)

Zuroff DC, Schwarz JC. Effects of transcendental meditation and muscle relaxation on trait anxiety, maladjustment, locus of control, and drug use. J Consult Clin Psychol. 1978;46(2):264-71. PMID: 348732. Excluded: Other wrong population (e.g., schizophrenia focus)

Criteria for Assessing Internal Validity of Individual Studies

RCTs and Cohort Studies

Criteria:

Initial assembly of comparable groups:
For RCTs: Adequate randomization, including first concealment and whether potential confounders were distributed equally among groups
For cohort studies: Consideration of potential confounders, with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts
Maintenance of comparable groups (includes attrition, cross-overs, adherence, contamination)
Important differential loss to followup or overall high loss to followup
Measurements: equal, reliable, and valid (includes masking of outcome assessment)
Clear definition of interventions
All important outcomes considered
Analysis: adjustment for potential confounders for cohort studies or intention-to treat analysis for RCTs

Definition of ratings based on above criteria:

Good: Meets all criteria: Comparable groups are assembled initially and maintained throughout the study (followup ≥80%); reliable and valid measurement instruments are used and applied equally to all groups; interventions are spelled out clearly; all important outcomes are considered; and appropriate attention to confounders in analysis. In addition, intention-to-treat analysis is used for RCTs.
Fair: Studies are graded "fair" if any or all of the following problems occur, without the fatal flaws noted in the "poor" category below: Generally comparable groups are assembled initially, but some question remains whether some (although not major) differences occurred with followup; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for. Intention-to-treat analysis is used for RCTs.
Poor: Studies are graded "poor" if any of the following fatal flaws exists: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. Intention-to-treat analysis is lacking for RCTs.

Systematic Reviews

Criteria:

Comprehensiveness of sources considered/search strategy used
Standard appraisal of included studies
Validity of conclusions
Recency and relevance (especially important for systematic reviews)

Definition of ratings based on above criteria:

Good: Recent, relevant review with comprehensive sources and search strategies; explicit and relevant selection criteria; standard appraisal of included studies; and valid conclusions
Fair: Recent, relevant review that is not clearly biased but lacks comprehensive sources and search strategies
Poor: Outdated, irrelevant, or biased review without systematic search for studies, explicit selection criteria, or standard appraisal of studies

Source: U.S. Preventive Services Task Force Procedure Manual. Accessed at https://www.uspreventiveservicestaskforce.org/Page/Name/methods-and-processes

Appendix A7. Reviewers of the Draft Report

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Note: Reviewers provided comments on a prior version of the draft report and may or may not agree with the report findings.

Appendix B1. Naltrexone Trials—Study Characteristics

Author, year Type of opioid used	Number of centers Country	Duration of followup	Intervention described and comparisons	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Cornish, 1997[71] Primarily heroin	Single center U.S.	6 months	A. Oral naltrexone 25 mg/day for 2 days, 50 mg/day for 3 days; after approximately 1 week titrated to 100 mg/day on Tuesday and 150 mg/day on Friday + counseling (n=34) B. Counseling alone (n=17)	Federal parolees/probationers (minimum of 2 years) with a history of opioid addiction	*NR by intervention group* Mean age 39 years 10% female 24% white; 62% black; 14% Hispanic Duration or severity of opioid use NR	N=51 Loss to followup: NR	NR	Fair	NIDA
Guo, 2001[5] Heroin	3 centers China	6 months	A. Oral naltrexone 50 mg/day (n=35) B. Placebo (n=14)	Age 16-45 years; DSM-IV criteria for opioid dependence; history of relapse; successful detoxification without using opioids for 7 to 10 days and negative urine test for morphine; relatives and/or friends guaranteed to supervise treatment Excluded: currently receiving opiate treatment; acute withdrawal symptoms or withdrawals symptoms after naloxone challenge test; positive urine test for morphine; naltrexone allergy; severe physical or mental disease	A vs. B Mean age 25 vs. 27 years 11% vs. 7% female Race/ethnicity NR Duration of drug abuse: 3.6 vs. 3.6 years Previous episodes of detoxification: 6 vs. 5 Drug-free duration after previous detoxification: 1.05 vs. 1.71 months	N=49 Loss to followup: 10% (5/49)	NR	Fair	NR

Appendix B1. Naltrexone Trials—Study Characteristics

Author, year Type of opioid used	Number of centers Country	Duration of followup	Intervention described and comparisons	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Hollister, 1978[72] Not specified	5 centers (2 centers for post-addicts; 2 centers for methadone maintenance therapy; 1 clinic for "street addicts") U.S.	9 months	A. Oral naltrexone syrup 50 mg/day for 5 days, 100 mg/day sixth day, no drug seventh day, titrated to 100 mg/day 2 days a week + 150 mg/day 1 day a week (n=NR) B. Oral placebo syrup (n=NR) No description of any counseling component for either group	Men age ≥18 years with diagnosis of opioid dependence based on history of past or current dependence, symptoms of opioid withdrawal, positive urine screen Excluded: chronic or severe physical or psychiatric problems or history of alcoholism	A vs. B Mean age NR 0% vs. 0% female Race NR Clinical characteristics NR	N=192 Loss to followup: NR	NR	Fair	NIDA

Appendix B1. Naltrexone Trials—Study Characteristics

Author, year Type of opioid used	Number of centers Country	Duration of followup	Intervention described and comparisons	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Krupitsky, 2004[73] Heroin	2 centers Russia	6 months	A. Oral naltrexone 50 mg/day (n=27) B. Placebo (n=25) Biweekly counseling delivered by trained therapists to both groups	Age 18-40 years; DSM-IV criteria for heroin dependence for at least 1 year; education at the high school level or above; abstinence from heroin and other substances of abuse, including alcohol, for at least 1 week prior to beginning the study; negative urine opiate drug screen and alcohol breath test; at least one relative willing to participate in treatment and monitor administration of medications, assist in followup, and provide outcome data; if female, a negative pregnancy test and willingness to use adequate contraception; no regular use of psychotropic medication Excluded: clinically significant cognitive impairment; schizophrenia; paranoid, bipolar or seizure disorder; advanced neurological, cardiovascular, renal, or hepatic disease; active tuberculosis or current febrile illness; a significant laboratory abnormality such as severe anemia, unstable diabetes, or liver function tests >3X above normal; pregnancy; legal charges with impending incarceration; current participation in another treatment study; or treatment in another substance abuse program.	A vs. B Mean age 23 vs. 21 years 11% vs. 28% female Race/ethnicity NR Duration of heroin use: 2.3 vs. 2.9 years Average daily dose of heroin: 171.5 vs. 161.3 mg Proportion using stimulants: 7% vs. 12%; hallucinogens: 15% vs. 8%; sedatives: 0% vs. 4% Daily alcohol use: 4.8 vs. 4.3 grams/day RAB HIV drug use score: 8.2 vs. 7.0 RAB HIV sexual behavior risk score: 5.0 vs. 5.0 Narrative report no significant differences between groups; p values NR	N=52 Loss to followup: NR	A vs. B Narrative report of 85-100% adherence based on riboflavin positive urine tests. No data stratified according to intervention group	Fair	NIH; VA; study drug provided by DuPont Pharma-ceutical

Appendix B1. Naltrexone Trials—Study Characteristics

Author, year Type of opioid used	Number of centers Country	Duration of followup	Intervention described and comparisons	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Krupitsky, 2006[74] Heroin	2 centers Russia	6 months	A. Oral naltrexone 50 mg/day with and without fluoxetine 20 mg/day (n=140; n=70 in each group) B. Placebo with and without fluoxetine 20 mg/day (n=140; n=70 in each group) Biweekly counseling delivered by trained therapists to both groups	Age 18-40 years; DSM-IV criteria for opioid dependence for at least 1 year; abstinence from heroin and other substances of abuse for at least 1 week; negative urine opiate drug screen and alcohol breath test; at least one relative willing to participate in treatment, monitor medication adherence; no regular use of psychotropic medication Excluded: clinically significant cognitive impairment; serious psychiatric or medical disease; significant lab abnormality; legal charges with impending incarceration; current participation in another treatment study or treatment program	A vs. B Mean age 24 vs. 24 years 24% vs. 31% female Race NR Duration of heroin use: 3.8 vs. 3.4 years Previous drug treatment episodes: 3.7 vs. 3.4	N=280 Loss to followup: NR	A vs. B Narrative report of 80-100% adherence based on riboflavin positive urine tests. No data stratified according to intervention group.	Fair	NIH; study drugs provided by DuPont (naltrexone) and Gideon Richter (fluoxetine)
Krupitsky, 2011[26] Heroin (88%), methadone (12%), other opioids and analgesics (13%)	13 centers Russia	24 weeks	A. Injectable naltrexone 300 mg/every 4 weeks (n=126) B. Injectable placebo every 4 weeks (n=124) Participants were offered 12 biweekly sessions of individual drug counseling adapted for opioid dependence	Age ≥18 years; DSM-IV criteria for opioid dependence disorder; completing inpatient opioid detoxification (≤30 days); off opioids for at least 7 days; voluntarily seeking treatment; spouse or relative available to supervise study procedures Excluded: treatment sought due to justice system coercion; pending legal proceedings with potential for incarceration	A vs. B Mean age 29 vs. 30 years 10% vs. 14% female 98% vs. 100% white; other races/ethnicities NR Duration of opioid dependence: 9.1 vs. 10.0 years	N=250 Loss to followup: 4.8% (12/250)	A vs. B Number of missing urine samples: 33.1% (833/2520) vs. 50.6% (1255/2480) Number of scheduled counseling sessions received: 99.7% (1191/1194) vs. 99.6% (922/926)	Good	Alkermes

Appendix B1. Naltrexone Trials—Study Characteristics

Author, year Type of opioid used	Number of centers Country	Duration of followup	Intervention described and comparisons	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Krupsky, 2012[25] and Krupitsky, 2016[76] Heroin	2 centers Russia	6 months	A. Naltrexone bimonthly implant 1000 mg + oral placebo (n=102) B. Placebo implant + oral naltrexone 50 mg/day (n=102) C. Placebo implant + oral placebo (n=102) All patients received individual counseling based on a modified version of the treatment used in the NIDA Collaborative Cocaine Treatment Study, delivered by experienced masters' level psychologists and addiction psychiatrists. Counselors were provided with a copy of the treatment manual given an overview of counseling techniques by the manual's authors, and supervised by one of the study investigators.	Age 18-40 years; DSM-IV criteria for opioid dependence with physiological features for at least 1 year as determined by results of clinical examination and the Composite International Diagnostic Interview; abstinence from heroin and other substances for the past week or more; negative results of urine toxicology and alcohol breath tests; no psychotropic medication; ability to provide informed consent; passed naloxone challenge Excluded: major psychiatric disorder; advanced neurological, cardiovascular, renal, or hepatic disease; active tuberculosis or current febrile illness; AIDS definingillness; significant laboratory abnormality; participation in another treatment study or substance abuse program.	A vs. B vs. C Mean age 28 vs. 28 vs. 29 years 28% vs. 28% vs. 28% female Race NR Duration of heroin abuse: 7.8 vs. 7.9 vs. 8.3 years Previous drug treatment episodes: 4.9 vs. 4.3 vs. 3.8 HIV positive: 43% vs. 52% vs. 46% Hepatitis B positive: 18% vs. 16% vs. 13% Hepatitis C positive: 96% vs. 96% vs. 94% RAB drug risk score: 8.0 vs. 8.1 vs. 8.7 GAF score: 64.7 vs. 62.8 vs. 62.5 ASI medical problems score: 0.13 vs. 0.07 vs. 0.09 ASI work problems score: 0.68 vs. 0.72 vs. 0.76 ASI alcohol use problems score: 0.11 vs. 0.08 vs. 0.10 ASI drug use problems score: 0.29 vs. 0.29 vs. 0.29 ASI legal problems score: 0.11 vs. 0.07 vs. 0.10 ASI family problems score: 0.34 vs. 0.31 vs. 0.30 ASI psychiatric problems score: 0.15 vs. 0.19 vs. 0.18	N=306 Loss to followup: 21% (65/306)	A vs. B vs. C Narrative report of 70-100% adherence based on riboflavin positive samples, consistent with capsule counts and self report	Good	NIDA; Fidelity Capital and Zambon (study drugs)

Appendix B1. Naltrexone Trials—Study Characteristics

Author, year Type of opioid used	Number of centers Country	Duration of followup	Intervention described and comparisons	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Krupitsky, 2013[75] Heroin	2 centers Russia	6 months of treatment with followup through 12 months	A. Oral naltrexone 50 mg/day with or without guanfacine 1 mg/day (n=151; n=75 with and n=76 without guanfacine) B. Placebo with or without guanfacine 1 mg/day (n=150; n=75 in each group) Participants were offered 12 biweekly sessions of individual drug counseling adapted for opioid dependence	Age 18-50 years; DSM-IV criteria for opioid dependence present for at least a year; abstinent from heroin and other substances of abuse for at least one week; negative urine screen; at least one relative willing to participate in treatment, monitor medication adherence and assist in follow-up Excluded: significant cognitive impairment; schizophrenia; major depression; bipolar or seizure disorder; advanced clinical disease; significant laboratory abnormality; legal charges with impending incarceration; participation in another treatment study; concurrent treatment in another substance abuse program	A vs. B Mean age 29 vs. 29 years 16% vs. 19% female Race NR Duration of heroin use: 8.1 vs. 8.5 years Previous drug treatment episodes: 4.2 vs. 4.2 Opioid craving scale score (Visual Analog Scale NR): 3.4 vs. 3.3 HIV positive: 42% vs. 55% RAB drug risk score: 8.7 vs. 8.2 RAB sex risk score: 4.6 vs. 4.7 GAF score: 62.6 vs. 63.1 ASI medical problems score: 0.11 vs. 0.12 ASI work problems score: 0.76 vs. 0.75 ASI alcohol score: 0.11 vs. 0.11 ASI drug use problems score: 0.33 vs. 0.29 ASI legal problems score: 0.09 vs. 0.08 ASI family problems score: 0.33 vs. 0.39 ASI psychiatric problems score: 0.21 to 0.23	N=301 Loss to followup: 37% (112/301)	A vs. B Narrative report of adherence ranging from 75-100% in the naltrexone group, based on urine screening tests	Good	NIH

Appendix B1. Naltrexone Trials—Study Characteristics

Author, year Type of opioid used	Number of centers Country	Duration of followup	Intervention described and comparisons	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Lerner, 1992[77] Heroin	3 centers Israel	2 months treatment, with follow-up through 1 year	A. Oral naltrexone 12.5 mg/day titrated to 50 mg/day by day 3 continuing to day 10, followed by 100 mg/day Monday, Wednesday and 150 mg/day Friday for total 2 months treatment (n=15) B. Oral placebo (n=16) All patients received counseling and individual and group psychotherapy when deemed necessary.	DSM-III criteria for opioid dependence applying for treatment, recently abstinent, pharmacologically detoxified and opioid-free for 1 to 2 weeks, negative naloxone challenge test.	*NR by intervention group* Mean age 27 (range 22-34; SD 3.2) years % female NR Race NR Duration of heroin use: 2.8 years Previous drug treatment: 1.2 (range 1-4; SD 1.01)	N=31 Loss to followup: NR	NR	Fair	NR

Appendix B1. Naltrexone Trials—Study Characteristics

Author, year Type of opioid used	Number of centers Country	Duration of followup	Intervention described and comparisons	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
San, 1991[78] Heroin	Single center Spain	6 months of treatment with followup through 1 year	Oral naltrexone 12.5 mg/day on day one titrated to 50 mg on day 3, 50 mg/day on days 4 to 7, 100 mg/day Monday, Wednesday and 150 mg/day Friday for total of 1 month, then: A. Oral naltrexone 100 mg/day Monday, Wednesday, 150 mg/day Friday for 5 months (n=28) B. Placebo with quinine (10 mcg/day) for 5 months (n=22) "Supportive psychotherapy" provided at scheduled visits. Patients has 3 visits/week, but it is unclear if psychotherapy was provided at every visit.	Age 18-30 years meeting DSM-III criteria for opioid/heroin dependence, completed detoxification Excluded: organic disease; psychiatric disorder; unable to follow scheduled attendance program; pregnant or breastfeeding; co-occurring alcoholism	A vs. B Mean age 26 vs. 27 years 21% vs. 27% female Race/ethnicity NR Duration of heroin use: 6.5 vs. 8.0 years Previous drug treatment: 2.4 vs. 2.4 Number of drugs consumed before treatment: 6.0 vs. 5.9 Employed: 75% vs. 55%	N=50 Loss to followup: 14% (7/50)	A vs. B Adherence (compliance with regimen): 94.4% vs. 82.2%	Fair	Centro para la Investigacion y Rehabilitacion de Adictos a Narcoticos

Appendix B1. Naltrexone Trials—Study Characteristics

Author, year Type of opioid used	Number of centers Country	Duration of followup	Intervention described and comparisons	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Schottenfeld, 2008[70] **Study also compares buprenorphine vs. placebo** Heroin	Single center Malaysia	6 months	A. Oral naltrexone 50 mg/day week 1, titrated to 100-150 mg/day Monday, Wednesday and Friday weeks 2-24 (n=43) B. Placebo (n=39) Manual-guided weekly individual counseling 45 minutes/session and group therapy aimed at relapse prevention, coping skills training, and HIV risk reduction delivered to all groups	DSM-IV criteria for heroin dependence and opioid-positive urine screen, completed residential detoxification program Excluded: Alcohol, benzodiazepine or sedative dependent; alkaline phosphatase or alanine transaminase >3x upper limit of normal; danger to themselves or others; psychotic/major depression; life-threatening medical problems	A vs. B Mean age 38 vs. 38 years Gender NR Malay ethnicity: 65% vs. 69%; other races/ ethnicities NR Duration of heroin use: 16.4 vs.14.8 years Previous drug treatment: 70% vs. 59% Heroin use in past 30 days: 26 vs. 28 days History of incarceration: 70% vs. 59%	N=82 Loss to followup: NR *Total N=126, including N=44 in the buprenorphine group*	NR	Fair	NIDA
Shufman, 1994[79] Heroin	Single center Israel	12 weeks	A. Oral naltrexone 25 mg/day day 1 and day 4 for 2 weeks; 50 mg/day 3 days/week weeks 3-12 (n=16) B. Placebo (n=16) Voluntary individual behavioral and supportive psychotherapy, 1 hour/week	DSM-II-R criteria for opioid dependence; abstinence from all drugs commonly used in Israel (opiates, hashish, benzodiazepines) for between 10 days and 1 year, following detoxification Excluded: heroin mean use of >1 g/day; injection drug user; severe mental disorder or physical illness	A vs. B Mean age 34 vs. 32 years 0% vs. 0% female 81% vs. 63% Jewish; 19% vs. 37% Arab Duration of opioid use: 6.7 vs. 5.9 years Mean daily heroin dose: 0.41 vs. 0.44 grams	N=32 Loss to followup: NR	NR	Fair	Anti-Drug Authority of Israel
Stella, 2005[80] NR	Single center Italy	6 months	A. Oral naltrexone 50 mg/day + psychological support (n=28) B. Psychological support alone (n=14)	DSM-IV criteria for opioid dependence Excluded: severe personality disorders	*NR by intervention group* Mean age 27 (range 22-34; SD 3.2) years 9% female Race NR Duration of heroin use: 2.8 years Previous drug treatment: 1.2 (range 1-4; SD 1.01)	N=42 Loss to followup: NR	NR	Fair	NR

Appendix B1. Naltrexone Trials—Study Characteristics

Abbreviations: ASI = Addiction Severity Index; DSM = Diagnostic and Statistical Manual of Mental Disorders; GAF = Global Assessment of Function; NIDA = National Institute on Drug Abuse; NIH = National Institutes of Health; NR = not reported; RAB = Risk Assessment Battery; SD = standard deviation; U.S. = United States; VA = United States Department of Veterans Affairs.

Appendix B2. Naltrexone Trials—Intervention Characteristics

Author, year Type of opioid used	Intervention described and comparisons	Recruitment setting	Treatment setting	Mentions training required for practitioners?	Mode of delivery	Intensity of intervention	Mentions intervention materials?
Cornish, 1997[71] Primarily heroin	A. Oral naltrexone 25 mg/day for 2 days, 50 mg/day for 3 days; after approximately 1 week titrated to 100 mg/day on Tuesday and 150 mg/day on Friday + counseling (n=34) B. Counseling alone (n=17)	Subjects assigned minimum 2 years of probation or parole	Outpatient, coordinated through probation office	NR	Medication dispensed by staff at office visits	Naltrexone: 5 days/week initially, then 2 days a week Counseling: 3 sessions/week for 2 weeks	NR
Guo, 2001[5] Heroin	A. Oral naltrexone 50 mg/day (n=35) B. Placebo (n=14)	NR	Outpatient treatment center	NR	Medication administered after breakfast, supervised by sponsor (family or friend)	Daily	NR
Hollister, 1978[72] Not specified	A. Oral naltrexone syrup 50 mg/day for 5 days, 100 mg/day sixth day, no drug seventh day, titrated to 100 mg/day 2 days a week + 150 mg/day 1 day a week (n=NR) B. Oral placebo syrup (n=NR) No description of any counseling component for either group	Recent detoxification from street drugs (22%), methadone maintenance program (30%), drug-free following incarceration or in a drug-free therapeutic program (48%)	Outpatient specialty clinic	NR	NR	3-6 days/week	NR
Krupitsky, 2004[73] Heroin	A. Oral naltrexone 50 mg/day (n=27) B. Placebo (n=25) Biweekly counseling delivered by trained therapists to both groups	Inpatient (40%) and outpatient (60%)	Outpatient specialty clinic	Counseling: Therapists were trained over 5 days prior to study initiation	Counseling: individual therapy	Counseling: every 2 weeks	Counseling: delivered according to standards in The Penn-VA Addiction Counseling Manual (Mercer and Woody, 1998)

Appendix B2. Naltrexone Trials—Intervention Characteristics

Author, year Type of opioid used	Intervention described and comparisons	Recruitment setting	Treatment setting	Mentions training required for practitioners?	Mode of delivery	Intensity of intervention	Mentions intervention materials?
Krupitsky, 2006[74] Heroin	A. Oral naltrexone 50 mg/day with and without fluoxetine 20 mg/day (n=140; n=70 in each group) B. Placebo with and without fluoxetine 20 mg/day (n=140; n=70 in each group) Biweekly counseling delivered by trained therapists to both groups	Inpatient (~45%) and outpatient (~55%)	Outpatient specialty clinic	Counseling: Therapists were trained over 5 days prior to study initiation	Counseling: individual therapy	Counseling: every 2 weeks	Counseling: delivered according to standards in The Penn-VA Addiction Counseling Manual (Mercer and Woody, 1998)
Krupitsky, 2011[26] Heroin (88%), methadone (12%), other opioids and analgesics (13%)	A. Injectable naltrexone 300 mg/every 4 weeks (n=126) B. Injectable placebo every 4 weeks (n=124) Participants were offered 12 biweekly sessions of individual drug counseling adapted for opioid dependence	Inpatient	Setting not described	NR	Counseling: individual therapy	Counseling: every 2 weeks	NR

Appendix B2. Naltrexone Trials—Intervention Characteristics

Author, year Type of opioid used	Intervention described and comparisons	Recruitment setting	Treatment setting	Mentions training required for practitioners?	Mode of delivery	Intensity of intervention	Mentions intervention materials?
Krupitsky, 2012[25] and Krupitsky, 2016[76] Heroin	A. Naltrexone bimonthly implant 1000 mg + oral placebo (n=102) B. Placebo implant + oral naltrexone 50 mg/day (n=102) C. Placebo implant + oral placebo (n=102) All patients received individual counseling based on a modified version of the treatment used in the NIDA Collaborative Cocaine Treatment Study, delivered by experienced masters' level psychologists and addiction psychiatrists. Counselors were provided with a copy of the treatment manual given an overview of counseling techniques by the manual's authors, and supervised by one of the study investigators.	Inpatient (93%) or outpatient (7%)	Outpatient specialty clinic (after inpatient detoxification)	Counseling: Experienced therapists given overview of counseling techniques by treatment manual's authors	Counseling: individual therapy	Counseling: 45 minute sessions every 2 weeks	Counseling: http://archives.drugabuse.gov/TXManuals/IDCA/IDCA16.html
Krupitsky, 2013[75] Heroin	A. Oral naltrexone 50 mg/day with or without guanfacine 1 mg/day (n=151; n=75 with and n=76 without guanfacine) B. Placebo with or without guanfacine 1 mg/day (n=150; n=75 in each group) Participants were offered 12 biweekly sessions of individual drug counseling adapted for opioid dependence	Inpatient (80%) or outpatient (20%)	Outpatient specialty clinic	Counseling: Experienced therapists were trained in counseling techniques prior to study and supervised biweekly by study author	Counseling: individual therapy	Counseling: every 2 weeks	Counseling: delivered according to standards in The Penn-VA Addiction Counseling Manual (Mercer and Woody, 1998) modified for use in opioid dependence and Russian language

Appendix B2. Naltrexone Trials—Intervention Characteristics

Author, year Type of opioid used	Intervention described and comparisons	Recruitment setting	Treatment setting	Mentions training required for practitioners?	Mode of delivery	Intensity of intervention	Mentions intervention materials?
Lerner, 1992[77] Heroin	A. Oral naltrexone 12.5 mg/day titrated to 50 mg/day by day 3 continuing to day 10, followed by 100 mg/day Monday, Wednesday and 150 mg/day Friday for total 2 months treatment (n=15) B. Oral placebo (n=16) All patients received counseling and individual and group psychotherapy when deemed necessary.	Outpatient (housing project or mental health clinic)	Outpatient specialty clinic	NR	Counseling: individual and group therapy	NR	NR
San, 1991[78] Heroin	Oral naltrexone 12.5 mg/day on day 1 titrated to 50 mg on day 3, then 50 mg/day on days 4 to 7, then 100 mg/day Monday, Wednesday and 150 mg/day Friday for total of 1 month, then: A. Oral naltrexone 100 mg/day Monday, Wednesday, 150 mg/day Friday for 5 months (n=28) B. Placebo with quinine (10 mcg/day) for 5 months (n=22) "Supportive psychotherapy" provided at scheduled visits. Patients has 3 visits/week, but it is unclear if psychotherapy was provided at every visit.	Inpatient	Outpatient specialty clinic (after inpatient detoxification)	NR	Unclear	Unclear	NR

Appendix B2. Naltrexone Trials—Intervention Characteristics

Author, year Type of opioid used	Intervention described and comparisons	Recruitment setting	Treatment setting	Mentions training required for practitioners?	Mode of delivery	Intensity of intervention	Mentions intervention materials?
Schottenfeld, 2008[70] **Study also compares buprenorphine vs. placebo** Heroin	A. Oral naltrexone 50 mg/day week 1, titrated to 100-150 mg/day Monday, Wednesday and Friday weeks 2-24 (n=43) B. Placebo (n=39) Manual-guided weekly individual counseling 45 minutes/session and group therapy aimed at relapse prevention, coping skills training, and HIV risk reduction delivered to all groups	Community	Outpatient specialty clinic (after inpatient detoxification)	Counseling: nurses trained over 4 days in delivering individual therapy	Counseling: group and individual therapy	Counseling: weekly 45 minute sessions	Counseling: manual guided therapy; proprietary information NR
Shufman, 1994[79] Heroin	A. Oral naltrexone 25 mg/day day 1 and day 4 for 2 weeks; 50 mg/day 3 days/week weeks 3-12 (n=16) B. Placebo (n=16) Voluntary individual behavioral and supportive psychotherapy, 1 hour/week	Unclear	Outpatient specialty clinic	NR	Counseling: individual therapy	Counseling: 1 hour/week	NR
Stella, 2005[80] NR	A. Oral naltrexone 50 mg/day + psychological support (n=28) B. Psychological support alone (n=14)	Unclear	Setting not described	NR	NR	NR	NR

Abbreviations: NIDA = National Institute on Drug Abuse; NR = not reported; VA = United States Department of Veterans Affairs.

Appendix B3. Naltrexone Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Cornish, 1997[71] Primarily heroin	A. Oral naltrexone 25 mg/day for 2 days, 50 mg/day for 3 days; after approximately 1 week titrated to 100 mg/day on Tuesday and 150 mg/day on Friday + counseling (n=34) B. Counseling alone (n=17)	A vs. B Retained in care (compliant with protocol and no absences for ≥2 consecutive weeks) at 6 months: 52% (18/34) vs. 33% (6/17); RR 1.50 (95% CI 0.73 to 3.07) Duration of retention (weeks): 16.6 vs. 14.2; p NR	A vs. B Proportion of opioid-positive urine tests: 8% vs. 30% (n/N NR); p<0.05	NR	A vs. B Reincarceration: 26% (9/34) vs. 56% (10/17); RR 0.45 (95% CI 0.23 to 0.89)	A vs. B Narrative report of higher level of "distress" in control group; data not shown, p=NR
Guo, 2001[5] Heroin	A. Oral naltrexone 50 mg/day (n=35) B. Placebo (n=14)	NR	A vs. B Relapse (not defined): 71% (25/35) vs. 93% (13/14); RR 0.77 (95% CI 0.60 to 0.99) Positive urine test for morphine (based on total samples): 24.7% (39/158) vs. 40.5% (17/42); p<0.05 Abstinence duration, months (mean): 3.34 (SD 2.29) vs. 2.08 (SD 1.59)	Anxiety 48.6% (17/35) vs. 21.4% (3/14); RR 2.27 (95% CI 0.79 to 6.54)	NR	A vs. B Narrative report that most adverse events were mild; no serious adverse events or withdrawals due to adverse events reported Diarrhea 51.4% (18/35) vs. 28.6% (4/14); RR 1.80 (95% CI 0.74 to 4.38) Nausea/vomiting 20% (7/35) vs. 14.3% (2/14); RR 1.40 (95% CI 0.33 to 5.93) Constipation 11.4% (4/35) vs. 14.3% (2/14); RR 0.80 (95% CI 0.16 to 3.88)

Appendix B3. Naltrexone Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Hollister, 1978[72] Not specified	A. Oral naltrexone syrup 50 mg/day for 5 days, 100 mg/day sixth day, no drug seventh day, titrated to 100 mg/day two days a week + 150 mg/day 1 day a week (n=NR) B. Oral placebo syrup (n=NR) No description of any counseling component for either group	A vs. B Retained in care at ≥8 months: 7 vs. 6 (denominators NR)	A vs. B Proportion with ≥1 positive urine test, among patients with ≥5 samples: 35% (21/60) vs. 41% (26/64); RR 0.86 (95% CI 0.55 to 1.36) Narrative report of no difference between groups in heroin, marijuana and alcohol use	NR	A vs. B Narrative report of no differences between groups in law enforcement contact	A vs. B Withdrawals due to adverse events: 12 vs. 5 Serious adverse events: 5 vs. 1 Narrative report that none of the problems for which patients were dropped from the study were serious

Appendix B3. Naltrexone Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Krupitsky, 2004[73] Heroin	A. Oral naltrexone 50 mg/day (n=27) B. Placebo (n=25) Biweekly counseling delivered by trained therapists to both groups	A vs. B Retained in care without relapse, 6 months: 44% (12/27) vs. 16% (4/25); RR 2.78 (95% CI 1.03 to 7.49)	A vs. B Relapse (≥3 consecutive opioid-positive urine tests, or signs/symptoms of withdrawal): 29.6% (8/27) vs. 72.0% (18/25), RR 0.41 (95% CI 0.22 to 0.77) Addiction Severity Index score, mean score ranges across both groups, 6 months: drug and alcohol use: 0.27 to 0.06, p=NS; legal status: 0.25 to 0.03, p=NS; family/social relationships: 0.34 to 0.04; p=NS; psychiatric status: 0.18 to 0.05; p=NS Alcohol use: Significant increase in naltrexone patients after 4 months; data reported in figure, p value NR Other drug use: Narrative report of no difference between groups RAB drug use score, 3 months: 1.5 vs. 0.9; 6 months: 1.4 vs. 0.0; p=NS RAB sexual behavior score, 3 months: 3.9 vs. 3.3; 6 months: 3.9 vs. 5.2; p=NS	A vs. B Mortality, drug overdose: 0% (0/27) vs. 4% (1/25); RR 0.31 (95% CI 0.01 to 7.26) Brief Psychiatric Rating Scale: no difference between groups at any time point BDI score, 3 months: 3.7 (SE 1.3) vs. 5.6 (SE 1.5); 6 months: 2.4 (SE 1.3) vs. 4.5 (SE 3.1) SSAI, 3 months: 36.4 (SE 2.8) vs. 33.0 (SE 2.3); 6 months: 32.3 (SE 2.7) vs. 30.0 (SE 5.7) STAI, 3 months: 38.1 (SE 2.1) vs. 36.3 (SE 1.9); 6 months: 35.3 (SE 2.1) vs. 34.3 (SE 4.6)	NR	A vs. B Suicide attempt: 4% (1/27) vs. 0% (0/25); RR 2.39 (95% CI 0.12 to 65)

Appendix B3. Naltrexone Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Krupitsky, 2006[74] Heroin	A. Oral naltrexone 50 mg/day with and without fluoxetine 20 mg/day (n=140; n=70 in each group) B. Placebo with and without fluoxetine 20 mg/day (n=140; n=70 in each group) Biweekly counseling delivered by trained therapists to both groups	A vs. B Retained in care without relapse: 39% (55/140) vs. 16% (22/140); RR 2.50 (95% CI 1.62 to 3.86)	A vs. B Relapse (reported everyday heroin use, three consecutive opioid-positive urine tests, or signs/symptoms of withdrawal): 31% (43/140) vs. 60% (84/140); RR 0.51 (95% CI 0.39 to 0.68) Proportion of urine tests that were positive: 5.6% (53/946) vs. 10.3% (63/610); RR 0.54 (95% CI 0.38 to 0.77) Narrative report of no difference between groups in use of stimulants and marijuana Narrative report of no difference between groups in RAB drug risk or risky sexual behavior scores	Mortality, drug overdose: none Narrative report of no difference between groups in psychiatric symptoms, including depression, anxiety, and anhedonia Narrative report of no difference between groups in composite Addiction Severity Index scores	NR	A vs. B Withdrawals due to adverse events: 0.7% (1/140) vs. 0% (0/140); RR 3.00 (95% CI 0.12 to 73) Any adverse effects (for those who remained in treatment): 7.3% (4/55) vs. 4.5% (1/22) RR 1.6 (95% CI 0.19 to 13.5)

Appendix B3. Naltrexone Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Krupitsky, 2011[26] Heroin (88%), methadone (12%), other opioids and analgesics (13%)	A. Injectable naltrexone 300 mg/every 4 weeks (n=126) B. Injectable placebo every 4 weeks (n=124) Participants were offered 12 biweekly sessions of individual drug counseling adapted for opioid dependence	A vs. B Proportion of patients completing trial without positive naloxone challenge: 53.2% (67/126) vs. 37.9% (47/124); RR 1.40 (95% CI 1.06 to 1.85)	A vs. B Non-abstinent (positive urine drug test or self-reported opioid use): 64% (81/126) vs. 77% (96/124); RR 0.83 (95% CI 0.71 to 0.98) Proportion of self-reported opioid-free days: 99.2% vs. 60.4%; p=0.0004 Mean change in opioid craving scale score: -10.1 (95% CI -12.3 to -7.8) vs. 0.7 (95% CI -3.1 to 4.4); p<0.0001Mean change in HIV risk behavior score: -0.187 (95% CI -0.224 to -0.150) vs. -0.130 (95% CI -0.173 to -0.087); p=0.02	A vs. B Mortality: no deaths in either group Overdose: no overdose events in either group Mean change from baseline on Euro-Qol-5 scale: 14.1 (95% CI 9.6 to 18.7) vs. 2.7 (95% CI 1.9 to 7.8); p=0.0005 Proportion rated "much improved" on clinical global impressions scale: 85.9% (95% CI 77.8 to 94%) vs. 57.5% (95% CI 45.7 vs. 69.5%); p=0.0002 Short Form-36 Item Health Survey mental component score: 50.37 (SD 9.18) vs. 45.28 (SD 10.47); mean difference 5.09 (95% CI 2.09 to 8.09); p=0.004	NR	A vs. B Withdrawals due to adverse events: 1.6% (2/126) vs. 2% (2/124); RR 0.98 (95% CI 0.14 to 6.88) >1 serious adverse event: 2.4% (3/126) vs. 3% (4/124); RR 0.74 (95% CI 0.17 to 3.23) >1 Drug-related adverse event: 26% (33/126) vs. 10% (10/124); RR 3.25 (95% CI 1.67 to 6.30) >1 Adverse event: 50% (63/126) vs. 32% (40/124); RR 1.55 (95% CI 1.14 to 2.11) Suicide: no events in either group

Appendix B3. Naltrexone Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Krupitsky, 2012[25] and Krupitsky, 2016[76] Heroin	A. Naltrexone bimonthly implant 1000 mg + oral placebo (n=102) B. Placebo implant + oral naltrexone 50 mg/day (n=102) C. Placebo implant + oral placebo (n=102) All patients received individual counseling based on a modified version of the treatment used in the National Institute on Drug Abuse Collaborative Cocaine Treatment Study, delivered by experienced masters' level psychologists and addiction psychiatrists. Counselors were provided with a copy of the treatment manual given an overview of counseling techniques by the manual's authors, and supervised by one of the study investigators.	A vs. B vs. C: Retained in care without relapse, 6 months: 52.9% (54/102) vs. 15.7% (16/102) vs. 10.8% (11/102); A vs. C: RR 4.91 (95% CI 2.73 vs. 8.83); B vs. C: RR 1.45 (95% CI 0.71 to 2.98)	A vs. B vs. C Relapse (daily heroin use, signs and symptoms of withdrawal, or positive naloxone challenge): 12.7% (13/102) vs. 56.9% (58/102) vs. 68.6% (70/102); A vs. C: RR 0.19 (95% CI 0.11 to 0.31); B vs. C: RR 0.22 (95% CI 0.13 to 0.38) Proportion of negative urine screening tests (of total urine tests): 63.6% (908/1428) vs. 42.7% (610/1428) vs. 34.1% (487/1428); A vs. C: RR 1.86 (95% CI 1.72 to 2.02); B vs. C: RR 1.25 (95% CI 1.14 to 1.38) Opioid craving score, 6 months (scale 1-10; higher score=more craving): 0.33 (SE 0.19) vs. 0.29 (SE 0.11) vs. 1.09 (SE 0.84)	A vs. B vs. C BDI: 2.80 (SE 0.49) vs. 6.11 (SE 2.03) vs. 1.50 (SE 0.73) SSAI: 34.4 (SE 1.34) vs. 38.8 (SE 2.14) vs. 36.6 (SE 3.82) STAI: 37.7 (SE 0.93) vs. 40.3 (SE 1.47) vs. 39.2 (SE 2.27) Narrative report of no evidence of increased risk of death due to overdose after naltrexone treatment	NR	A vs. B vs. C Withdrawals due to adverse events: 2.0% (2/102) vs. 0% (0/102) vs. 0% (0/102); RR 5.00 (95% CI 0.24 to 103) Severe AE: 0% (0/102) vs. 0% (0/102) vs. 0.98% (1/102) Infections at implant site: 8.8% (9/102) vs. 2.0% (2/102) vs. 1.1% (1/102) Local site redness and swelling: 3.9% (4/102) vs. 0% (0/102) vs. 0% (0/102) AEs per no. of implantations: wound infections 4.9% (12/244) vs. 1.1% (2/181) vs. 0.7% (1/148) Other AEs: 7.8% (8/102) vs. 3.9% (4/102) vs. 2.9% (3/102)

Appendix B3. Naltrexone Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Krupitsky, 2013[75] Heroin	A. Oral naltrexone 50 mg/day with or without guanfacine 1 mg/day (n=151; n=75 with and n=76 without guanfacine) B. Placebo with or without guanfacine 1 mg/day (n=150; n=75 in each group) Participants were offered 12 biweekly sessions of individual drug counseling adapted for opioid dependence	A vs. B Retained in care without relapse, 6 months: 23% (35/151) vs. 8.7% (13/150); RR 2.67 (95% CI 1.47 to 4.85)	A vs. B Relapse (reported daily heroin use, three consecutive opioid positive urine tests, or signs/symptoms of withdrawal): 36.4% (55/151) vs. 52.0% (78/150); RR 0.70 (95% CI 0.54 to 0.91) Proportion of negative urine screening tests (of all urine samples), naloxone vs. placebo: NR vs. 26.9% (268/1050); OR 1.6 (95% CI 1.33 to 1.93); naloxone + guanfacine vs. placebo + guanfacine: 34.5% (367/1064) vs. 24.6% (255/1037); OR 1.6 (95% CI 1.35 to 1.77) n/N NR for the naltrexone arm	A vs. B Narrative report of no difference in depression, anxiety, Global Assessment of Function, or HIV risk behavior between groups (data NR)	NR	A vs. B Narrative report of no differences between groups in adverse events, and 4.7% overall reported any side effect
Lerner, 1992[77] Heroin	A. Oral naltrexone 12.5 mg/day titrated to 50 mg/day by day 3 continuing to day 10, followed by 100 mg/day Monday, Wednesday and 150 mg/day Friday for total 2 months treatment (n=15) B. Oral placebo (n=16) All patients received counseling and individual and group psychotherapy when deemed necessary.	A vs. B Still in treatment, 2 months: 60.0% (9/15) vs. 50.0% (8/16)	A vs. B Non-abstinent (positive urinalysis), 1 year (10 months after completing treatment): 47% (7/15) vs. 62% (10/16); RR 0.75 (95% CI 0.39 to 1.45) One or more attempts to take opioids (self-report): 53.3% (8/15) vs. 50.0% (8/16); RR 1.07 (95% CI 0.54 to 2.11)	NR	A vs. B Narrative report of fewer police records among subjects who completed two-month treatment; between group difference NR	NR

Appendix B3. Naltrexone Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
San, 1991[78] Heroin	Oral naltrexone 12.5 mg/day on day 1 titrated to 50 mg on day 3, then 50 mg/day on days 4 to 7, then 100 mg/day Monday, Wednesday and 150 mg/day Friday for total of 1 month, then: A. Oral naltrexone 100 mg/day Monday, Wednesday, 150 mg/day Friday for 5 months (n=28) B. Placebo with quinine (10 mcg/day) for 5 months (n=22) "Supportive psychotherapy" provided at scheduled visits. Patients has 3 visits/week, but it is unclear if psychotherapy was provided at every visit.	A vs. B Completed treatment without dropout, 6 months: 14% (4/28) vs. 36% (8/22); RR 0.39 (95% CI 0.14 to 1.14) Duration of treatment, weeks (mean): 7.5 (SD 5.7) vs. 8.9 (SD 4.8); p=NS	A vs. B Non-abstinent (positive urinalysis), 12 months (6 months after completing treatment): 57% (16/28) vs. 55% (12/22); RR 1.05 (95% CI 0.64 to 1.72) Mean number of urine tests: 23.6 (SD 16.6) vs. 38.1 (SD 21.6) Proportion of urine tests positive for opioids: 12.8% vs. 9.6%; cocaine: 15.1% vs. 20.3%; cannabinoids: 52.4% vs. 26.9%; p values NR Drug-free, 1 year: 32% vs. 36% (n/N NR, denominator unclear)	A vs. B Mortality: 7.1% (2/28) vs. 0% (0/22); RR 3.97 (95% CI 0.20 to 79) Minnesota Multiphasic Personality Inventory depression score: 73.7 vs. 65.5; p<0.02 Narrative report of no difference between groups in STAI and SSS	A vs. B Narrative report of no significant difference between groups in number of employed at 6 months (similar to baseline rates)	A vs. B Withdrawals due to adverse events: None in either group Any adverse effect, number of events: 32 vs. 69

Appendix B3. Naltrexone Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Schottenfeld, 2008[70] **Study also compares buprenorphine vs. placebo** Heroin	A. Oral naltrexone 50 mg/day week 1, titrated to 100-150 mg/day Monday, Wednesday and Friday weeks 2-24 (n=43) B. Placebo (n=39) Manual-guided weekly individual counseling 45 minutes/session and group therapy aimed at relapse prevention, coping skills training, and HIV risk reduction delivered to all groups	A vs. B Retained in care, 6 months: 21% (9/43) vs. 13% (5/39); RR 1.63 (95% CI 0.60 to 4.45) Days in treatment: 84 vs. 70; p=0.52	A vs. B 3 consecutive positive urine tests or opiate positive test followed by two consecutive positive or missing tests: 91% (39/43) vs. 92% (36/39); RR 0.98 (95% CI 0.86 to 1.12) Abstinent at study completion: 2% (1/43) vs. 3%(1/39); RR 0.91 (95% CI 0.06 to 14) Injection drug use in past 30 days: 6.9% (2/29) vs. 8.7% (2/23); RR 0.79 (95% CI 0.12 to 5.21) Maximum consecutive days abstinent: 42 (95% CI 28 to 57) vs. 24 (95% CI 13 to 35); p=0.18 HIV risk behavior, AIDS Risk Inventory mean score, 6 months: 43.1 (95% CI 33.5 to 52.7) vs. 43.6 (95% CI 34.9 vs. 52.4); p=0.14 Days in treatment without heroin use: 24 vs. 18; p=0.80 Days in treatment without heroin relapse: 64 vs. 39; p=0.12	A vs. B vs. C Mortality: No deaths in either group	NR	A vs. B Withdrawals due to adverse events: None in either group Serious medication-related adverse events (hospitalization): 7.0% (3/43) vs. 0% (0/39); RR 6.36 (95% CI 0.34 to 119) Severe constipation: 23% (8/35) vs. 22% (8/36); RR 1.03 (95% CI 0.43 to 2.44) Urinary hesitancy: 9% (3/35) vs. 22% (8/36); RR 0.39 (95% CI 0.11 to 1.34) Drowsiness: 17% (6/35) vs. 28% (10/36); RR 0.62 (95% CI 0.25 to 1.52) Sweating: 11% (4/35) vs. 14% (5/36); RR 0.82 (95% CI 0.24 to 2.81)

Appendix B3. Naltrexone Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Shufman, 1994[79] Heroin	A. Oral naltrexone 25 mg/day on day 1 and day 4 for 2 weeks; 50 mg/day 3 days/week weeks 3-12 (n=16) B. Placebo (n=16) Voluntary individual behavioral and supportive psychotherapy, 1 hour/week	A vs. B Retained in care, 12 weeks: 50.0% (8/16) vs. 56.3% (9/16); RR 0.89 (95% CI 0.46 to 1.71)	A vs. B ≥1 positive urine opioid drug test: 62% (10/16) vs. 81% (13/16), RR 0.77 (95% CI 0.49 to 1.20) Narrative report of no difference between groups in number of positive urine tests (p=0.24)	A vs. B Depression: 31.3% (5/16) vs. 56.3% (9/16); RR 0.56 (95% CI 0.24 to 1.29)	NR	A vs. B, frequency of events Nausea and vomiting: 0% vs. 0% Diarrhea: 19% (3/16) vs. 6% (1/16); RR 3.0 (95% CI 0.35 to 25.9) Note: 1 patient's results are omitted, which accounted for the majority of AEs
Stella, 2005[80] NR	A. Oral naltrexone 50 mg/day + psychological support (n=28) B. Psychological support alone (n=14)	NR	A vs. B Relapse (not defined): 57% (16/28) vs. 79% (11/14), RR 0.73 (95% CI 0.48 to 1.11)	A vs B, % of symptoms Anxiety: 33% (9/28) vs. 7% (1/14); RR 4.50 (95% CI 0.63 to 32.1) Panic attack: 26% (7/28) vs. 5% (1/14); RR 3.50 (95% CI 0.48 to 25.7) Insomnia: 35% (10/28) vs. 8% (1/14): RR 5.00 (95% CI 0.71 to 35.2)	NR	NR

Abbreviations: BDI = Beck Depression Index; CI = confidence interval; NS = not significant; NR = not reported; RAB = Risk Assessment Battery; RR = risk ratio; SD = standard deviation; SE = standard error; SSAI = Spielberger State Anxiety Scale; STAI = Spielberger Trait Anxiety Scale.

Appendix B4. Naltrexone Trials—Quality Assessment

Author, year	Valid random assignment/ random sequence generation methods	Allocation concealment	Balance in baseline characteristics	Fidelity to intervention protocol	Low risk of contamination between groups	Participants analyzed as originally allocated	No, or minimal, post-randomization exclusions	Outcome data reasonably complete and comparable between groups
Cornish, 1997[71]	Unclear	Unclear	Yes	Yes	Yes	Yes	Unclear	No (not complete)
Guo, 2001[5]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Hollister, 1978[72]	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear	Yes
Krupitsky, 2004[73]	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Krupitsky, 2006[74]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Krupitsky, 2011[26]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Krupitsky, 2012[25] and Krupitsky, 2016[76]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Krupitsky, 2013[75]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Lerner, 1992[77]	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear	Yes
San, 1991[78]	Unclear	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes
Schottenfeld, 2008[70]	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes
Shufman, 1994[79]	Unclear	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes
Stella, 2005[80]	Unclear	Unclear	Unclear	Yes	Yes	Yes	Unclear	Yes

Appendix B4. Naltrexone Trials—Quality Assessment

Author, year	Time point and followup	Reasons for missing data similar across groups	Missing data unlikely to bias results	Blinding of outcome assessors	Blinding of clinicians/ care provider	Blinding of patients	Outcomes measured using consistent and appropriate procedures and instruments across treatment groups	No evidence of biased use of inferential statistics	No evidence that measures, analyses, or subgroup analyses selectively reported	Quality Rating
Cornish, 1997[71]	6 months; unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Guo, 2001[5]	6 months: 90% (44/49)	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Unclear	Fair
Hollister, 1978[72]	9 months: unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Krupitsky, 2004[73]	6 months: unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Krupitsky, 2006[74]	6 months: unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Krupitsky, 2011[26]	6 months: 95% (238/250)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Good
Krupitsky, 2012[25] and Krupitsky, 2016[76]	6 months: 79% (241/306)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Good
Krupitsky, 2013[75]	6 months: 63% (189/301)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Good
Lerner, 1992[77]	2 months: unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Fair
San, 1991[78]	6 months: 86% (43/50)	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Schottenfeld, 2008[70]	6 months: unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Shufman, 1994[79]	3 months: unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Stella, 2005[80]	6 months: unclear	Yes	Unclear	Yes (naltrexone group only)	Yes (naltrexone group only)	Yes (naltrexone group only)	Yes	Yes	Yes	Fair

Appendix B5. Methadone and Buprenorphine Trials—Study Characteristics

Author, year Type of opioid used	Number of centers Country	Duration of followup	Intervention described and comparisons	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Gruber, 2008[81] Heroin	Single center U.S.	6 months	A. Methadone, up to 90 mg/day for 6 months + minimal counseling, followed by 6 week taper (n=35) B. Methadone, up to 90 mg/day for 6 months + standard counseling, followed by 6 week taper (n=37) C. Usual care with 21-day methadone detoxification (n=39) Methadone administered with supervised dosing	Injection drug users aged 21-59 years with latent tuberculosis infection, opioid dependence, and willingness to be treated with isoniazid and methadone therapy	A vs. B vs. C Age: 43 vs. 40 vs. 43 years Female: 46% vs. 46% vs. 26% white: 37% vs. 46% vs. 41% black: 24% vs. 30% vs. 27% Latino: 20% vs. 22% vs. 19% Native American: 3% vs. 3% vs. 5% Asian/Pacific islander: 6% vs. 0% vs. 8% Years of heroin abuse: 16.6 vs. 16.9 vs. 20.4 years Days of heroin use in last 30 days: 19.3 (SD 9.5) vs. 19.1 (SD 9.8) vs. 17.7 (SD 10.3) Days of cocaine use: 5.5 (SD 8.5) vs. 6.2 (SD 9.5) vs. 5.1 (SD 9.1) Days of alcohol use: 5.9 (SD 9.8) vs. 7.6 (SD 10.6) vs. 5.3 (SD 9.4)	N=111 Loss to followup at 8.5 months: 51.4% (18/35) vs. 48.6% (18/37) vs. 61.5% (24/39)	NR	Fair	NIDA
Kakko, 2003[82] Heroin	Single center Sweden	12 months	A. Buprenorphine 16 mg sublingual (n=20) B. Buprenorphine taper (6 days) followed by placebo (n=20)	Newly admitted inpatients to a chemical-dependence clinic, aged 20 years or older, with a history of heroin dependence (DSM-IV) for at least 1 year	A vs. B Age: 29 vs. 32 years Female: 25% vs. 30% Race: NR Duration of heroin use: 5.8 vs. 4.8 years	N=40 Loss to followup: none	NR	Fair	Schering Plough, Swedish Medical Council, NIDA
Krook, 2002[83] Heroin	Single center Norway	3 months	A. Buprenorphine 16 mg sublingual (double dose on Saturday and no dose on Sunday), supervised dosing (n=55) B. Placebo (n=51)	Age 25 years or older, with more than 10 years of opioid dependence and failure of a traditional treatment program	A vs. B Age: 38 vs. 38 years Female: 35% vs. 33% Race: NR Homeless: 16% vs. 26% Institutionalized: 20% vs. 13% Previous maintenance treatment: 15% vs. 12% Years of heroin addiction: 20 vs. 20 years	N=106 Loss to followup: 7% (7/106)	A vs. B Compliance (% of doses taken per day of participation): 83% vs. 85%	Fair	Schering Plough, Norwegian Social and Health Department

Appendix B5. Methadone and Buprenorphine Trials—Study Characteristics

Author, year Type of opioid used	Number of centers Country	Duration of followup	Intervention described and comparisons	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Ling, 2010[84] Heroin: 63% Prescription pain medication: 37%	18 centers U.S.	6 months	A. Buprenorphine implant, 4 implants of 80 mg each (n=108) B. Placebo implant (n=55)	Men and non-pregnant women age 18-65 years with current opioid dependence (DSM-IV)	A vs. B Age: 36 vs. 39 years Female: 33% vs. 27% Race/ethnicity: white: 76% vs. 73%, black: 13% vs. 11%, other: 11% vs. 16% Opioid dependence >5 years: 16% vs. 14% Previous pharmacotherapy for opioid dependence: 23% vs. 26%	N=163 Loss to followup: 9% (10/108) vs. 7% (4/55)	A vs. B Adherent: 89% (96/108) vs. 87% (48/55)	Fair	Titan Pharma-ceuticals
Rosenthal, 2013[85] Heroin: 62% Prescription pain medication: 37%	20 centers U.S.	6 months	A. Buprenorphine implant, 4 implants of 80 mg each (n=114) B: Open-label buprenorphine-naloxone sublingual 12-16 mg/day, supervised dosing (n=119) C. Placebo implant (n=54)	Men and non-pregnant women age 18-65 years with current opioid dependence (DSM-IV)	A vs. B vs. C Age: 36 vs. 35 vs. 35 years Female: 37% vs. 40% vs. 43% Race/ethnicity: white: 83% vs. 82% vs. 83%, black: 12% vs. 13% vs. 13% Opioid dependence >5 years: 25% vs. 31% vs. 22% Previous treatment for opioid dependence: 55% vs. 57% vs. 57%	N=287 Loss to followup: 8% (9/114) vs. 14% (17/119) vs. 6% (3/54)	NR	Good	Titan Pharma-ceuticals, Reckit/ Benckiser Pharma-ceuticals

Appendix B5. Methadone and Buprenorphine Trials—Study Characteristics

Author, year Type of opioid used	Number of centers Country	Duration of followup	Intervention described and comparisons	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Schottenfeld, 2008[70] Heroin	Single center Malaysia	6 months	A. Buprenorphine sublingual 8 mg/day week 1, titrated to 16-24 mg/day Monday, Wednesday and Friday weeks 2-24. Further dose titration to 24-36 mg/day was allowed in patients reporting craving, withdrawal or persistent heroin use (n=44) B. Placebo (n=39) Manual-guided weekly individual counseling 45 minutes/session and group therapy aimed at relapse prevention, coping skills training, and HIV risk reduction delivered to all groups	DSM-IV criteria for heroin dependence and opioid-positive urine screen, completed residential detoxification program Excluded: Alcohol, benzodiazepine or sedative dependent; alkaline phosphatase or alanine transaminase >3x upper limit of normal; danger to themselves or others; psychotic/major depression; life-threatening medical problems	A vs. B Mean age 36 vs. 38 years Gender NR Malaysian ethnicity: 71% vs. 69%; other races/ethnicities NR Duration of heroin use: 14.5 vs. 14.8 years Previous drug treatment: 64% vs. 59% Heroin use in past 30 days: 27 vs. 28 days History of incarceration: 64% vs. 59% HIV-positive: 26% vs. 13% Hepatitis C-positive: 89% vs. 92% Current injection drug use: 46% vs. 41%	N=83 Loss to followup: NR *Total N=126, including 43 in the naltrexone arm*	NR	Fair	NIDA
Schwartz, 2007[86] Schwartz, 2006[6] Schwartz, 2009[87] Heroin	Single center U.S.	4 months treatment (follow-up up to 24 months)	A. Methadone, mean dose 78.4 mg/day, supervised dosing, for up to 120 days (n=199) B. Waitlist (n=120)	Heroin-dependent (at least 1 year) adults (DSM-IV) seeking treatment, on wait-list for methadone maintenance treatment at opioid treatment program	A vs. B Age: 41 vs. 42 years Female: 42% vs. 38% Race/ethnicity: white: 7% vs. 7%black: 93% vs. 93% Hispanic: 0.5% vs. 0% Age of onset of heroin use: 23 vs. 23 years Age of onset of cocaine use: 24 vs. 25 years Heroin use in last 30 days (days): 29.5 (SD 2.1) vs. 29.8 (SD 1.0) Cocaine use in last 30 days (days): 24.3 (SD 7.3) vs. 24.8 (SD 7.3)	N=319 Loss to followup at 6 months: 6% (11/199) vs. 11% (13/120)	NR	Good	NIDA

Abbreviations: DSM-IV = Diagnostic and Statistical Manual of Mental Disorders Fourth Edition; NIDA = National Institute on Drug Abuse; NR = not reported; SD = standard deviation; U.S. = United States.

Appendix B6. Methadone and Buprenorphine Trials—Intervention Characteristics

Author, year Type of opioid used	Intervention described and comparisons	Recruitment setting	Treatment setting	Mentions training required for practitioners?	Mode of delivery	Intensity of intervention	Mentions intervention materials?
Gruber, 2008[81] Heroin	A. Methadone, up to 90 mg/day for 6 months + minimal counseling, followed by 6 week taper (n=35) B. Methadone, up to 90 mg/day for 6 months + standard counseling, followed by 6 week taper (n=37) C. Usual care with 21-day methadone detoxification (n=39) Methadone administered with supervised dosing	Outpatient detoxification program (recent inpatient discharge)	Outpatient treatment center	NR	Individual	A: Not described B: Only on emergency basis or to enforce program rules (~once a month for no more than 15 minutes) C: Twice per month; participants could earn 2 take-home doses per week for negative weekly urine drug tests and alcohol breathalyzer test. Additional onsite counseling if needed.	No
Kakko, 2003[82] Heroin	A. Buprenorphine 16 mg sublingual (n=20) B. Buprenorphine taper (6 days) followed by placebo (n=20)	Inpatient addiction treatment unit	Inpatient treatment center	Group counseling led by nurse practitioners trained in Marlatt's relapse prevention manual; training otherwise NR	Group and individual	Group: Weekly for 10 sessions, followed by 2 booster sessions Individual: Weekly for 45 minutes, with contingency management	No
Krook, 2002[83] Heroin	A. Buprenorphine 16 mg sublingual (double dose on Saturday and no dose on Sunday), supervised dosing (n=55) B. Placebo (n=51)	Opioid treatment program	Addiction treatment center	Not Applicable	No counseling or rehabilitation services	No counseling or rehabilitation services	No
Ling, 2010[84] Heroin: 63% Prescription pain medication: 37%	A. Buprenorphine implant, 4 implants of 80 mg each (n=108) B. Placebo implant (n=55)	Outpatient addiction treatment centers	Outpatient addiction treatment clinics	Not required (all counselors were familiar with the treatment model)	Counseling: Individual	Twice weekly for 12 weeks then weekly for 6 weeks	No
Rosenthal, 2013[85] Heroin: 62% Prescription pain medication: 37%	A. Buprenorphine implant, 4 implants of 80 mg each (n=114) B: Open-label buprenorphine-naloxone sublingual 12-16 mg/day, supervised dosing (n=119) C. Placebo implant (n=54)	Addiction treatment centers	Addiction treatment centers	"Experienced" counselors	Counseling: Individual	Counseling: Twice weekly weeks 1-12, then weekly for 12 weeks	No

Appendix B6. Methadone and Buprenorphine Trials—Intervention Characteristics

Author, year Type of opioid used	Intervention described and comparisons	Recruitment setting	Treatment setting	Mentions training required for practitioners?	Mode of delivery	Intensity of intervention	Mentions intervention materials?
Schottenfeld, 2008[70] Heroin	A. Buprenorphine sublingual 8 mg/day week 1, titrated to 16-24 mg/day Monday, Wednesday and Friday weeks 2-24. Further dose titration to 24-36 mg/day was allowed in patients reporting craving, withdrawal or persistent heroin use (n=44) B. Placebo (n=39)Manual-guided weekly individual counseling 45 minutes/session and group therapy aimed at relapse prevention, coping skills training, and HIV risk reduction delivered to all groups	Community	Outpatient specialty clinic (after inpatient detoxification)	Counseling: nurses trained over 4 days in delivering individual therapy	Counseling: group and individual therapy	Counseling: weekly 45 minute sessions	Counseling: manual guided therapy; proprietary information NR
Schwartz, 2007[86] Schwartz, 2006[6] Schwartz, 2009[87] Heroin	A. Methadone, mean dose 78.4 mg/day, supervised dosing, for up to 120 days (n=199) B. Waitlist (n=120)	Opioid treatment program	Outpatient addiction treatment center	NR	No counseling or rehabilitation services	No counseling or rehabilitation services	No

Abbreviation: NR = not reported.

Appendix B7. Methadone and Buprenorphine Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Gruber, 2008[81] Heroin	A. Methadone, up to 90 mg/day for 6 months + minimal counseling, followed by 6 week taper (n=35) B. Methadone, up to 90 mg/day for 6 months + standard counseling, followed by 6 week taper (n=37) C. Usual care with 21-day methadone detoxification (n=39) Methadone administered with supervised dosing	A vs. B vs. C Retention at 8.5 months: 48.6% (17/35) vs. 51.4% (19/37) vs. 38.5% (15/39), RR 1.30 (95% CI 0.82 to 2.06) for A or B vs. C Retention, mean duration (days): 176 vs. 158 vs. NR	A vs. B vs. C 6 months (end of treatment) Proportion of positive urine tests: 65.4% vs. 62.5% vs. 77.8% Self-reported heroin use, mean days: 5.9 (SD 7.7) vs. 4.2 (SD 6.7) vs. 18.4 (SD 12.8); p=0.0003 for A vs. C months 1-6 Self-reported cocaine use, mean days: 2.2 (SD 3.9) vs. 4.0 (SD 6.3) vs. 4.6 (SD 9.9); p>0.05 for A vs. C or B vs. C Self-reported alcohol use, mean days: 6.5 (SD 9.7) vs. 8.4 (SD 11.1) vs. 7.2 (SD 11.2); p=0.02 for A vs. C months 1-6 Addiction Severity Index: No difference in psychiatric or family composite scores, data NR	Beck Depression Index: No difference, data NR	NR	NR
Kakko, 2003[82] Heroin	A. Buprenorphine 16 mg sublingual (n=20) B. Buprenorphine taper (6 days) followed by placebo (n=20)	A vs. B Retention at 250 days (no voluntary or involuntary withdrawal due to relapse): 75% (15/20) vs. 0% (0/20); Hazard Ratio 58.7 (95% CI 7.4-467.4), RR 33.00 (95% CI 2.11 to 515.05)	A vs. B ≥2 positive urine samples within 3 months: 20% (4/20) vs. 100% (20/20); RR 0.20 (95% CI 0.08 to 0.48)	A vs. B Mortality: 0% (0/20) vs. 20% (4/20); p=0.015; RR 0.11 (95% CI 0.006 to 1.94)	NR	NR

Appendix B7. Methadone and Buprenorphine Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Krook, 2002[83] Heroin	A. Buprenorphine 16 mg sublingual (double dose on Saturday and no dose on Sunday), supervised dosing (n=55) B. Placebo (n=51)	A vs. B Retention at end of treatment: 29% (16/55) vs. 2% (1/51), RR 14.84 (95% CI 2.04 to 107.89) Retention, mean days: 42 vs. 14, p<0.001	A vs. B Self-reported heroin use, mean change from baseline (0-10 VAS): -3.21 (95% CI -4.29 to -2.13) vs. 0.52 (95% CI -0.64 to 1.68); p<0.001 Self-reported other drug use, mean change from baseline (0-10 VAS): -0.66 (95% CI -1.77 to 0.44) vs. 1.11 (95% CI 0.18 to 2.05); p<0.01	A vs. B Wellbeing, mean change from baseline (0-10 VAS): -2.00 (95% CI -2.95 to -1.04) vs. -0.43 (95% CI -1.32 to 0.45); p<0.001 Life satisfaction, mean change from baseline (Temporal Satisfaction with Life Scale, 0 to 10): -0.65 (95% CI -1.00 to -0.31) vs. -0.24 (95% CI -0.57 to 0.09); p<0.05 Anxiety and depression, mean change from baseline (Symptom Checklist-5): -0.30 (95% CI -0.52 to -0.08) vs. -0.17 (95% CI -0.40 to 0.07); p>0.05 Mortality: None	NR	Serious adverse events: None Diaphoresis: 23.6% (13/55) vs. 29.4% (15/51); RR 0.80 (95% CI 0.42 to 1.52) Edema: 5.5% (3/55) vs. 3.9% (2/51); RR 1.39 (95% CI 0.24 to 8.00) Nausea: 16.4% (9/55) vs. 17.6% (9/51); RR 0.93 (95% CI 0.40 to 2.15) Exanthema: 1.8% (1/55) vs. 11.8% (6/51); RR 0.15 (95% CI 0.02 to 1.24)

Appendix B7. Methadone and Buprenorphine Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Ling, 2010[84] Heroin: 63% Prescription pain medication: 37%	A. Buprenorphine implant, 4 implants of 80 mg each (n=108) B. Placebo implant (n=55)	A vs. B Retention at 24 weeks: 66% (71/108) vs. 31% (17/55), RR 2.13 (95% CI 1.40 to 3.23)	A vs. B Treatment failure (required fifth implant and subsequently requiring 3 or more days per week of supplemental sublingual buprenorphine for 2 consecutive weeks or 8 or more days: 0% (0/108) vs. 30.9% (17/55); RR 0.01 (95% CI 0.001 to 0.24) Mean proportion of negative urine tests (72 samples per patient): 36.6% (95% CI 30.5% to 42.6%) vs. 22.4% (15.3% vs. 29.5%); p=0.01 Clinical Opiate Withdrawal Scale: 2.3 vs. 3.4; p<0.001 Subjective Opiate Withdrawal Scale: 4.1 vs. 6.5; p=0.004 VAS-opioid craving: 9.9 vs. 15.8; p<0.001	A vs. B Clinical Global Impressions-severity, normal or borderline normal: 57.1% (52/91) vs. 34.0% (16/47); RR 1.68 (95% CI 1.09 to 2.60) Clinical Global Impressions-improvement, very much or much improved: 80.2% (73/91) vs. 51.1% (24/47); RR 1.57 (95% CI 1.17 to 2.12) Anxiety: 10.2% (11/108) vs. 9.1% (5/55); RR 1.12 (95% CI 0.41 to 3.06) Insomnia: 21.3% (23/108) vs. 21.8% (12/55); RR 0.98 (95% CI 0.53 to 1.81)	NR	A vs. B Serious adverse events: 1.9% (2/108) vs. 7.3% (4/55); RR 0.25 (95% CI 0.05 to 1.35) Any implant site adverse event: 56.5% (61/108) vs. 52.7% (29/55); RR 1.07 (95% CI 0.79 to 1.45) Constipation: 13.9% (15/108) vs. 5.5% (3/55); RR 2.55 (95% CI 0.77 to 8.42) Diarrhea: 5.6% (6/108) vs. 12.7% (7/55); RR 0.44 (95% CI 0.15 to 1.24) Nausea: 13.9% (15/108) vs. 12.7% (7/55); RR 1.09 (95% CI 0.47 to 2.52)

Appendix B7. Methadone and Buprenorphine Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Rosenthal, 2013[85] Heroin: 62% Prescription pain medication: 37%	A. Buprenorphine implant, 4 implants of 80 mg each (n=114) B: Open-label buprenorphine-naloxone sublingual 12-16 mg/day, supervised dosing (n=119) C. Placebo implant (n=54)	A vs. B vs. C Completed trial: 64% (73/114) vs. 64% (76/119) vs. 26% (14/54), RR 2.5 (95% CI 1.6 to 3.9) for A or B vs. C	A vs. B vs. C >50% of urines positive for opioids: 72.8% (83/114) vs. NR vs. 94.4% (51/54), RR 0.77 (95% CI 0.68 to 0.88) for A vs. C Proportion of urine tests positive, weeks 1-24: 64.0% vs. 64.9% vs. 85.6%; p<0.0001 for A vs. C Proportion of urine tests positive, weeks 17-24: 71.1% vs. 70.4% vs. 92.8%; p<0.0001 for A vs. C Clinical Opiate Withdrawal Scale, weeks 1-24: 2.49 vs. 1.71 vs. 4.52, p=0.0005 for A vs. B and p<0.0001 for A vs. C Subjective Opiate Withdrawal Scale, weeks 1-24: 5.30 vs. 2.83 vs. 8.42; A vs. C, p<0.0001; A vs. B, p=0.0006 VAS-craving, weeks 1-24: 10.2 vs. 7.1 vs. 21.8; A vs. C, p<0.0001; A vs. B, p=0.054	Clinical Global Impressions-patient-rated, very much or much improved, week 24: 71.9% (82/114) vs. 72.2% (86/119) vs. 59.3% (32/54); RR 1.22 (95% CI 0.96 to 1.54) Death, accidental overdose: 1 in group B Depression: 8.8% (10/114) vs. 3.4% (4/119) vs. 5.6% (3/54); RR 1.08 (95% CI 0.32 to 3.63) Anxiety: 1.8% (2/114) vs. 5.9% (7/119) vs. 5.6% (3/54); RR 0.70 (95% CI 0.19 to 2.48) Insomnia: 7.9% (9/114) vs. 13.4% (16/119) vs. 14.8% (8/54); RR 0.72 (95% CI 0.35 to 1.52)	NR	A vs. B vs. C Any adverse event: 67.5% (77/114) vs. 71.4% (85/119) vs. 61.1% (33/54); RR 1.14 (95% CI 0.90 to 1.43) Serious adverse event: 5.3% (6/114) vs. 5.9% (7/119) vs. 5.6% (3/54); RR 1.00 (95% CI 0.30 to 3.40) Severe adverse events: 7.9% (9/114) vs. 11.8% (14/119) vs. 5.6% (3/54); RR 1.78 (95% CI 0.55 to 5.70) Nausea: 6.1% (7/114) vs. 6.7% (8/119) vs. 1.9% (1/54); RR 3.48 (95% CI 0.47 to 25.75) Hyperhidrosis: 2.6% (3/114) vs. 1.7% (2/119) vs. 5.6% (3/54); RR 0.39 (95% CI 0.10 to 1.57) Diarrhea: 1.8% (2/114) vs. 1.7% (2/119) vs. 5.6% (3/54); RR 0.31 (95% CI 0.07 to 1.34)

Appendix B7. Methadone and Buprenorphine Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Schottenfeld, 2008[70] Heroin	A. Buprenorphine sublingual 8 mg/day week 1, titrated to 16-24 mg/day Monday, Wednesday and Friday weeks 2-24. Further dose titration to 24-36 mg/day was allowed in patients reporting craving, withdrawal or persistent heroin use (n=44) B. Placebo (n=39) Manual-guided weekly individual counseling 45 minutes/session and group therapy aimed at relapse prevention, coping skills training, and HIV risk reduction delivered to all groups	A vs. B Retained in care, 6 months: 41% (18/44) vs. 13% (5/39); RR 3.19 (95% CI 1.31 to 7.79) Days in treatment (mean): 117 (95% CI 102 to 132) vs. 70 (95% CI 54 to 87); p=0.0009	A vs. B Relapse (3 consecutive positive urine tests or opiate positive test followed by two consecutive positive or missing tests): 75% (33/44) vs. 92% (36/39); RR 0.81 (95% CI 0.67 to 0.99) Abstinent at study completion: 11% (5/44) vs. 3%(1/39); RR 4.43 (95% CI 0.54 to 36) Maximum consecutive days abstinent: 59 (95% CI 43 to 76) vs. 24 (95% CI 13 to 35); p<0.01 Days in treatment without heroin relapse: 79 (95% CI 61 to 98) vs. 39 (95% CI 25 to 53); p=0.007 HIV risk behavior, AIDS Risk Inventory mean score, 6 months: 53.7 (95% CI 41.7 vs. 53.0) vs. 43.6 (95% CI 34.9 vs. 52.4); p=0.14 IDU past 30 days, at 6 months: 14% (5/36) vs. 8.7% (2/23), p=0.716	A vs. B vs. C Mortality: No deaths in either group	NR	A vs. B Withdrawals due to adverse events: 2.3% (1/44) vs. 2.6% (1/39); RR 0.89 (95% CI 0.06 to 13.7) Serious medication-related adverse events (hospitalization): None Severe constipation: 51% (22/43) vs. 22% (8/36); RR 2.30 (95% CI 1.17 to 4.53) Drowsiness: 47% (20/43) vs. 28% (10/36); RR 1.67 (95% CI 0.90 to 3.10) Urinary hesitancy: 54% (23/43) vs. 22% (8/36); RR 2.41 (95% CI 1.23 to 4.71) Sweating: 33% (14/43) vs. 14% (5/36); RR 2.34 (95% CI 0.93 to 5.88)

Appendix B7. Methadone and Buprenorphine Trials—Results

Author, year Type of opioid used	Intervention described and comparisons	Retention in care	Drug use and behavior	Clinical health outcomes	Social or legal outcomes	Adverse events
Schwartz, 2007[86] Schwartz, 2006[6] Schwartz, 2009[87] Heroin	A. Methadone, mean dose 78.4 mg/day, supervised dosing, for up to 120 days (n=199) B. Waitlist (n=120)	Entered into comprehensive methadone treatment, 4 months: 76% (151/199) vs. 21% (25/120), RR 3.64 (95% CI 2.55 to 5.21)	A vs. B Opioid-positive drug test, 4 months: 57% (99/175) vs. 79% (80/101), RR 0.71 (95% CI 0.61 to 0.84) Cocaine-positive drug test, 4 months: 62% (107/174) vs. 63% (62/99), RR 0.98 (95% CI 0.81 to 1.19) Cocaine-positive drug test, 6 months: 52% (79/153) vs. 59% (60/101), RR 0.87 (95% CI 0.70 to 1.09) Days of heroin use, last 30 days: 4.2 (SD 8.6) vs. 26.4 (SD 8.8); p<0.001 for overall time trend Days of cocaine use, last 30 days: 2.4 (SD 5.5) vs. 5.8 (SD 8.8); p=0.001 for overall time trend	NR	A vs. B 6 months Days of illegal activity in past 30 days: 1.7 vs. 6.9; p<0.001 for overall time trend Arrests, at 6 months: 16% (31/198) vs. 20% (24/119); RR 0.78 (95% CI 0.48 to 1.26)	NR

Abbreviations: CI = confidence interval; NR = not reported; RR = risk ratio; SD = standard deviation; VAS = Visual Analog Scale.

Appendix B8. Methadone and Buprenorphine Trials—Quality Assessment

Author, year	Valid random assignment/ random sequence generation methods	Allocation concealment	Balance in baseline characteristics	Fidelity to intervention protocol	Low risk of contamination between groups	Participants analyzed as originally allocated	No, or minimal, post-randomization exclusions	Outcome data reasonably complete and comparable between groups
Gruber, 2008[81]	Unclear; "generated by a statistician"	Yes; sealed envelopes	No; not age or depressive symptoms	Yes	Yes	Yes	Yes	No; final urinalysis data available for half of each group or less
Kakko, 2003[82]	Yes; random numbers table	Yes	Yes	Yes	Yes	Yes	Yes	No
Krook, 2002[83]	Unclear	Yes; sealed envelopes	Yes	Yes	Yes	Yes	Yes	Yes
Ling, 2010[84]	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Rosenthal, 2013[85]	Yes	Yes	Yes	Yes	Yes	Yes	No; 14 excluded after randomization but before receiving medication	Yes
Schottenfeld, 2008[70]	Yes; computer	Yes; central	Yes	Yes	Yes	Yes	Yes	No
Schwartz, 2007[86] See also: Schwartz, 2006[6]; Schwartz, 2009[87]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Appendix B8. Methadone and Buprenorphine Trials—Quality Assessment

Author, year	Time point and followup	Reasons for missing data similar across groups	Missing data unlikely to bias results	Blinding of outcome assessors	Blinding of clinicians/ care provider	Blinding of patients	Outcomes measured using consistent and appropriate procedures and instruments across treatment groups	No evidence of biased use of inferential statistics	No evidence that measures, analyses, or subgroup analyses selectively reported	Quality rating
Gruber, 2008[81]	8.5 months: 49% vs. 51% vs. 39%	Unclear	No	No	No	No	Yes	Yes	Yes	Fair
Kakko, 2003[82]	12 months: 94% vs. 0%	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Krook, 2002[83]	3 months: 93% (99/106)	Yes	Unclear	Yes; mostly self-report	Yes	Yes	Yes	Yes	Yes	Fair
Ling, 2010[84]	6 months: 91% vs. 93%	Yes	Yes	Yes	Yes	Yes; placebo implants	Yes	Yes	Yes	Fair
Rosenthal, 2013[85]	6 months: 92% vs. 94% vs. 86%	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Good
Schottenfeld, 2008[70]	6 months: 41% (18/44) vs. 13% (5/39); RR 3.19 (95% CI 1.31 to 7.79)	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Schwartz, 2007[86] See also: Schwartz, 2006[6]; Schwartz, 2009[87]	4 months: 94.7%	Yes	Yes	Unclear	No	No	Yes	Yes	Yes	Fair

Abbreviations: CI = confidence interval; RR = relative risk.

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Babor, 2004[30]	3 sites U.S.	4 months (for all treatment groups)	A. Multi-component therapy: motivational enhancement + CBT + case management (n=156) B. Motivational enhancement (n=146) C. Control: delayed treatment (n=148)	Age ≥18 years; current DSM-IV diagnosis of marijuana dependence; marijuana use at least 40/90 days prior to study entry	A vs. B vs. C Mean age 36 vs. 35 vs. 37 years % female: 29% vs. 36% vs. 29% Race/ethnicity: 67% vs. 65% vs. 67% white; 16% vs. 21% vs. 16% Hispanic; 15% vs. 13% vs. 8% black; 2% vs. 1% vs. 0% other Characteristics NR by intervention group: Duration of regular marijuana use: 17.9 years Duration of self-defined problem marijuana use: 9.2 years Dependence symptoms (DSM-IV, 0 to 7): 5.62 (SD 1.17) vs. 5.70 (SD 1.20) vs. 5.56 (SD 1.33) Abuse symptoms (DSM-IV, 0 to 4): 2.06 (SD 0.77) vs. 2.10 (SD 0.87) vs. 2.11 (SD 0.84) Marijuana problems (Marijuana Problem Scale, 0 to 19): 9.47 (SD 3.51) vs. 10.18 (SD 3.47) vs. 9.07 (SD 3.53) Days of marijuana use in 90 days prior to study entry: 82 days Number of marijuana use episodes/day: 3.7 Proportion with prior treatment for drug abuse: 18% Proportion of days marijuana used: 87.56% (SD 17.24) vs. 86.92% (SD 17.15) vs. 89.88 (SD 14.11)	N=450 Loss to followup: 7.1% (32/450)	A vs. B vs. C Proportion attending all allocated sessions: 47.3% (74/156) vs. 71.9% (105/146) vs. NA	Good	SAMHSA, Center for Substance Abuse Treatment

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Baker, 2001[88] Baker, 2001[89]	Unclear Australia	6 months	A. 4-session CBT: MI (Session 1) + cognitive behavioral coping strategies + relapse prevention (Sessions 2-4) + self-help booklet (n=16) B. 2-session CBT: same as Session 1 and 2 + self-help booklet (n=16) C. Control: self-help booklet only (n=32)	Regular amphetamine users residing in Newcastle New South Wales, Australia	(A + B) vs. C Mean age 33 vs. 31 years33% vs. 43% female Race/ethnicity NR Duration of regular amphetamine use: 10.92 (SD 7.84) vs. 10.25 (SD 7.03) years Mean OTI score: 1.20 (SD 1.65) vs. 0.83 (SD 1.03) Enrolled in methadone maintenance treatment: 33% vs. 39% Characteristics not stratified by intervention group: Previous substance use treatment: 72% Current substance use treatment: 48% Mean SDS score: 6.41 (SD 3.23) Mean GHQ-28 score: 11.20 (SD 7.65) Proportion with other daily drug use: 94% tobacco; 30% heroin; 47% cannabis; 38% tranquilizers; 10% alcohol; 1% cocaine	N=64 Loss to followup: 19% (12/64)	A vs. B vs. C Proportion completing ≥75% of sessions: 56.3% (9/16) vs. 68.8% (11/16) vs. NA	Fair	University of Newcastle
Baker, 2005[90]	Unclear Australia	6 months	A. 4-session CBT: MI (Session 1) + cognitive behavioral coping strategies + relapse prevention (Sessions 2-4; n=66) B. 2-session CBT: same as Session 1 and 2 (n=74) C. Control (n=74)	Regular amphetamine users, defined as OTI weekly use score ≥0.14 Excluded: suicidality or acute psychosis; acquired cognitive impairment; current enrolment or treatment for amphetamine use	(A + B) vs. C Mean age 30 vs. 30 years 39% vs. 35% female Race/ethnicity NR Duration of regular amphetamine use: 9.24 (SD 6.87) vs. 8.49 (SD 7.07) years Mean OTI score: 1.48 (SD 1.67) vs. 1.55 (SD 1.61) Enrolled in methadone maintenance treatment: 28% vs. 23%	N=214 Loss to followup: 29% (61/214)	A vs. B vs. C Proportion completing ≥75% of sessions: 68.2% (45/66) vs. 75.7% (56/74) vs. NA	Fair	Australian Commonwealth Department of Health and Ageing

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Bernstein, 2005[4]	Multi-center U.S.	6 months	A. MI + telephone booster session: Participants received a semi scripted, brief (10-45 minute) motivational interview delivered by a peer, a substance abuse outreach worker in recovery. (n=490) B. Minimal: Participants received only a handout stating that "based on your screening responses, you would benefit from help with your drug use" (n=472)	Adults aged ≥18 years using cocaine, heroin recruited during a primary care visit using the DAST-10 tool. Cocaine and/or heroin use in last 30 days and DAST-10 score ≥3 (moderate-to-severe problems related to drug use)	Mean age 38 vs. 38 years 31% vs. 28% female 62% vs. 63% black; 14% vs. 15% white; 24% vs. 22% Hispanic; 0.7% vs. 0.5% other Education: 37% vs. 38% less than high school Working: 43% vs. 49% DAST-10 score: 8.0 (SD 1.7) vs. 7.9 (SD 1.8) Readiness to change score: 7.0 (SD 2.5) vs. 7.0 (SD 2.6) ≥1 prior admission for detox or substance abuse treatment: 44% vs. 49% ASI, drug subscale score: mean 0.3 (SD 0.1) vs. 0.2 (SD 0.1) ASI, medical subscale score: mean 0.6 (SD 0.3) vs. 0.5 (SD 0.4)	N=1,175 Loss to followup: 33.8%	31% could be reached for phone booster session	Fair	NIDA
Bernstein, 2009[45]	Single center U.S.	12 months	A. Brief intervention, based on a MI approach (n=47) B. Usual care (not described) (n=55)	Adolescents and young adults aged 14-21 years using cannabis recruited during pediatric emergency department visit using Youth and Young Adult Health and Safety Needs Survey. Smoked marijuana ≥3 times in the past 30 days or risky behavior related to marijuana use = included	Mean age NR; ≤17 years: 29% vs. 30%; ≥18 years: 71% vs. 70% % female: 66.2 Race/ethnicity: black 84% vs. 78%; Hispanic 10% vs. 16%; white 4% vs. 7%; other 2% vs. 0% Cannabis use, days per month, mean (SD): 19.0 (10.9) vs. 15.3 (10.1) Cannabis abstinence, days per month, mean: 0 vs. 0 Drove after cannabis use, n (%): 8 (14.5) vs. 9 (14.1) Rode in a car with person high after cannabis use, n (%): 12 (21.8) vs. 11 (17.2)	N=139 (Full study randomized 210; the non-assessed control group was not included in this report) Loss to followup: 26.6%	92.5% reported receiving emails about feedback, 75.2% reported linking to and viewing feedback, and 5.6% reported printing the feedback	Fair	NIH/NIDA supplement to The Youth Alcohol Prevention Center

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Blow, 2017[46] Bonar, 2018[91] HealthiER You	Single center U.S.	52 weeks	A. Computerized brief motivational interview, targeting drug and alcohol use (n=257); A1 with (n=130) or A2 without (n=127) additional MET B. Therapist brief motivational interview, targeting drug and alcohol use (n=257); B1 with (n=127) or B2 without (n=130) additional MET C. Educational control: 3 minute review of community resources and HIV prevention (n=266); C1 with (n=136) or C2 without (n=130) additional MET	Age 18-60 years presenting to the emergency department with reported drug use in the past 3 months	A vs. B vs. C Age: 31 vs. 32 vs. 31 years Gender: 54% vs. 55% vs. 57% female Race: 54% black, 36% white, 10% other vs. 51% black, 42% white, 7% other vs. 52% black, 39% white, 9% other Cannabis use in past 3 months: 90% vs. 90% vs. 93% Using other illegal drugs in past 3 months: 16% vs. 22% vs. 17%	N=780 12 month Loss to followup: 12% (32/257) vs. 19% (48/257) vs. 12% (33/266)	NR	Good	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Bogen-schutz 2014[47] Bogen-schutz 2011[115] SMART-ED	6 centers U.S.	12 months	A. Brief intervention based on MI principles + telephone booster sessions. In addition to an informational pamphlet about drug use and misuse (n=427) B. Minimal: informational pamphlet about drug use and misuse, its potential consequences, and treatment options and optional referral to addiction treatment, consisting of a recommendation to seek treatment and a standardized list of available options (n=427)	Adults aged ≥18 years using all drugs recruited during an emergency department visit using the DAST-10 tool. At least 1 day of drug use in past 30 days and DAST-10 score ≥ 3 (moderate-to-severe problems related to drug use)	Mean age 36 vs. 36 years 30% vs. 33% female Race/ethnicity: 2% vs. 2% American Indian/Alaska Native; 1% vs. 1% Asian; 34% vs. 36% black; 48% vs. 49% white; 5% vs. 4% other; 5% vs. 5% multiracial; 5% vs. 2% other/did not answer Education: 31% vs. 30% less than high school DAST-10 score: 5.8 (2.3) vs. 5.9 (SD 2.3) AUDIT-C score: 5.5 (SD 3.8) vs. 5.5 (SD 3.8) Drug use days in past 30 days: 15.7 (SD 11.5) vs. 17.4 (SD 11.6) Primary drug used: 44% vs. 43% cannabis; 26% vs. 27% cocaine; 18% vs. 19% street opioids; 5% vs. 5% prescription opioids; 4% vs. 4% methamphetamine; 3% vs. 2% other Drug use days for the most frequently used drug, mean (SD): 14.8 (11.2) vs. 16.3 (11.4) Drug use days, mean (SD): 16.4 (11.0) vs. 18.5 (10.9) Drug use abstinence (n (%)) Based on hair sample (units = ng/10 mg) for the most frequency used drug: 20 (5.7) vs. 25 (7.4) Drug use abstinence (n (%)) Based on hair sample (units = ng/10 mg): 9 (2.4) vs. 9 (2.6)	N=854 (Full study randomized N=1285. Minimal screening only group was not included in this report given no baseline measures for outcome variables) Loss to followup: 19.7%	421 (99%) participants received the initial brief intervention, 243 (57%) received the first booster call, and 166 (39%) received the second booster call. 250 (58.5%) of participants were referred to addiction treatment	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Copeland, 2001a[31] Copeland, 2001b[92]	Single center Australia	6 months; median followup 8 months	A. 6CBT: intervention package incorporating motivational interview + standard relapse prevention (n=78) B. 1CBT: single session of 6CBT + self-help booklet (n=82) C. Delayed treatment control (n=69)	Age ≥18 years with a desire to cease cannabis use. Excluded: more than weekly use of other drugs, nicotine or alcohol in the past 6 months; previous treatment for cannabis dependence in the past 3 months; current treatment for any other substance use	NR by intervention group Mean age 32 years 31% female 3% Aboriginal; other race/ethnicity NR Age of first cannabis use: 15 (range 7-45) Duration of weekly cannabis use: 13.9 years (SD 7.0; range 1-34) Proportion meeting DSM-IV cannabis dependence diagnosis: 96.4% SDS score: 9.2 (SD 3.2) vs. 9.8 (SD 2.9) vs. 9.3 (SD 2.6) OTI score: 2.1 (SD 0.8) vs. 2.0 (SD 0.8) vs. 2.2 (SD 0.9)	N=229 Loss to followup: 26% (59/229)	A vs. B vs. C Proportion completing ≥75% of sessions: 59% (46/78) vs. 87.8% (72/82) vs. NA	Fair	Australian Common-wealth Department of Health and Family Services
D'Amico, 2018[44]	4 clinics U.S.	1 year	A. Brief, 15-20 minute motivational interview delivered in primary care (CHAT) (n=153) B. Control: brochure with information on the effects of alcohol and drug use, how to prepare for risky situations, and online and telephone resources (n=141) Paid $25 (baseline), $40 (3 months), $50 (6 months), $75 (12 months)	Adolescents ages 12-18 years, screened as at-risk on NIAAA Screening Guide;	A vs. B Mean age: 16 vs. 16 years Female: 59.6% vs. 55.4% Race/ethnicity: 12.4% vs. 10.6% white, 20.3% vs. 12.8% black, 64.7% vs. 68.1% Hispanic, 2.6% vs. 8.5% other/multiracial Ever used marijuana: 82.4% vs. 82.3% Past year marijuana use (number of times), mean (SD): 10.02 (8.51) vs. 9.51 (8.31) On days using marijuana, number of times used, mean (SD): 1.54 (1.15) vs. 1.51 (1.15) Number of negative consequences from marijuana use, mean (SD): 3.58 (10.46) vs. 463 (12.54) Cannabis use disorder: 38.6% (56/153) vs. 40.7% (57/141)	N=294 Loss to followup, A vs. B: 20% (31/153) vs. 20% (27/141)	A. 7.2% (11/153) did not receive the intervention	Fair	NIAAA grant

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
de Dios, 2012[93]	Unclear U.S.	3 months	A. MI + mindfulness meditation (n=22) B. Control: assessment only (n=12)	Age 18-29 female participants who smoked marijuana at least three times in the previous month; desire to quit or reduce marijuana use; endorsed the following item from the Marijuana Expectancies Questionnaire: "In the past month, have you used marijuana as a way to relax, relieve anxiety or calm down?" Excluded: severe psychiatric disorder; using alcohol or other substances at NIAAA criteria for Hazardous Use; use of any cocaine, heroin, methamphetamines or other drugs in the past month	A vs. B Mean age 23 vs. 24 years 100% vs. 100% female 46% vs. 58% white; other races/ethnicities NR Days of marijuana use past month: 17.05 (SD 9.96) vs. 18.83 (SD 8.09) Psychiatric Diagnostic Screening Questionnaire general anxiety disorder score: 5.95 (SD 2.9) vs. 4.92 (SD 3.12)	N=34 Loss to followup: 27% (9/34)	A vs. B Proportion with 1 or more followup visits: 77.3% (17/22) vs. 83.3% (10/12); p=0.68	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
de Gee, 2014[94]	8 centers The Nether-lands	3 months	A. Intervention: MI-based, aimed at changing adolescents' cannabis use by increasing their awareness of the possible negative consequences of cannabis use and by helping them to make informed choices about their own use (n=58) B. Control: information session (n=61)	Age 14-21 years with weekly cannabis use and no intention to seek help for cannabis use Excluded: significant cognitive impairment; treatment for drug or alcohol use during previous 3 months; heavy alcohol consumption; use of illicit drugs other than cannabis more than twice weekly in the past 3 months	A vs. B Mean age 18 vs. 18 years 26% vs. 28% female Race NR (79% vs. 77% Dutch; 14% vs. 10% Western, non-Dutch; 7% vs. 11% non-Western) Mean SDS score: 3.2 (SD 2.5) vs. 3.2 (SD 2.8) Mean CUPIT Impaired Control score: 29.0 (SD 8.3) vs. 28.9 (SD 8.1) Mean CUPIT Problems score: 6.2 (SD 4.3) vs. 5.7 (SD 3.7) Mean YSR Internalizing Problems score: 15.5 (SD 11.5) vs. 10.7 (SD 9.0); p<0.001 Mean YSR Externalizing Problems score: 17.7 (SD 10.0) vs. 17.3 (SD 8.8) Mean age of cannabis use onset: 14 vs. 14 years Days of cannabis use/week: 4.6 vs. 4.3	N=119 Loss to followup: 18% (21/119)	NR	Good	The Netherlands Organi-sation for Health Research and Develop-ment

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Dembo, 2016[95]	In home U.S	18 months	A. Brief, 2-session youth only session, integrates MI, CBT rational-emotive therapy, and problem-solving therapy B. Brief, 2- session youth and separate 1-session parent session C. Standard truancy services plus a referral service overlay of 3 visits by a project staff member; no counseling was offered $15 was paid for completing the interviews	Ages 11 to 17, no official record of delinquency or up to 2 misdemeanor arrests, some indication of alcohol or other drug use, as determined, for example, by a screening instrument (Person Experience Screening Questionnaire), or as reported by a social worker, lived within a 25 mile radius of the Truancy Intake Center Eligible participants recruited from a Truancy Intake Center located at the Hillsborough Country Juvenile Assessment Center and referrals were accepted from social workers and guidance counselors within the Hillsborough County School District	*NR by group; reports no significant differences at baseline between groups* Mean age: 14.8 years (1.3 years SD) Female: 37% Race/ethnicity: 37.3% white, 28.7% Hispanic, 25.7% black, 7,0% other (mixed race), 1.0% Asian, 0.3% Native American Legal problem resulting in jail time or detention 26.4% Unemployment of parent: 50.3% Divorce of parents: 38.7% Death of a loved one: 57.7% Serious illness: 31.0% Victim of a violent crime: 17.3% Eviction from house or apartment: 17.0% Accidental injury requiring hospitalization: 12.0% Other stressful/traumatic event: 48.8%	N=300 Loss to followup on marijuana use: 28% (85/300)	NR	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Dupont, 2016[96]	4 sites Nether-lands	6 months	A. MOTI-4(n=71) B. Usual care, 1 hour session in which the effects of cannabis on the body were discussed, including a computerized animation, followed by a quiz and receipt of information leaflet (n=60)	Dutch youth aged 14 to 24 years who had used cannabis in the previous month and had to meet 1 or more of the below criteria: a clear relationship between cannabis use and problems at school, work or in relationships, as reported by teachers, parents, or others; experiencing physical or mental health problems as a possible result of cannabis use, as reported by parents, teachers, or others; high risk of developing problematic use (homelessness marginalization, truancy, having addicted parents, attending special education); age-inappropriate experimentation (weekly use under age 16) Youth referred by the parents, agencies for youth care and drop out, prevention field workers, and by student counselors	Mean age: 17.9 vs. 18.2 years Female: 12.7% vs. 20.0% Living with at least 1 parent: 74.6% vs. 61.7% Mean cannabis use in Euros, per week: 18.2 vs. 19.4 Cannabis use sessions per week: 3.87 vs. 4.02 Average number of cigarettes per day: 9.6 vs. 9.2 Alcohol, glasses per week: 8.9 vs. 14.6, p<0.05 Reported use of other drugs: 67.2% vs. 57.1%	N=131 Loss to followup: 17% vs. 27% (all included in analysis)	NR	Fair	Potentially Mondriaan Institute

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Fischer, 2012[98] Fischer, 2013[97]	Unclear Canada	12 months	A. Brief intervention: oral or written intervention consisting of short, fact-based and nonjudgmental information on cannabis-related health risks (n=72) B. Control: general health information delivered in a manner similar to the brief intervention (n=62)	Marijuana-using adults who represented who responded to advertisements and were screened for participation Excluded: <15 days of marijuana use out of the last 30 days, heavy alcohol or other drug use, involved in other substance abuse treatment	A vs. B Mean age 20 vs. 21 years 35% vs. 31% female 74% white; 10% Middle Eastern/Arabic; 8% Asian; 8% other race/ethnicity (NR by intervention group) Days of cannabis use in last 30 days: 24.0 (SD 5.81) vs. 23.9 (SD 6.06) Cannabis use episodes/day: 2.3 (SD 1.14) vs. 2.0 (SD 0.87)	N=134 Loss to followup: 46% (62/134)	NA	Fair	Canadian Institutes of Health Research
Gates, 2012[99] Project Cannabis Assistance Help Line	Unclear Australia	12 weeks	A. MI and CBT (n=68)B. Delayed treatment control (n=81)	Participants >16 years old who used cannabis within the past month	A vs. B Age: 36 vs. 36 years Gender: 38% vs. 38% female Race: NR Age at first cannabis use: 16 vs. 16 years SDS: 10.4 (SD 3.0) vs. 9.7 (SD 3.6) Cannabis Problems Questionnaire: 28-day cannabis use frequency (days): 22.6 (SD 6.7) vs. 22.3 (SD 5.9) Cannabis use quantity per day: 15.6 (SD 12.1) vs. 14.2 (SD 10.9)	N=149 Loss to followup: 27% (22/81) or 25% (20/81)* vs. 28% (19/68)* Inconsistentl y reported numbers	Mean sessions attended: 3.25 (SD 1.2)	Fair	NR

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Gelberg, 2015[48] Bau-meister, 2014[114] Project QUIT	5 centers U.S.	3 months	A. Brief intervention + telephone coaching sessions: clinicians followed a paper scripted protocol; covering drug addiction as a chronic brain disease, the need to quit or reduce using drugs to prevent this disease, the physical and mental consequences of drug use, and the potential accelerated progression towards severe substance use disorders caused by poly-substance use. (n=129) B. Attention control: video doctor and information booklet on cancer screening. At study exit, participants were given all intervention materials. (n=132)	Adults aged ≥18 years using all drugs recruited during a primary care visit using ASSIST screening tool. ASSIST score 4 to 26 (Moderate risk for drug use).	A vs. B Mean age: 42 vs. 41 years 34% vs. 40% female Race/ethnicity: 37% vs. 39% white; 25% vs. 23% black; 33% vs. 34% Hispanic; 5% vs. 6% other Education: 83% vs. 84% ≥12 years ASSIST score (for primary drug): 14.6 vs. 14.3 Duration of drug use, years (for primary drug): 22 vs. 20 years Prevalence of drug use (for primary drug): 53% vs. 50% cannabis; 24% vs. 16% cocaine/crack; 12% vs. 13% amphetamines; 6% vs. 11% sedatives; 5% vs. 9% opiates: 6.6%; 0% vs. 1% other Drug use days for the most frequently used drug, mean (SD): 10.6 (NR) vs. 10.7 (NR) QOL, mental health component (As measured by SF-12), mean (SD): 42.69 (12.57) vs. 42.94 (12.28) QOL, physical health component (As measured by SF-12), mean (SD): 42.97 (12.11) vs. 43.1 (12.01)	N=334 Loss to followup: 21.0%	All 171 intervention participants received clinician brief advice, and 134 (78%) had at least 1 telephone session (93 [54%] 2 sessions, 41 [24%] 1 session)	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Gelberg, 2017[49] Project QUIT (Pilot Repli-cation)	5 centers U.S.	3 months	A. Brief intervention + telephone coaching sessions. Replication of Gelberg, 2015[48] intervention with minor modifications. (n=23) B. Attention control. Participants received a video doctor and information booklet on cancer screening. (n=28)	Adults aged ≥18 years using all drugs recruited during a primary care visit using ASSIST screening tool. ASSIST score 4 to 26 (Moderate risk for drug use)	A vs. B Mean age: 30 vs. 32 years 41% vs. 42% female 97% vs. 91% Hispanic Education: 78% vs. 88% ≥12 years U.S. born: 87.5% ASSIST score (for primary drug): 14.4 vs. 14.5 Duration of drug use, years (for primary drug): 10.4 vs. 15.4 years Prevalence of drug use (for primary drug): 63% vs. 72% cannabis; 9% vs. 9% cocaine/crack; 6% vs. 9% amphetamine; 6% vs. 0% sedative; 16% vs. 9% opiates Drug use days (in past 30 days) for the most frequently used drug, mean (95% CI): 6.6 (NR) vs. 10.7 (NR) Any drug use based on urine samples: 21 (100) vs. 26 (100)	N=65 Loss to followup: 21.5%	All 32 intervention participants received clinician brief advice (as reported on the clinician Intervention Plan), and 22 (69%) had at least 1 telephone session and 15 (47%) had both sessions	Fair	NIDA and U.S. State Department's Bureau of International Narcotics and Law Enforcement

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Gryczyn-ski, 2016[50]	Single center U.S.	3 months	A. Brief intervention: Computerized brief intervention consisting of a short, single-session interactive program led by an animated talking avatar. Participants' choice was emphasized throughout, and participants were free to choose which substances to focus on (up to 2) and what kinds of behavioral changes they were willing to make. The computer brief intervention included questions about substance use problems, gender-specific normative feedback messaging, rating importance to change, and rating confidence (self-efficacy) to change. Participants received tailored messages and options based on their responses. (n=40) B. Wait list: Received the allocated intervention 3 months after study enrollment (n=5/40 lost to followup at that time)	Adults aged ≥18 years using all drugs recruited at a community health center using ASSIST screening tool. ASSIST score 4 to 26 (Moderate risk for drug use)	A vs. B Mean age 34.3 vs. 36 years 62.5% vs. 42.5% female 82.5% vs. 90.0% white 37.5% vs. 47.5% Hispanic ASSIST, total score, mean (SD): 26.4 (9.5) vs. 34.2 (13.8) p=0.04 Marijuana, mean (SD): 9.6 (5.5) vs. 11.2 (5.7) Cocaine, mean (SD): 0.4 (1.3) vs. 0.8 (2.3) Amphetamines, mean (SD): 1.2 (3.4) vs. 1.8 (3.8) Opioids, mean (SD): 1.8 (4.0) vs. 4.0 (7.5) Moderate risk (ASSIST score 4-26), % (n): Cannabis: 87.5 (35) vs. 92.5 (37) Cocaine: 2.5 (1) vs. 7.5 (3) Amphetamines: 12.5 (5) vs. 20.0 (8) Opioids: 20.0 (8) vs. 27.5 (11) Drug positive hair tests, % (n): Any drug: 47.6 (10) vs. 37.5 (6) Cannabis: 28.6 (6) vs. 31.3 (5) Cocaine: 4.8 (1) vs. 0 (0) Opiates: 4.8 (1) vs. 0 (0)	N=80 Loss to followup: 11.2%	NR	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Humeniuk, 2012[51]	Multi-center Australia, Brazil, India, U.S. (Country-specific data for only Australia and the U.S. reported where available. Full N randomized=731; Australia N=171; U.S. N=218)	3 months	A. Brief intervention with MI techniques: brief intervention linked to the results of the ASSIST+ a take-home guide. (n=103) B. Wait list: participants were invited to contact the clinical interviewer if they had concerns about their substance use and were administered the brief intervention following the intervention period. (n=115)	Adolescents and adults aged 16-62 years using all drugs recruited at a university-affiliated community clinic, walk-in health clinic, walk-in sexually transmitted disease clinic visit using ASSIST screening tool. ASSIST score 4 to 26 (Moderate risk for cannabis, cocaine, amphetamine-type stimulant, or opioid use)	*NR by intervention group* Mean age: 31.4 years 28% female Race/ethnicity: 60% white; 24% Indian; 2% Hispanic; 1% Asian/Pacific Islander; 0.4% Native American; 0.3% Aboriginal/Torres Strait Islander; 3% mixed race; 2% other Education: 9.5 years Prior drug/alcohol treatment: 15% Moderate risk (ASSIST score 4-26) for primary drug, for full sample (proportion of participants at moderate risk for each drug class NR by country): 54% cannabis; 13% cocaine; 21% amphetamines; 13% opioids A vs. B ASSIST, total score, mean (SD): 34.9 (22.3) vs. 39.0 (24.6) ASSIST, cannabis score, mean (SD): 16.8 (7.7) vs. 16.2 (6.7) ASSIST, stimulant score (Among those eligible for a cocaine or amphetamine-type stimulant brief intervention), mean (SD): 20.9 (7.9) vs. 18.5 (7.6)	N=389 Loss to followup: 14.9%	Assume 100% of participants received brief intervention	Fair	WHO, Geneva, Switzerland and the Australian Commonwealth Department of Health and Ageing, NIDA, WHO Department of Mental Health and Substance Abuse and the Drug and Alcohol Services South Australia
Jones, 2005[100]	2 centers U.S.	26 weeks	A. Contingency management, rewarding negative urine screens with access to the full range of counseling services; positive screens received individual 1 hour counseling sessions (n=66) B. Usual care, providing a list of referrals for aftercare options (n=64)	Age 18-60 years with DSM-IV opioid dependence who completed a residential tapering program	A vs. B Age: 38 vs. 38 years Gender: 61% vs. 63% female Race: 72% vs. 70% black Positive for cocaine at detox intake: 70% vs. 66%	N=130 Loss to followup: NR	NR	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Lee, 2010[53]	Single U.S.	6 months	A. Computer-based personalized feedback: In addition to brief written materials about risks associated with marijuana use and a list of community resources and adolescent treatment facilities, participants received a 20- to 30-minute structured intervention delivered by a peer educator. (n=171) B. Usual Care: Participants received brief written materials about risks associated with marijuana use and a list of community resources and adolescent treatment facilities. (n=170)	Incoming college students aged 17-19 years using cannabis recruited via direct mailing using a GAIN-1 screening criteria. Any cannabis use in the past 3 months.	Mean age 18 years (NR by intervention group) 57% vs. 52% female Race/ethnicity: white 68% white; 2% black; 6% Hispanic; Asian 16%, 0.9% American Indian/Native American; 0.7% other (NR by intervention group) Days used cannabis in past 90 days: 9.9 (15.8 SD) vs. 9.8 (16.2 SD) Cannabis related consequences in the last 3 months: 2.11 (SD 2.69) vs. 1.86 (SD 2.23)	N=341 Loss to followup: 5.6%	NR	Fair	NIDA
Lee, 2013[52]	Single U.S.	6 months	A. In-person personalized feedback: 1-hour intervention designed to provide the opportunity to discuss their cannabis use and review personalized graphic feedback. Facilitators used MI principles. (n=121) B. Control: assessment only (n=121)	College students aged 18-25 years using cannabis recruited via direct mailing using an unreported screening criteria. Cannabis used ≥5 days in the past month	*NR by intervention group* Mean age 20 years 45% female Race/ethnicity: white 75%; 6% Hispanic; 11% Asian; 15% other A vs. B Days used cannabis in past 30 days: 16.5 (SD 8.2) vs. 16.5 (SD 8.2) Number of joints smoked in typical week): 9.4 (SD 9.8) vs. 8.3 (SD 8.8) Cannabis-related problems: 10.45 (SD 4.9) vs. 10.38 (SD 5.90)	N=212 Loss to followup: 17.5%	54.7% participants attended the in-person intervention Overall, 90 (84.9%) of participants received either the in-person or mailed feedback.	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Litt, 2005[103] Marijuana Treatment Project	3 centers U.S.	64 weeks Only 16 weeks of relevant comparison data	A. MET + CBT (n=NR) B. MET (n=NR) C. Delayed treatment (n=NR)	Adults with DSM-IV diagnosis of cannabis dependence who had used at least 40 of the preceding 90 days	Age: 36 years Gender: 32% female Race: 69% white, 12% black, 17% Hispanic Frequency of cannabis use: 82 of previous 90 days Joints per day: 3.7 Duration of cannabis use: 17.9 years *Baseline demographics NR by group	N=450 4 months Loss to followup: 11% 9 months Loss to followup: 13% 15 months Loss to followup: 17%	NR	Fair	SAMHSA, Center for Substance Abuse Treatment
Litt, 2008[101] Kadden, 2007[121]	Single center U.S.	60 weeks	A. MET, cognitive behavioral skills training, and contingency management (n=63) B. MET and cognitive behavioral skills training (n=61) C. Contingency management (n=54) D. Case management control (n=62)	Adults who used cannabis heavily, met DSM-IV criteria for cannabis dependence, and were unable to stop using on their own	A vs. B vs. C vs. D Age: 32 vs. 34 vs. 33 vs. 32 years Gender: 36% vs. 28% vs. 20% vs. 31% female Race: 59% vs. 56% vs. 72% vs. 57% white Cannabis Problems Scale: 13.42 vs. 13.97 vs. 12.62 vs. 15.19 Joints per day: 4.76 vs. 4.67 vs. 3.24 vs. 5.20	N=240 Loss to followup: 19% (12/63) vs. 20% (12/61) vs. 11% (6/54) 16% (10/62)	Mean sessions attended: 5.2 (SD 3.5); no differences among treatments, p>0.36	Fair	NIDA, NIH
Litt, 2013[102]	Single center U.S.	9 weeks	A. MET, cognitive behavioral skills training, and contingency reinforcement for completing homework assignments (n=71) B. MET, cognitive behavioral skills training, and contingency reinforcement for providing cannabis-free urine samples (n=73) C. Case management without MET or substance abuse skills training (n=71)	Age at least 18 years and meeting DSM-IV criteria for cannabis dependence or abuse	A vs. B vs. C Age: 32 vs. 32 vs. 34 years Gender: 27% vs. 30% vs. 38% female Race: 73% white, 9% black, 14% Hispanic, 4% other vs. 69% white, 11% black, 19% Hispanic, 1% other vs. 63% white, 17% black, 16% Hispanic, 4% other Estimated joints per day: 2.0 vs. 1.8 vs. 1.6	N=215 Loss to followup: 14% (10/71) vs. 18% (13/73) vs. 14% (10/71)	A vs. B vs. C Mean sessions completed: 5.7 vs. 5.5 vs. 6.0; p=NS	Fair	NIDA/NIH

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Lozano, 2006[104]	Unclear U.S.	68 weeks Only 16 weeks of relevant comparison data	A. CBT relapse prevention (n=117) B. MET (n=88) C. Delayed treatment control (n=86)	Age 18 years or older, smoked cannabis at least 50 times in the preceding 90 days, and not dependent on alcohol or other drugs	Age: 34 years Gender: 23% female Race: 95% white Days smoking cannabis in preceding 90 days: 75 Met criteria for cannabis dependence: 94%	N=290 4 months Loss to followup: 14% 7 months Loss to followup: 19% 13 months Loss to followup: 13% 16 months Loss to followup: 11%	NR	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Marsden, 2006[105]	5 sites London	6 months	A. Brief adapted motivational intervention, manual guided, plus standard printed health risk information (n=166) B. Received printed health risk information (n=176) All received £15 plus travel expenses at recruitment and again at followup	Adolescent and young adult (ages 16-22), self-identified main substance to be ecstasy, cocaine powder or crack cocaine, regular use of 1 or more of these drugs in the previous month (on at least 4 occasions) and willingness to provide 2 person contacts for use in case of difficulty in arranging followup Excluded life-time treatment for nonmedical opioid drug use, current dependence and more than 1 injection of illicit drugs in the previous year Recruited via detached outreach contact, direction nomination by other participants, and by advertisements in the community (e.g., colleges) Period June 2002 to January 2003	A vs. B Mean age: 18.3 vs. 18.5 Female: 33.1% vs. 34.1% Race/ethnicity: 75.3% vs. 76.7% white, 12.7% vs. 10.2% black, 8.4% vs. 9.1% Asian 3.6% vs. 4.0% other Living with parents: 68.1% vs. 63.6% Ecstasy use in last 90 days (days): 18.8 (SD 17.8) vs. 17.3 (SD 16.2) Cocaine power use in last 90 days (days): 9.5 (SD 13.8) vs. 9.4 (SD 14.2) Crack cocaine use in last 90 days (days): 9.5 (SD 21.4) vs. 11.7 (SD 22.9) SDS score ≥4: 54.2% vs. 58.0% Cannabis use in last 90 days (days): 57.1 (SD 34.7) vs. 59.3 (SD 34.3)	N=342 Loss to followup: 13.3 vs. 11.9%	NR	Good	Department of Health for England and Wales, cost of toxicology testing were partly met by Altrix Healthcare Limited

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Martin, 2008[106]	NR Australia	3 months	A. "The Adolescent Cannabis Check-Up"; a brief, manualized, motivational and cognitive behavioral intervention, consisting of 2 sessions. Optional discussion of skills for quitting drug use (n=20) B. Delayed treatment control (n=20) All participants were given a $25 gift card at completion of the 3 month interview	Ages 14-19 years, non-treatment-seeking adolescents that have used cannabis at least once in the past month, and were reasonably fluent in English Excluded if showed evidence of significant cognitive impairment, had used more than 80 grams of alcohol per day (8 Australian standard drinks) on mean and/or other illicit drugs more than twice weekly in the past 90 days, or if they had received treatment for drug or alcohol issues in the past 90 days Recruited from the general community via advertisements, some aimed at parents to enroll their adolescents, and presentations to various potential referral sources such as youth services and juvenile justice offices	A vs. B Mean age: 16.6 vs. 16.2 Female: 45% vs. 20% Country of birth Australia, nonindigenous: 90% vs. 85% Living with parents: 80% vs. 75% Age of first cannabis use: 12.5 vs. 12.3 Days of cannabis use in past 90 days: 74.1 (SD 24.6) vs. 55.4 (SD 31.4), p=0.019 Cannabis dependence (DSM-IV) symptoms: 5.8 (SD 1.2) vs. 4.8 (SD 2.1) Cannabis dependence (DSM-IV): 100% vs. 85% SDS: 7.6 (SD 4.1) vs. 7.2 (SD 3.4)	N=40 Loss to followup: 20% vs. 20%	Completed intervention: 90% (18/20)	Fair	Australian National Heatlh and Medical Research Council

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Martino, 2018[54]	2 centers U.S.	6 months	A. In-person brief intervention based on MI. Following screening, 1 20 minute intervention based on MI to support the importance of, and a woman's confidence in, cutting down or quitting substances and obtaining treatment. (n=145) B. Computer-based brief intervention. Following screening, 1 20 minute computer-based, self-directed intervention based on MI to support the importance of, and a woman's confidence in, cutting down or quitting substances and obtaining treatment. The electronic sessions featured an interactive, 3-dimensional, mobile narrator that delivered the intervention. (n=143) C. Usual care. Received 2 minute interaction based on their ASSIST score and told about local treatments. (n=151)	Pregnant and nonpregnant women aged ≥18 years who scored positive on the ASSIST screening tool. ASSIST score 4 to 26 (Moderate risk for drug use) or ≥11 for nonpregnant women and ≥6 for pregnant women for alcohol	A vs. B vs. C Mean age 34 vs. 35 vs. 34 years 100% vs. 100% vs. 100% female 70% vs. 65% vs. 65% black; 13% vs. 11% vs. 15% white; 13% vs. 15% vs. 16% Hispanic; 4% vs. 8% vs. 4% other Primary substance used: 56% vs. 56% vs. 60% nicotine; 10% vs. 16% vs. 9% alcohol; 22% vs. 19% vs. 21% cannabis; 12% vs. 9% vs. 11% other Substance use disorders: 57% vs. 53% vs. 59% nicotine; 27% vs. 25% vs. 31% alcohol; 36% vs. 29% vs. 37% cannabis Education less than high school: 32% vs. 34% vs. 34% Mean ASSIST score (for primary drug): 22.2 (SD 8.1) vs. 22.8 (SD 8.5) vs. 22.5 (SD 7.9) Cannabis use disorder: 36% vs. 29% vs. 37% Other illicit drug use disorder: 18% vs. 18% vs. 24% Any substance use, days per month: 22.8 (95% CI 21.4 to 25.5) vs. 23.9 (95% CI 22.4 to 25.5) vs. 23.5 (95% CI 22.2 to 24.9)	N=439 Loss to followup: 12.1%	99% received the intervention	Good	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Mason, 2015[55] Mason, 2017[119]	2 centers U.S.	6 months	A. Peer Network Counseling: MI guided by 5 key MI clinical issues: rapport, acceptance, collaboration, reflections, and non-confrontation. (n=59) B. Attention control. (n=60)	Adolescents aged 14-18 years using alcohol and any drugs recruited during primary care visit using CRAFFT screening tool. CRAFFT score of 2 or 3 = at risk for substance use disorder	*NR by intervention group* Mean age 16 years 71% female black 84%; other 16% Cannabis use in past 30 days (scale 0-7; 0=0 days; 1=1-2 days; 2=NR; 3=3-5 days; 4=6-9 days; 5=10-19 days; 6=20-29 days; 7=30 days): 1.4 (SD 1.3) Intentions to use cannabis in next 90 days (Scale 0-4; 0=definitely no; 1=probably no; 2=unsure; 3=probably yes; and 4=definitely yes): 1.9 (SD 1.3)	N=119 Loss to followup: 1.7%	100% received intervention	Fair	NIDA
McCam-bridge, 2004[108] McCam-bridge, 2005[32]	10 further education colleges London	12 months	A. MI, single session adapted from work of Miller & Rollnick 1991 and Rollnick 1992 (n=105) B. Non-intervention education-as-usual control (n=95)	Students ages 16-20 years of age in Further Education colleges in London who had weekly cannabis use or stimulant drug use within the previous 3 months; excluded those with opiate and injecting drug use Recruited by peer interviewers who conducted baseline questionnaires	A vs. B Age 16 years: 22% vs. 17% Age 17 years: 32% vs. 33% Age 18 years: 27% vs. 24% Age 19 years: 12% vs. 20% Age 20 years: 7% vs. 6% Gender: 46% vs. 45% female Race: 32% white, 61% black, 8% Asian/other vs. 46% white, 37% black, 20% Asian/other; p=0.003 Current cannabis use, monthly or less: 13% vs. 22% Current cannabis use, weekly: 35% vs. 28% Current cannabis use, daily/near daily: 49% vs. 48% Irregular stimulant use: 19% vs. 18% Monthly or more stimulant use: 8% vs. 23%; p=0.03 Other illicit drug use: 16% vs. 21% Frequency of cannabis use (per week): 15.7 vs. 13.3	N=200 Loss to followup: 10.5% (21/200) Proportion with followup, 3 months: 92.4% (97/105) vs. 86.3% (82/95), p>0.01	The intervention was delivered successfully to all participants	Fair	Research Training Fellowship awarded by the National Health Services Executive (London/ South Thames)

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
McCambridge, 2008[107]	11 Further education colleges London	6 months	A. MI (n=164) B. Control, received drug information on harm reduction and advice (n=162)	Students ages 16-19 years of age in Further Education colleges in London who smoked cannabis weekly or more frequently Recruited by college staff or researches in informal areas such as coffee bars and game rooms	A vs. B Mean age: 18.0 vs. 17.9 years Female: 32% vs. 30% Race: 11% vs. 10% white, 53% vs. 51% black, 20% vs. 19% Asian, 16% vs. 20% mixed/other Cannabis, mean 30-day frequency: 17.3 (SD 9.8) vs. 18.3 (SD 10.4) Cannabis, mean joints past week: 10.3 vs. 11.1 SDS: 4.1 (SD 2.9) vs. 4.6 (SD 3.2) Cannabis, mean interactional problems score: 1.0 vs. 1.0 Cannabis, mean problems score (Cannabis Problems Questionnaire): 6.5 (SD 4.3) vs. 7.0 (SD 4.0) Ever used amphetamines: 4% vs. 2% Ever used ecstasy: 7% vs. 8% Ever used cocaine: 9% vs. 4% Ever offered heroin: 9% vs. 10% Ever offered crack: 11% vs. 15% Sold drug to friends: 20% vs. 25% Sold drugs to others: 15% vs. 17% Mean General Health Questionnaire-28 score: 11.2 vs. 11.1	N=326 Loss to followup: 20% vs. 18%	Received intervention: 90% vs. 91%	Fair	Wellcome Truist, Health Services Research Fellowship, Big Lottery Fund, Action on Addiction

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Onders-ma, 2007[56]	Single center U.S.	4 months	A. Computer-based brief intervention: three components based on MI and brief intervention principles: (1) feedback regarding the negative consequences of drug use that the participant reported, as well as self-reported readiness to change, and drug use as compared to that of all adult women; (2) pros and cons of drug use and related change, in which the participant chose from lists of positive and negative aspects of drug use from their perspective; and (3) a summary and query regarding the participant's interest in change, followed by optional goal-setting regarding drug use (n=55) B. None. Control group received no intervention (n=52)	Postpartum women in post-delivery recovery aged ≥18 years using all drugs recruited during inpatient hospitalization for childbirth using a single question screener. Any illicit drug use in the month before becoming pregnant	A vs. B Mean age: 26 vs. 24 years 100% vs. 100% female 100% vs. 94% black Education less than high school: 40% vs. 42% Daily or weekly cannabis use in 3 months prior to pregnancy: 66% vs. 60% Drug use other than cannabis in 3 months prior to pregnancy: 11% vs. 14%	N=107 Loss to followup: 29%	NR	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Onders-ma, 2014[58]	3 centers U.S.	6 months	A. Computer-based personalized feedback combining CBT and MET (eCHECKUP TO GO): 6 30-minute individual behavioral therapy sessions that involved a combination of MET and CBT (n=72) B. Attention control: 1 minute of brief advice based on a manualized version of standard interventions offered by obstetrical doctors and nurses (n=71)	Postpartum women in post-delivery recovery aged ≥18 years using all drugs recruited during inpatient hospitalization for childbirth using a single question screener. Any illicit drug use in the month before becoming pregnant	A vs. B Mean age: 26 vs. 27 years 100% vs. 100% female 88% vs. 93% black; 6% vs. 6% white; 6% vs. 1% other Education high school graduate or higher: 65% vs. 52% ASSIST marijuana score: 14.5 (SD 10.8) vs. 14.4 (SD 10.5) ASSIST cocaine score: 1.7 (SD 7.1) vs. 2.0 (SD 7.7) ASSIST opiates score: 2.2 (SD 6.9) vs. 1.8 (SD 6.6) ASSIST amphetamine score: 0.3 (SD 2.2) vs. 0.2 (SD 1.0) Prior drug use treatment: 15% vs. 19% Daily/near daily cannabis use: 87% vs. 86%	N=143 Loss to followup: 34.1%	4.3% did not receive the inter-vention, 23.9% received 1-2 sessions, and 60.9% received ≥3 sessions A vs. B Mean 7 vs. 5 treatment visits Average time in treatment 148.17 (SD 97.34) minutes vs. 7.12 (SD 3.57) minutes Average # of sessions and 3.89 vs. 5.88	Fair	NIH, Interva, Inc.

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Onders-ma, 2018[57]	Single center U.S.	6 months	A. Computer-based brief intervention focused on parenting patterned after MI principles and was tailored to each participant. Participants received a video-based orientation ("The Parent Check-up"), tailored to their ethnic identity and religiosity. The video touched on substance use but did not focus on it exclusively. Participants received feedback and offered the option of changing in 1 of the 4 areas or ending The Parent Check-up (n=252) B. Attention control: Participants watched educational videos about infant nutrition from birth to age 1 (i.e., breastfeeding, formula feeding, when to introduce solids) with no mention of safety, emotional health, or substance use (n=248)	Postpartum women in post-delivery recovery aged 18-45 years using all drugs recruited during inpatient hospitalization for childbirth using the WIDUS screening tool. WIDUS score ≥3	Mean age: 25 vs. 24 years 100% vs. 100% female 72% vs. 74% black; 3% vs. 2% white; 25% vs. 23% other; 4% vs. 4% Hispanic Pre-pregnancy prescription opioid misuse: 14% vs. 10%	N=500 Loss to followup: 34.7%	100% received intervention	Fair	NIH

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Palfai, 2014[59]	Single center U.S.	6 months	A. Computer-based personalized feedback (eCHECKUP TO GO) Following assessment, participants were provided with detailed personalized feedback about their cannabis use, including costs, norms, risks, consequences, and alternative activities (n=54) B. Attention Control: Participants were provided minimal general health feedback regarding recommended guidelines for sleep, exercise, and nutrition (n=49)	Undergraduate students using cannabis recruited during a primary care visit using the ASSIST screening tool. At least monthly cannabis use in the past 3 months (Persons with ASSIST score >27 at baseline (indicating a high likelihood of substance dependence) were excluded)	*NR by intervention group* Mean age 19 years 58% female 87% white; 3% black; 17% Hispanic 6%; Asian 5.7%; 2% American Indian/Native American ASSIST score: 11.9 (6.5) Readiness to change (Computed by subtracting the mean precontemplation score from the sum of the contemplation and action scores, range NR): 1.34 (2.3) A vs. B Cannabis use, days in past 90 days, mean (SD): 30.3 (28.4) vs. 39.6 (28.4) Cannabis related consequences (19 items from Marijuana Problem Scale with binary coding of 0 (not experienced) and 1 (experienced)), mean (SD): 3.74 (3.89) vs. 4.51 (3.72)	N=123 Loss to followup: 16.3%	NR	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Poblete, 2017[60]	32 sites Chile	3 months	A. Brief intervention based on FRAMES: ASSIST-linked brief intervention for the substance with the highest score, and the ASSIST self-help guide, with additional information regarding substances and high-risk situation management. When 2 substances had the same score, the participant had the choice to decide which substance to receive counseling for. The intervention was based on the FRAME model, which provides specific feedback, offers a menu of options, and enhances motivation to change (n=400) B. Usual care: Participants received a pamphlet of their own choosing containing broad information on substance use risk and harm (n=406)	Adults aged 19-55 years using alcohol, all drugs recruited at primary care, emergency department or police station visit using ASSIST, Chilean version. ASSIST score 11 to 20 for alcohol or ASSIST score 4 to 20 for drug use (moderate risk)	A vs. B Mean age: 29 vs. 30 years 71% vs. 70% females Race/ethnicity NR ASSIST (Chilean) total score (mean): 27.1 (SD 9.2) vs. 26.6 (SD 9.7) ASSIST, cannabis score: 9.6 (SD 4.6) vs. 10.0 (SD 4.3) ASSIST, cocaine score: 11.1 (SD 5.1) vs. 10.4 (SD 5.1) Participants with moderate risk drug use: cannabis: 47% vs. 51%; cocaine: 18% vs. 20%	N=806 Loss to followup: 38.3%	Assume 100% of participants received brief intervention	Fair	The Chilean National Service for the Prevention and Rehabilitation of Drugs and Alcohol

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Rooke, 2013[109]	NR Inter-national	12 weeks	A. Web-based CBT + MI, 6 modules (n=119) B. Educational control, 6 modules (n=111)	Adults who used cannabis at least once during the preceding month and expressed a desire to reduce or quit use	A vs. B Age: 32 vs. 30 years Gender: 40% vs. 37% female Race: NR SDS: 8.97 (SD 3.61) vs. 8.78 (SD 3.61) Frequency of cannabis use: 21.33 vs. 20.76 days/month	N=230 Loss to followup: 46% (55/119) vs. 43% (48/111)	"If participants completed 1 module per week as recom-mended, the 6-week followup approx-imates a short term post-treatment assessment Participants may not have completed all modules or completed them more quickly than in 6 weeks"	Fair	Department of Health and Aging

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Roy-Byrne, 2014[61] Krupitski, 2012[118]	7 centers U.S.	12 months	A. In-person personalized feedback using a MI approach + telephone booster session: brief (30 minute) intervention in which interventionists used a MI approach and tailored the intervention to allow for flexibility as to which or how many drugs to target, as well as in how to guide the participant (e.g., specialty treatment, abstinence, harm reduction). The same interventionist attempted a follow-up telephone booster session within 2 weeks of the intervention (n=435) B. Enhanced usual care: participants received an illustrated handout depicting their DAST-10 drug problem severity score and list of substance abuse resources. Resembled the "notification and referral" strategy that might be implemented in high-quality usual care (n=433)	Adults aged ≥18 years using all drugs recruited at primary care visit using unreported screener. Any illegal drug or nonprescribed medication use at least once in the past 3 months.	A vs. B Mean age: 48 vs. 48 years 32% vs. 29% female 44% vs. 45% white; 36% vs. 38% black; 19% vs. 16% other; 9% vs. 10% Hispanic Education less than high school: 21% vs. 17% Days used most frequently used drug past 30 days (mean): 14.4 (SD 11.3) vs. 13.3 (SD 10.7) Drugs used in the last 30 days: marijuana: 77% vs. 75%; stimulants: 42% vs. 41%; opiates: 24% vs. 28% DAST-10 drug use severity: low (score 1-2): 32% vs. 32%; intermediate (score 3-5): 39% vs. 37%; substantial/severe (score ≥6): 29% vs. 32% Drug use days (For the most frequently used drug), mean (SD): 14.4 (11.3) vs. 13.3 (10.7) Severity of disorder (ASI -Drug) (For the most frequently used drug), mean (SD): 0.11 (0.1) vs. 0.1 (0.1)	N=868 Loss to followup: 10.5%	97% received a brief intervention and 47% received a booster call Brief intervention averaged 27 minutes	Good	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Saitz, 2014[62] Fuster, 2016[116] Kim, 2016[117] ASPIRE	Single center U.S.	6 months	A. Brief interview using some MI. Participants received single 10- to 15-minute structured interview included feedback, review of the "pros and cons" of use, and a plan for change (n=169) B. MI + telephone booster. Participants received 30 to 45 minutes of MI with an offered 20- to 30-minute booster followup session. Interview elicited possible links between drug use and health concerns, heightening discrepancies between negative drug use outcomes and valued goals, enhancing self-efficacy about behavior change, and providing options for change (n=173) C. Minimal. Participants given contact information for Alcoholics Anonymous, Narcotics Anonymous, the hospital behavioral health clinic and emergency team, a state hotline, a city triage line, and websites for alcohol and drug screening (n=175)	Adults aged ≥18 years using all drugs recruited during primary care visit using ASSIST. ASSIST score ≥4 (drug use weekly or more in past 3 months or less frequent use but with consequences)	A vs. B vs. C Mean age: 40 vs. 43 vs. 41 years 29% vs. 29% vs. 33% female 68% vs. 72% vs. 66% black; 11% vs. 6% vs. 12% Hispanic; 19% vs. 21% vs. 21% white; 2% vs. 0% vs. 2% other High school graduate: 68% vs. 72% vs. 79% Medicaid/ Medicare: 79% vs. 86% vs. 78% No insurance: 7% vs. 3% vs. 7% Primary drug of use: opioids (including prescription): 18% vs. 16% vs. 18%; cocaine: 18% vs. 19% vs. 19%; marijuana: 63% vs. 63% vs. 63% Drug use days using the 30-day timeline followback, mean (SD): 15.1 (11.7) vs. 13.8 (11.2) vs. 14.3 (11.4) Drug use days >1 time using the 30-day timeline followback, mean (SD):10.5 (11.1) vs. 9.4 (11.1) vs. 9.6 (11.1) Any drug use (n (%)) Cocaine or opiates: 160 (97.0) vs. 157 (95.7) vs. 157 (95.7) Severity of disorder (ASSIST score) Scale range 0-273, where lower scores indicate better outcomes, mean (SD): 21.8 (18.4) vs. 22.0 (18.6) vs. 22.9 (19.50)	N=528 Loss to followup: 2.1%	A. All participants received intervention B. All participants received 30-45 minute MI session, and 31% received the optional 20-30 minute booster session	Good	NIDA, center for substance abuse treatment, SAMHSA, National Center for Research Resources

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Schaub, 2015[110] Can Reduce	NR Germany	12 weeks	A. Self-help with chat, based on MI and CBT (n=114) B. Self-help without chat, based on MI and CBT (n=101) C. Waitlist control (n=93)	Age 18 years or older, using cannabis at least once a week over the preceding 30 days	A vs. B vs. C Age 20 years or less: 21% vs. 12% vs. 19% Age 21-25 years: 27% vs. 19% vs. 14% Age 26-30 years: 14% vs. 29% vs. 20% Age 31-35 years: 15% vs. 18% vs. 16% Age 36-40 years: 12% vs. 10% vs. 12% Age 41-45 years: 5% vs. 5% vs. 8% Age 46 years or older: 5% vs. 8% vs. 11% Gender: 31% vs. 24% vs. 18% female Race: NR Cannabis use (days per week): 6.1 (SD 1.6) vs. 6.1 (SD 1.7) vs. 6.7 (SD 0.9) Cannabis use (standardized cannabis joints): 23.0 (SD 15.1) vs. 25.1 (SD 25.2) vs. 23.6 (SD 13.2) SDS: 7.7 (SD 3.5) vs. 7.5 (SD 3.6) vs. 7.3 (SD 3.1)	N=308 Loss to followup: 67% (76/114) vs. 59% (60/101) vs. 59% (55/93)	A. Received self-help and chat: 24% (27/114) Received self-help but not chat: 76% (87/114) Mean modules completed: 3.2 B. Received self-help: 100% (101/101)	Fair	Infodrog
Stein, 2009[111]	NR U.S.	26 weeks	A. MI, 4 sessions (n=97) B. Written handout of treatment resources (n=101)	Age 18 years or older, who used cocaine at least weekly during the previous 6 months	A vs. B Age: 38 vs. 38 years Gender: 39% vs. 38% female Race: 39% vs. 41% white Duration of cocaine use: 16.0 vs. 16.7 years Current injector: 22% vs. 25% Days of cocaine use in last month: 15.9 (SD 9.4) vs. 16.7 (SD 8.5)	N=198 Loss to followup: 17% vs. 21%	Mean MI sessions: 2.9 Attended all MI sessions: 54% Attended no MI sessions: 10%	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Stein, 2011[63]	Single center U.S.	6 months	A. MI: Participants received 2 45-minute MI sessions spaced 1 month apart (n=163) B. Control: assessment only (n=169)	Women aged 18-24 years using cannabis recruited using generic advertising for a health study. Screening tool or survey NR. Cannabis use ≥3 times in past 3 months.	A vs. B Mean age 21 vs. 21 years 100% vs. 100% female 72% vs. 63% white; 10% vs. 11% black; 10% vs. 13% Hispanic; 7% vs. 12% other Years of regular cannabis use: 3.8 (SD 2.7) vs. 4.1 (SD 2.5) Cannabis dependence: 39.5% Desire to quit using cannabis: 57% vs. 64% Proportion of days used cannabis, in past 90 days: 0.59 (SD 0.34) vs. 0.55 (SD 0.34) Any cannabis use: 100% vs. 100% Cannabis related consequences: 4.82 (SD 4.66) vs. 4.99 (SD 4.71)	N=332 Loss to followup: 21.1%	80.3% received both MI sessions, 9.8% received 1 MI session, and 9.8% received none of the MI sessions	Fair	NIDA
Stephens, 2000[33]	Single center U.S.	4 months	A. Relapse Prevention Support Group: combination CBT and social support (n=117) B. Individualized Assessment and Advice: sessions with therapist feedback, MI and advice on CBT techniques (n=88) C. Delayed treatment control (n=86)	Adult marijuana users who wanted help quitting Excluded: use <50 times in the past 90 days; severe psychological distress or suicidal ideation; currently in formal treatment for marijuana use	*NR by intervention group* Mean age 34 years 23% female 95% white; other race/ethnicity NR Age of first marijuana use: 15.9 (SD 3.9) Years of marijuana use: 17.4 (SD 5.21) Marijuana Dependence Scale (0-9): 6.84 (SD 2.13) vs. 6.65 (SD 1.95) vs. 6.71 (SD 1.77) Proportion meeting 1 or more DSM-III dependence criteria: 93% (range 58-93%) Cannabis use in last month (days): 25.38 (SD 6.15) vs. 24.24 (SD 6.29) vs. 24.85 (SD 6.13)	N=291 Loss to followup: 14% (42/291)	A vs. B vs. C A. Proportion attending ≥10 sessions: 50% B. Proportion attending both sessions: 86% (76/88) C. NR	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Stephens, 2007[112]	Single center U.S.	12 months	A. Personal feedback: therapist reviewed a personal feedback report with the participant (n=62) B. Attention control (multi-media feedback): a balanced presentation of the multiple points of view on the consequences associated with marijuana use; participants were invited to ask questions at any time but no feedback regarding the participant's use of marijuana was provided and therapists avoided using MI techniques (n=62) C. Delayed feedback: educational control condition that provided information about the latest research on marijuana delivered in an objective, stimulating, but largely didactic manner. (n=64)	Marijuana-using adults who represented who responded to advertisements and were screened for participation Excluded: <15 days of marijuana use out of the last 30 days, heavy alcohol or other drug use, involved in other substance abuse, treatment or a self-help group, had severe psychiatric difficulties, legal status that might have interfered with participation, planned to move out of the area within the next 12 months, did not live within 60 miles of the study site, living with someone already enrolled in the study, not fluent in English	A vs. B Mean age 31.48 (SD 9.22) vs. 32.48 (SD 11.11) 77.4% vs. 69.4% male 87.1% vs. 87.1% white race Age of first marijuana use: 14.71 (SD 3.81) vs. 14.74 (SD 3.55) Days of marijuana use in the last 90 days: 74.84 (SD 16.71) vs. 74.84 (SD 16.44) Dependence symptoms (DSM-IV, 0-7): 3.92 (SD 1.78) vs. 3.26 (SD 1.93) Marijuana Problem Scale (0-19): 6.37 (SD 3.71) vs. 5.31 (SD 3.53) Proportion meeting DSM-IV criteria for cannabis dependence (total population): 64% Proportion meeting DSM-IV criteria for cannabis abuse (total population): 29%	N=188 Loss to followup: 19% (groups A and B only)	88.7% and 93.5 received allocated intervention (groups A and B)	Good	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Tait, 2015[113]	Community recruitment (social media and clinic posters) Australia	24 weeks	A. MET + CBT (n=81) B. Waitlist (n=79)	Age 18 years or older, resident of Australia, with reported use of amphetamine-type stimulants in the preceding 3 months	A vs. B Age: 22 vs. 23 years Gender: 21% vs. 28% female Race: NR Age at first amphetamine-type stimulant use: 18 vs. 19 years Daily stimulant use: 9% vs. 14% Weekly stimulant use: 26% vs. 29% Monthly stimulant use: 41% vs. 23% 1-2 times stimulant use in previous 90 days: 25% vs. 34% SDS: 3.7 (SD 3.5) vs. 3.8 (SD 3.3) Amphetamine-type Stimulants Score: 17.0 (SD 10.1) vs. 16.8 (SD 11.1)	N=160 3 months Loss to followup: 57% (46/81) vs. 43% (34/79) 6 months Loss to followup: 53% (43/81) vs. 48% (38/79)	Did not complete any modules: 37% (30/81) Completed only 1 module: 7% (6/81) Completed only 2 modules: 7% 6/81) Completed all 3 modules: 48% (39/81)	Fair	Commonwealth of Australia Department of Health and Ageing, Australian National Health and Medical Research Council

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Tzilos Wernette, 2018[64]	Single center U.S.	4 months	A. Health Checkup for Expectant Moms: computerized program in a MI-consistent style (Intervention addressed both sexually transmitted infection/HIV and alcohol/drug risk). Participants interacted with a computer and were guided by an animated narrator, which engages in a MI-consistent style, can use emotionally expressive statements and empathic reflection. Participants also received brochures specifically designed to facilitate health risk behaviors during pregnancy (n=31) B. Attention control: participants interacted with the computer and were guided by the same narrator used for intervention group participants. Participants also received brochures specifically designed to facilitate health risk behaviors during pregnancy (n=19)	Pregnant women (<5 months gestation) using alcohol, cannabis recruited during obstetrics visit using T-ACE or SURP-P screening tools. Current alcohol or drug use or at -risk for prenatal alcohol/drug use (positive score on T-ACE or SURP-P)	A vs. B Mean age: 25 vs. 23 years 100% vs. 100% female Race/ethnicity: 23% vs. 42% white; 35% vs. 10% black; 12% vs. 15% multiracial; 6% vs. 0% Native American/Alaskan; 23% vs. 32% other/unknown High school grad: 25% vs. 32% Any alcohol or cannabis use by hair sample: 77% vs. 58%	N=50 Loss to followup: 2.0%	100% completed health check-up for expectant moms program; 97% completed booster session	Fair	Eunice Kennedy Schive National Institute of Health and Human Developme nt

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Walton, 2013[65] Project Chill	7 centers U.S.	12 months	A. In-person personalized feedback using MI (The intervention, delivered by a therapist and facilitated by a computer, incorporated MI, including tailored, parallel content. The therapist used an elicit-provide-elicit framework when reviewing tailored feedback, using summaries and open-ended questions to evoke change talk (n=118) B. Computer-based personalized feedback (n=100) C. Usual care (n=110)	Adolescents aged 12-18 years using cannabis recruited during primary care visit using Add Health screening tool. Any cannabis use in the past year = included	A vs. B vs. C Mean age 16 vs. 16 vs. 16 years 64% vs. 67% vs. 69% female 65% vs. 61% vs. 56% black; 7% vs. 16% vs. 11% Hispanic Cannabis use in past 90 days: 3.2 (1.9) Cannabis use, frequency, mean (SD): 3.14 (1.86) vs. 3.06 (1.90) vs. 3.25 (1.87) Other drug use, frequency, mean (SD): 0.47 (1.29) vs. 0.86 (3.01) vs. 1.16 (2.71) Note: Use and frequency defined as 0=never, 1=1–2 days, 2=once a month or less, 3=2–3 days per month, 4=1–2 days per week, 5=3–5 days per week, and 6=every day or almost every day Cannabis DUI (Categorical responses (assumed) 0=never, 1=1–2, 2=3–5, 3=6–9, 5=10 or more), mean (SD): 0.40 (0.93) vs. 0.48 (1.06) vs. 0.26 (0.66) Cannabis-related consequences scale range 0-28 (Included 23 items from the adapted version of the Rutgers Alcohol Problems Index (Marijuana Problem Inventory) and 5 items from the SDS where endorsement of an item =1 and no endorsement =0. Low value indicates better outcome.), mean (SD): 14.2 (15.3) vs. 14.3 (15.5) vs. 14.0 (15.0)	N=328 Loss to followup: 16.2%	NR	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Watkins, 2017[66] SUMMIT	2 centers U.S.	6 months	A. Collaborative care: the intervention included a population-based management approach, measurement-based care, and integration of addiction expertise through a RAND-based clinical psychologist affiliated with the MI Network of Trainers (n=138) B. Usual care: participants were told by the research team that the clinic provided opioid and/or alcohol use disorder treatment and given a number for appointment scheduling and list of community referrals. They did not receive any additional outreach or contact (n=123)	Adults aged ≥18 years using alcohol, opioids recruited during primary care visit with NIDA Quick Screen. Probable opioid or alcohol use disorder	Mean age: 42 vs. 43 years 21% vs. 20% female 42% vs. 45% white; 13% vs. 14% black; 1% vs. 2% American Indian/Alaska Native; 1% vs. 0% Native Hawaiian/Pacific Islander; 0.5% vs. 1% Asian; 28% vs. 26% other; 11% vs. 17% multiple; 32% vs. 30% Hispanic Less than high school education: 28% vs. 28% Alcohol abuse or dependence only: 56% vs. 52% Heroin abuse or dependence with or without co-occurring alcohol or prescription opioid abuse or dependence: 27% vs. 34% Prescription opioid abuse or dependence with or without co-occurring alcohol abuse or dependence: 17% vs. 14%	N=397 Loss to followup: 30.8%	98% were entered into the registry, 93% met with the care coordinator, 76% scheduled an appointment with a therapist, 45% kept the appointment, and 20% had at least 1 additional psychotherapy session	Fair	NIDA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Woolard, 2013[67] Project Reduce	Single center U.S.	12 months	A. MI: 2 brief interventions guided by the principles of MI. The goal of the first brief intervention was to engage the participant in reflection upon the pros and cons of alcohol and marijuana use. The focus of the second brief intervention session was to review and reinforce the change and create a change plan with those who had not made a change plan in the first session (n=206) B. Usual care: participants received routine emergency care for their presenting medical complaint and were offered information on local treatment resources for substance misuse (n= 220)	Adults aged ≥18 years using alcohol, cannabis recruited during emergency department visit using 10-item wellness questionnaire. Any past month alcohol use and past year marijuana use	A vs. B Mean age: 28 vs. 28 years 17% vs. 16% female 68% white; 17% Hispanic/Latino (NR by intervention group) Education years: 12.5 vs. 12.3 years AUDIT score mean: 10.7 (SD 1.5) vs. 11.2 (SD 1.3) Alcohol and cannabis use days in past 30 days, mean (95% CI): 6.5 (5.7 to 7.3) vs. 6.2 (5.4 to 7.0) Cannabis use days in past 30 days, mean (95% CI): 12.8 (11.4 to 14.3) vs. 12.4 (11.0 to 13.8) Heavy cannabis use in past 30 days (with or without co-occurring alcohol or prescription opioid/heroin abuse or dependence), mean (95% CI): 5.3 (4.5 to 6.2) vs. 4.9 (4.2 to 5.6) Negative consequences, total (Noteworthy Index of Problems): 3.1 (SD 2.2) vs. 3.3 (SD 2.0) Negative consequences, marijuana: 1.6 (SD 1.7) vs. 1.7 (SD 1.6)	N=515 Loss to followup: 17.3%	51% returned to second intervention session	Fair	NIAAA

Appendix B9. Psychosocial Trials—Study Characteristics

Author, year Study	Number of centers Country	Duration of followup	Intervention described and comparisons (A vs. B) Ns	Inclusion criteria	Patient characteristics	N Loss to followup	Adherence	Quality rating	Funding source
Yonkers, 2012[68]	2 centers U.S.	3 months	A. MET-CBT: motivational enhancement, functional analysis, safe sexual behavior, communication skills, relapse prevention and problem solving skills. Research nurse therapists had the flexibility to offeradditional sessions or repeat topics if there was time and need (n=92) B. Brief advice: a manualized version of standard interventions offered by obstetrical doctors and nurses (n=91)	Pregnant women (<28 weeks gestation), aged ≥16 years using alcohol, all drugs recruited during obstetrics visit using TWEAK. Any use of alcohol or illicit drug use (excluding opiates) in last 30 days or TWEAK score ≥3	A vs. B Mean age NR; <20: 20% vs. 15%; 20-34: 61% vs. 65%; 35+: 5% vs. 8% 100% vs. 100% vs. 100% female Race/ethnicity: 23% vs. 20% white; 51% vs. 55% black; 23% vs. 20% Hispanic Education <12 years: 38% vs. 30% Past month use: 23% vs. 39% alcohol; 4% vs. 1% heroin; 10% vs. 6% methadone; 5% vs. 7% opiates; 9% vs. 13% cocaine; 0% vs. 1% amphetamines; 41% vs. 47% marijuana Primary drug used: 32% vs. 29% alcohol; 17% vs. 17% cocaine; 45% vs. 47% marijuana; 6% vs. 7% other	N=183 Loss to followup: 8.2%	NR	Fair	NIDA
Zahradnik, 2009[69] Otto, 2009[120]	2 centers Germany	12 months	A. MI: Participants received 2 MI sessions. The first 30-45 minute session took place in the hospital; the second session, 4 weeks later, was conducted by phone. The intervention was based on the Transtheoretical Model of behavior change. Participants received an individualized feedback letter 8 weeks after the first intervention. (n=56) B. Usual care: informational booklet about prescription drugs (n=70)	Adults aged 18-69 years using prescription drugs recruited during admission to internal, surgical, or gynecological ward of hospital using questionnaire for prescription drug misuse, SDS screener. Prescription drug use (Includes opioids, anxiolytics, hypnotics, sedative, and caffeine with addiction potential) >60 days in past 3 months or prescription drug abuse or dependence	A vs. B Mean age 53 vs. 56 years 65% vs. 60% female Race/ethnicity NR Education less than 10 years: 44% vs. 49% Prescription drug misuse, M-CIDI: 23% vs. 20%; SCID-I: 11% vs. 23% Prescription drug dependence, M-CIDI: 23% vs. 20%; SCID-I: 54% vs. 36% Alcohol use disorder: 9% vs. 10%	N=126 Loss to followup: 11.1%	NR	Fair	German Federal Ministry of Health

Abbreviations: ASI = Addiction Severity Index; ASPIRE = The Assessing Screening Plus Brief Intervention's Resulting Efficacy to Stop Drug Use study; ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; AUDIT = Alcohol Use Disorders Identification Test; CBT = cognitive behavioral therapy; CI = confidence interval; CRAFFT = CRAFFT youth substance screening questionnaire; CUPIT = Cannabis Use Problems Identification Test; DAST-10 = Drug Abuse Screening Test; DSM = Diagnostic and Statistical Manual of

Mental Disorders; DUI = driving under the influence; FRAME = Feedback, Responsibility, Advice, Menu Options, Empathy, and Self-Efficacy; GAIN-1 = Global Appraisal of Individual Needs; M-CIDI = Munchener Composite International Diagnostic Interview; MET = motivational enhancement therapy; MI = motivational interviewing; MOTI-4 = brief motivational enhancement intervention designed for young vulnerable non-treatment-seeking cannabis users; NA = not applicable; NIAAA = National Institute on Alcohol Abuse and Alcoholism; NIDA = National Institute on Drug Abuse; NIH = National Institutes of Health; NR = not reported; OTI = Opioid Treatment Index; QOL = quality of life; QUIT = Quit Using Drugs Intervention Trial; RAND = RAND (Research and Development) Corporation; SAMHSA = Substance Abuse and Mental Health Services Administration; SCID-I = Structured Clinical Interview for DSM-IV Axis Disorders; SD = standard deviation; SDS = Severity of Dependence Scale; SF-12 = 12-Item Short Form Health Survey; SMART-ED = Screening, Motivational Assessment, Referral and Treatment in EDs; SUMMIT = Substance Use Motivation and Medication Integrated Treatment study; SURP-P = Substance Use Risk Profile-Pregnancy scale; T-ACE = screening tool for at-risk drinking developed for use in obstetrics/gynecological settings; TWEAK = five item alcohol screening tool; U.S. = United States; WHO = World Health Organization; WIDUS = The Wayne Indirect Drug Use Screener, YSR = Youth Self Report.

Appendix B10. Psychosocial Trials—Intervention Characteristics

Author, year Study	Intervention described and comparisons (A vs. B) Ns	Recruitment method	Treatment setting	Practitioner Mentions special training required?	Mode of delivery	Intensity of intervention (when and how much)	Mentions intervention materials?	Method(s) of outcome assessment
Babor, 2004[30]	A. Multicomponent therapy: MET + CBT + case management (n=156) B. MET (n=146) C. Control: delayed treatment (n=148)	84% referred via advertising that offered free treatment; 8% referred by a family member, friend, or relative; 5% referred from a general advertisement for the agency or clinic; and the remainder were from social service agencies, medical doctors, private practitioners (nonmedical), or self-referrals.	Research center and specialty outpatient clinics	Therapist Yes	Face to face	A. 9 sessions (session duration NR) delivered over 12 weeks B. 2 1-hour sessions delivered 1 month apart C. NA	NR	Self-report based on timeline followback and standardized questionnaires Interviews with spouse, partner, friends or other relatives Urine testing
Baker, 2001a[88] Baker, 2001b[89]	A. 4-session CBT: MI (Session 1) + cognitive behavioral coping strategies + relapse prevention (Sessions 2-4) + self-help booklet (n=16) B. 2-session CBT: same as Session 1 and 2 + self-help booklet (n=16) C. Control: self-help booklet only (n=32)	Notices placed within various agencies, cafes and treatment centres and an inner-city needle-exchange scheme; word of mouth.	Unclear	Student therapist Yes	Face to face	A. 4 30-60 minute sessions B. 2 30-60 minute sessions C. NA	NR	Self-report based on standardized questionnaires

Appendix B10. Psychosocial Trials—Intervention Characteristics

Author, year Study	Intervention described and comparisons (A vs. B) Ns	Recruitment method	Treatment setting	Practitioner Mentions special training required?	Mode of delivery	Intensity of intervention (when and how much)	Mentions intervention materials?	Method(s) of outcome assessment
Baker, 2005[90]	A. 4-session CBT: MI (Session 1) + cognitive behavioral coping strategies + relapse prevention (Sessions 2-4; n=66) B. 2-session CBT: same as Session 1 and 2 (n=74) C. Control (n=74)	Notices placed withinvarious agencies and treatment centres, media releases and via word of mouth. 54% referred by alcohol and other drug service; 14% word of mouth; 13% media advertisements; 10% general practitioners; 5% a youth service; 5% other community agencies	Unclear	Therapist (psychologist or social worker) Yes	Face to face; some assessments conducted over the telephone (9.7% post-treatment; 28.8% at 6 months)	A. 4 45-60 minute sessions B. 2 45-60 minute sessionsC. NA	Yes; published in Baker, A., Kay-Lambkin, F., Lee, N., Claire, M. & Jenner, L. (2003) A Brief Cognitive-Behavioural Intervention for Regular Amphetamine Users. Canberra: Australian Government Department of Health and Ageing	Self-report based on standardized questionnaires Urine testing (20% subset)
Bernstein, 2005[4]	A. MI + telephone booster session: Participants received a semi scripted, brief (10-45 minute) motivational interview delivered by a peer, a substance abuse outreach worker in recovery. (n=490) B. Minimal: Participants received only a handout stating that “based on your screening responses, you would benefit from help with your drug use” (n=472)	Screen-detected (DAST-10)	Primary care	Experienced substance abuse outreach workers who were themselves in recovery Yes	Face to face followed by phone	1 10-45 minute MI session followed by 1 5-10 minute phone call	NR	Self-report based on standardized questionnaires

Appendix B10. Psychosocial Trials—Intervention Characteristics

Author, year Study	Intervention described and comparisons (A vs. B) Ns	Recruitment method	Treatment setting	Practitioner Mentions special training required?	Mode of delivery	Intensity of intervention (when and how much)	Mentions intervention materials?	Method(s) of outcome assessment
Bernstein, 2009[45]	A. Brief intervention, based on a MI approach (n=47) B. Usual care (not described) (n=55)	Screen-detected (Youth and Young Adult Health and Safety Needs Survey)	Emergency department	Peer educator Yes	Face to face	1 20 to 30 minutes brief individual counseling session and 1 5 to 10 minute booster phone call	NR	Self-report based on timeline followback and standardized questionnaires
Blow, 2017[46] Bonar, 2018[91] HealthiER You	A. Computerized brief motivational interview, targeting drug and alcohol use (n=257); A1 with (n=130) or A2 without (n=127) additional MET B. Therapist brief motivational interview, targeting drug and alcohol use (n=257); B1 with (n=127) or B2 without (n=130) additional MET C. Educational control: 3 minute review of community resources and HIV prevention (n=266); C1 with (n=136) or C2 without (n=130) additional MET	Screen-detected (ASSIST)	Trauma center	Masters level therapist in one arm No	A. Computer B. Face to face	Single 30 minute session	No	Self-report based on standardized questionnaires Urine testing

Appendix B10. Psychosocial Trials—Intervention Characteristics

Author, year Study	Intervention described and comparisons (A vs. B) Ns	Recruitment method	Treatment setting	Practitioner Mentions special training required?	Mode of delivery	Intensity of intervention (when and how much)	Mentions intervention materials?	Method(s) of outcome assessment
Bogenschutz, 2014[47] Bogenschutz, 2011[115] SMART-ED	A. Brief intervention based on MI principles + telephone booster sessions. In addition to an informational pamphlet about drug use and misuse (n=427) B. Minimal: informational pamphlet about drug use and misuse, its potential consequences, and treatment options and optional referral to addiction treatment, consisting of a recommendation to seek treatment and a standardized list of available options (n=427)	Screen-detected (screening tool NR)	Emergency department	Research staff that were not required to have prior clinical training Yes	Face to face followed by phone	1 brief intervention and 2 telephone booster calls	NR	Self-report based on timeline followback and standardized questionnaires
Copeland, 2001a[31] Copeland, 2001b[92]	A. 6CBT: intervention package incorporating motivational interview + standard relapse prevention (n=78) B. 1CBT: single session of 6CBT + self-help booklet (n=82) C. Delayed treatment control (n=69)	Advertisements in local newspapers and radio interviews that promoted a treatment research program for persons seeking assistance in abstainingfrom cannabis use.	Research center	Psychologist familiar with CBT and alcohol and other drug interventions No	Face to face	A. 6 60-minute sessions B. 1 90-minute session C. NA	No	Self-report based on standardized questionnaires

Appendix B10. Psychosocial Trials—Intervention Characteristics

Author, year Study	Intervention described and comparisons (A vs. B) Ns	Recruitment method	Treatment setting	Practitioner Mentions special training required?	Mode of delivery	Intensity of intervention (when and how much)	Mentions intervention materials?	Method(s) of outcome assessment
D'Amico, 2018[44]	A. CHAT, brief, 15-20 minute motivational interview delivered in primary care (n=153) B. Usual care, including a brochure with information on the effects of alcohol and drug use, how to prepare for risky situations, and online and telephone resources (n=141)	Adolescents who came in for an appointment were invited to participate	Primary care, family-based community health clinic	Facilitator (38% had masters and the rest had bachelor's degrees) Yes	Face to face	A. 15-20 minutes, 1 session B. Usual care (received brochure)	CHAT intervention based on decision making theory, social learning theory	Self-report web surveys
de Dios, 2012[93]	A. Motivational interview + mindfulness meditation (n=22) B. Control: assessment only (n=12)	Advertisements in local newspapers and radio	Unclear	Master's level interventionist Yes	Face to face	A. 2 sessions; duration NR B. NA	Project MAPLE	Self-report based on standardized questionnaires; 14% of participants also used timeline followback diaries
de Gee, 2014[94]	A. Brief intervention: motivational interview-based aimed at changing adolescents' cannabis use by increasing their awareness of the possible negative consequences of cannabis use and by helping them to make informed choices about their own use (n=58) B. Control: information session (n=61)	Direct recruitment by Drug Information Line staff in educational settings, youth care, coffee shops, and peer education projects	Specialty outpatient clinic 8 centers The Netherlands	Prevention worker previously trained in MI Yes	A. Face to face B. Face to face and computer	A. 2 sessions; 90 minutes each B. Single session; mean 56 minutes	NR; intervention based on Australian Adolescent Cannabis Check-Up	Self-report based on standardized questionnaires

Appendix B10. Psychosocial Trials—Intervention Characteristics

Author, year Study	Intervention described and comparisons (A vs. B) Ns	Recruitment method	Treatment setting	Practitioner Mentions special training required?	Mode of delivery	Intensity of intervention (when and how much)	Mentions intervention materials?	Method(s) of outcome assessment
Dembo, 2016[95]	A. Brief, 2-session youth only session, integrates MI, CBT rational-emotive therapy, and problem-solving therapy B. Brief, 2- session youth and separate 1-session parent session C. Standard truancy services plus a referral service overlay of 3 visits by a project staff member; no counseling was offered $15 was paid for completing the interviews	Recruited from juvenile truancy intake and community diversion program; referrals accepted from any school district social worker orguidance counselor	In-home U.S.	Counselor Yes	Face to face	A and B. 2-3 sessions lasting 1.5 hours each, occurring a week apart C. Standard services plus 3 hour-long visits a week apart offering referral services	Winters KC, Fahnhorst T, Botzet A, et al. Brief intervention for drug-abusing adolescents in a school setting: outcomes and mediating factors. J Subst Abuse Treat. 2012;42(3):279-88. doi: 10.1016/j.jsat.2011.08.005. PMID: 22000326 and Winters KC, Leitten W. Brief intervention for drug-abusing adolescents in a school setting. Psychol Addict Behav. 2007;21(2):249-54.	Self-report based on standardized questionnaires Urine testing

Appendix B10. Psychosocial Trials—Intervention Characteristics

Author, year Study	Intervention described and comparisons (A vs. B) Ns	Recruitment method	Treatment setting	Practitioner Mentions special training required?	Mode of delivery	Intensity of intervention (when and how much)	Mentions intervention materials?	Method(s) of outcome assessment
Dupont, 2016[96]	A. MOTI-4 (n=71) B. Usual care, 1 hour session in which the effects of cannabis on the body were discussed, including a computerized animation, followed by a quiz and receipt of information leaflet (n=60)	Referred by parents, agencies for youth care and drop-out, prevention fieldworkers and student counselors in the school system	4 sites Netherlands	Previous training in MI and a higher vocational education degree Yes	Face to face	A. 4 sessions B. 1 1-hour session	Dupont HB, Lemmens P, Adriana G, et al. Developing the Moti-4 intervention, assessing its feasibility and pilot testing its effectiveness. BMC Public Health. 2015;15:500. doi: 10.1186/s12889-015-1826-y. PMID: 25990860	Self-report based on standardized questionnaires
Fischer, 2012[98] Fischer, 2013[97]	A. Brief intervention: oral or written intervention consisting of short, fact-based and nonjudgmental information on cannabis-related health risks (n=72) B. Control: general health information delivered in a manner similar to the brief intervention (n=62)	University campus posters	Setting unclear Canada	Therapists with training in substance use and health behavior counseling No	Face to face	Oral sessions: single 20-30 minute session Written information: NA	NR	Self-report based on standardized questionnaires
Gates, 2012[99] CAHL	A. MI and CBT (n=68) B. Delayed treatment control (n=81)	Telephone callers to Cannabis Information and Helpline	Community Australia	Counselor Yes	Telephone	4 weekly 60-minute counseling sessions	Manuals used to guide therapy	Self-report based on timeline followback and standardized questionnaires

Appendix B10. Psychosocial Trials—Intervention Characteristics

Author, year Study	Intervention described and comparisons (A vs. B) Ns	Recruitment method	Treatment setting	Practitioner Mentions special training required?	Mode of delivery	Intensity of intervention (when and how much)	Mentions intervention materials?	Method(s) of outcome assessment
Gelberg, 2015[48] Baumeister, 2014[114] Project QUIT	A. Brief intervention + telephone coaching sessions: clinicians followed a paper scripted protocol; covering drug addiction as a chronic brain disease, the need to quit or reduce using drugs to prevent this disease, the physical and mental consequences of drug use, and the potential accelerated progression towards severe substance use disorders caused by poly-substance use. (n=129) B. Attention control: video doctor and information booklet on cancer screening. At study exit, participants were given all intervention materials. (n=132)	Screen-detected (ASSIST)	Primary care 5 centers U.S.	Primary care physicians, lay counselors Yes	Face to face followed by phone	1 3-4 minute brief intervention followed by 2 20-30 minute phone calls	NR	Self-report based on standardized questionnaires Urine testing
Gelberg, 2017[49] Project QUIT (Pilot Replication)	A. Brief intervention + telephone coaching sessions. Replication of Gelberg, 2015 intervention with minor modifications. (n=23) B. Attention control. Participants received a video doctor and information booklet on cancer screening. (n=28)	Screen-detected (ASSIST)	Primary care 5 centers U.S.	Primary care physicians, lay counselors Yes	Face to face followed by phone	1 3-4 minute brief intervention followed by 2 20-30 minute phone calls	NR	Self-report based on standardized questionnaires Urine testing

Appendix B10. Psychosocial Trials—Intervention Characteristics

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Gryczynski, 2016[50]	A. Brief intervention: Computerized brief intervention consisting of a short, single-session interactive program led by an animated talking avatar. Participants' choice was emphasized throughout, and participants were free to choose which substances to focus on (up to 2) and what kinds of behavioral changes they were willing to make. The computer BI included questions about substance use problems, gender-specific normative feedback messaging, rating importance to change, and rating confidence (self-efficacy) to change. Participants received tailored messages and options based on their responses. (n=40) B. Wait list: Received the allocated intervention 3 months after study enrollment (n=5/40 lost to followup at that time)	Screen-detected (ASSIST)	Primary care Single center U.S.	Not relevant (computer-based)	Computer-based	1 10 minute computerized brief session	ASSIST manual	Self-report based on standardized questionnaires

Appendix B10. Psychosocial Trials—Intervention Characteristics

Author, year Study	Intervention described and comparisons (A vs. B) Ns	Recruitment method	Treatment setting	Practitioner Mentions special training required?	Mode of delivery	Intensity of intervention (when and how much)	Mentions intervention materials?	Method(s) of outcome assessment
Humeniuk, 2012[51]	A. Brief intervention with MI techniques: brief intervention linked to the results of the ASSIST+ a take-home guide (n=103) B. Wait list: participants were invited to contact the clinical interviewer if they had concerns about their substance use and were administered the brief intervention following the intervention period. (n=115)	Screen-detected (ASSIST)	Primary care Multicenter Australia, Brazil, India, U.S. (Country-specific data for only Australia and U.S. reported where available. Full N randomized=731; Australia N=171; U.S. N=218)	Clinical interviewers with some level of tertiary education within the health field Yes	Face to face	1 15 minute brief intervention session	ASSIST materials: https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1111%2Fj.1360-0443.2011.03740.x&file=ADD_3740_sm_apps1.pdf https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1111%2Fj.1360-0443.2011.03740.x&file=ADD_3740_sm_apps2.pdf	Self-report based on standardized questionnaires
Jones, 2005[100]	A. Contingency management, rewarding negative urine screens with access to the full range of counseling services; positive screens received individual 1 hour counseling sessions (n=66) B. Usual care, providing a list of referrals for aftercare options (n=64)	Consecutively enrolled from inpatient medically assisted taper program	Inpatient to outpatient 2 centers U.S.	Master's level counselor Yes	Face to face	7 days per week for first 3 weeks, followed by 4 days per week in weeks 4-12	No	Self-report based on standardized questionnaires Urine testing

Appendix B10. Psychosocial Trials—Intervention Characteristics

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Lee, 2010[53]	A. Computer-based personalized feedback: In addition to brief written materials about risks associated with marijuana use and a list of community resources and adolescent treatment facilities, participants received a 20- to 30-minute structured intervention delivered by a peer educator. (n=171) B. Usual Care: Participants received brief written materials about risks associated with marijuana use and a list of community resources and adolescent treatment facilities. (n=170)	Screen-detected (GAIN-1)	Home Online- single university U.S.	Not relevant (computer-based)	Computer-based	1 computer-ized, personalized feedback session with access to feedback for 3 months	NR	Self-report based on standardized questionnaires
Lee, 2013[52]	A. In-person personalized feedback: 1-hour intervention designed to provide the opportunity to discuss their cannabis use and review personalized graphic feedback. Facilitators used MI principles. (n=121) B. Control: assessment only (n=121)	Screen-detected (screening tool NR)	Setting NR U.S.	Facilitators (Doctoral level graduate students and professionals) Yes	Face to face	One 60-minute in-person personalized feedback session	NR	Self-report based on timeline followback and standardized questionnaires
Litt, 2005[103] Marijuana Treatment Project	A. MET + CBT (n=NR) B. MET (n=NR) C. Delayed treatment (n=NR)	Media advertisements and agency referrals	Community recruitment (newspaper and radio ads) U.S.	Therapist NR	Face to face	2 sessions of MET (weeks 1 and 5) and 9 sessions of MET-CBT (over 12 weeks)	Manuals used to guide therapy	Self-report based on timeline followback and standardized questionnaires

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Litt, 2008[101] Kadden, 2007[121]	A. MET, cognitive behavioral skills training, and contingency management (n=63) B. MET and cognitive behavioral skills training (n=61) C. Contingency management (n=54) D. Case management control (n=62)	Newspaper and radio advertisements	Community recruitment (newspaper and radio ads) U.S.	Experienced therapists Yes	Face to face	9 sessions: 2 sessions of MET + 7 sessions of CBT (relevant groups)	No	Self-report based on timeline followback and standardized questionnaires
Litt, 2013[102]	A. MET, cognitive behavioral skills training, and contingency reinforcement for completing homework assignments (n=71) B. MET, cognitive behavioral skills training, and contingency reinforcement for providing cannabis-free urine samples (n=73) C. Case management without MET or substance abuse skills training (n=71)	Newspaper and radio advertisements announcing free treatment for marijuana dependence	Single center U.S.	Therapists with graduate-level training and clinical experience with CBT and case management Yes	Face to face	9 hour-long sessions once per week	Manuals used to guide therapy	Self-report based on timeline followback and standardized questionnaires
Lozano, 2006[104]	A. CBT relapse prevention (n=117) B. MET (n=88) C. Delayed treatment control (n=86)	News stories, media announcements and paid advertisements in local newspapers and on radio stations targeted adult marijuana users who wanted help quitting marijuana use.	Community recruitment (radio and newspaper advertisements) U.S.	Therapist NR	Face to face	A. 14 2-hour group sessions over 4 months B. 2 90-minute individual sessions 1 month apart	No	Self-report based on standardized questionnaires for dependence and severity; method of ascertaining self-reported marijuana use NR

Appendix B10. Psychosocial Trials—Intervention Characteristics

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Marsden, 2006[105]	A. Brief adapted motivational intervention, manual guided, plus standard printed health risk information (n=166) B. Received printed health risk information (n=176) All received £15 plus travel expenses at recruitment and again at followup	Detached outreach contact, direct nomination by other participants (to a maximum of five friends and acquaintances) and by advertisements placed in community sites	5 community agency sites London	Non-specialist youth and drug workers with relatively limited counseling experience and skills Yes	Face to face	A Single session, 45-60 minutes	Influenced by Rollnick S., Bell A. Brief MI for the nonspecialist. In: Miller W. R., Rollnick S., eds. MI - preparing people for change. New York: GuildfordPress; 1991, p. 203–13 and Rollnick S., Heather N., Bell A. Negotiating behavioural change in medical settings: the development of brief MI. J Mental Health 1992; 1: 25–37	Self-report based on standardized questionnaires Saliva testing in a random subset

Appendix B10. Psychosocial Trials—Intervention Characteristics

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Martin, 2008[106]	A. "The Adolescent Cannabis Check-Up"; a brief, manualized, motivational and cognitive behavioral intervention, consisting of 2 sessions. Optional discussion of skills for quitting drug use (n=20) B. Delayed treatment control (n=20) All participants were given a $25 gift card at completion of the 3 month interview	Participants were targeted directly via media advertising; parents and concerned others were also targeted	NR Australia	Therapist Yes (manualized)	Face to face	A. 2 sessions, time NR B. None	MI style referenced: Miller, W. R., & Rollnick, S. (2002). MI: Preparing people for change. New York: The Guilford Press.	Self-report based on timeline followback and standardized questionnaires

Appendix B10. Psychosocial Trials—Intervention Characteristics

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Martino, 2018[54]	A. In-person brief intervention based on MI. Following screening, 1 20 minute intervention based on MI to support the importance of, and a woman's confidence in, cutting down or quitting substances and obtaining treatment. (n=145) B. Computer-based brief intervention. Following screening, 1 20 minute computer-based, self-directed intervention based on MI to support the importance of, and a woman's confidence in, cutting down or quitting substances and obtaining treatment. The electronic sessions featured an interactive, 3-dimensional, mobile narrator that delivered the intervention. (n=143) C. Usual care. Received 2 minute interaction based on their ASSIST score and told about local treatments (n=151)	Screen-detected (ASSIST)	Primary care 2 centers U.S.	Study nurse, social worker, obstetrician-gynecologist Yes	A. Face to face B. Computer C. Face to face	A. 1 20 minute brief intervention session B. 1 20 minute brief intervention session C. 1 2 minute interaction	NR	Self-report based on timeline followback and standardized questionnaires Urine testing
Mason, 2015[55] Mason, 2017[119]	A. Peer Network Counseling: MI guided by 5 key MI clinical issues: rapport, acceptance, collaboration, reflections, and non-confrontation. (n=59) B. Attention control (n=60)	Screen-detected (CRAFFT)	Primary care 2 centers U.S.	Masters level therapist Yes	Face to face	1 20-minute individual counseling session	NR	Self-report based on standardized questionnaires

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McCambridge, 2004[108] McCambridge, 2005[32]	A. MI, single session adapted from work of Miller & Rollnick 1991 and Rollnick 1992 (n=105) B. Non-intervention education-as-usual control (n=95)	Identified through peer interviews, referred by advertisement, or introductions made to groups of students, or both.	10 Further education colleges London	Lead author performed MI intervention, who has degrees in social work and psychology Yes	Face to face	A. 1 hour, single session B. Completed baseline and followup assessments only	Miller, W. R. & Rollnick, S. (1991) MI: PreparingPeople to Change Addictive Behavior. New York: Guilford Press.Rollnick, S., Heather, N. & Bell, A. (1992a) Negotiating behaviour change in medical settings: the development of brief MI. Journal of Mental Health, 1, 25–37.	Self-report based on standardized questionnaires
McCambridge, 2008[107]	A. MI (n=164) B. Control, received drug information on harm reduction and advice (n=162)	Approached individually by college staff, as well as by researchers, in informal areas such as coffeebars and games rooms and provided with information about the study	11 Further education colleges London	Practitioners Yes	Face to face	Single session, no longer than 1 hour	NR	Self-report based on standardized questionnaires; saliva testing was requested at baseline as a bogus pipeline measure

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Ondersma, 2007[56]	A. Computer-based brief intervention: three components based on MI and brief intervention principles: (1) feedback regarding the negative consequences of drug use that the participant reported, as well as self-reported readiness to change, and drug use as compared to that of all adult women; (2) pros and cons of drug use and related change, in which the participant chose from lists of positive and negative aspects of drug use from their perspective; and (3) a summary and query regarding the participant's interest in change, followed by optional goal-setting regarding drug use (n=55) B. None. Control group received no intervention (n=52)	Screen-detected (ASSIST)	Hospital Single center U.S.	Not relevant (computer-based)	Computer-based (tablet)	1 20 minute computer-delivered brief intervention session and 2 non-tailored mailings	NR	Self-report based on standardized questionnaires Urine testing

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Ondersma, 2014[58]	A. Computer-based personalized feedback combining CBT and MET (eCHECKUP TO GO): 6 30-minute individual behavioral therapy sessions that involved a combination of MET and CBT (n=72) B. Attention control: 1 minute of brief advice based on a manualized version of standard interventions offered by obstetrical doctors and nurses (n=71)	Screen-detected (ASSIST)	Hospital 3 centers U.S.	Not relevant (computer-based)	Computer-based	1 20 minute interactive computer-based personalized feedback session	NR	Self-report based on timeline followback Urine and hair sample testing

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Ondersma, 2018[57]	A. Computer-based brief intervention focused on parenting patterned after MI principles and was tailored to each participant. Participants received a video-based orientation ("The Parent Check-up"), tailored to their ethnic identity and religiosity. The video touched on substance use but did not focus on it exclusively. Participants received feedback and offered the option of changing in 1 of the 4 areas or ending The Parent Check-up (n=252) B. Attention control: Participants watched educational videos about infant nutrition from birth to age 1 (i.e., breastfeeding, formula feeding, when to introduce solids) with no mention of safety, emotional health, or substance use (n=248)	Screen-detected (WIDUS)	Hospital Single center U.S.	Not relevant (computer-based)	Computer-based	1 brief computer-based session and personalized feedback report	NR	Self-report based on timeline followback and standardized questionnaires Urine and hair sample testing

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Palfai, 2014[59]	A. Computer-based personalized feedback (eCHECKUP TO GO) Following assessment, participants were provided with detailed personalized feedback about their cannabis use, including costs, norms, risks, consequences, and alternative activities. (n=54) B. Attention Control: Participants were provided minimal general health feedback regarding recommended guidelines for sleep, exercise, and nutrition. (n=49)	Screen-detected (ASSIST)	College health clinic Single center U.S.	Not relevant (computer-based)	Computer-based	1 web-based personalized feedback session (minutes NR)	Yes; described as a commercially available intervention that is used widely in universities and colleges in U.S. and Canada	Self-report based on standardized questionnaires

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Poblete, 2017[60]	A. Brief intervention based on FRAMES: ASSIST-linked brief intervention for the substance with the highest score, and the ASSIST self-help guide, with additional information regarding substances and high-risk situation management. When 2 substances had the same score, the participant had the choice to decide which substance to receive counseling for. The intervention was based on the FRAME model, which provides specific feedback, offers a menu of options, and enhances motivation to change (n=400) B. Usual care: Participants received a pamphlet of their own choosing containing broad information on substance use risk and harm (n=406)	Screen-detected (ASSIST - Chilean version)	Primary care, emergency department, police station 32 centers Chile	Social worker, psychologist Yes	Face to face	1 18 minute brief individual counseling session	ASSIST manual	Self-report based on standardized questionnaires
Rooke, 2013[109]	A. Web-based CBT + MI, 6 modules (n=119) B. Educational control, 6 modules (n=111)	Advertisements seeking individuals who wished to reduce or quit their cannabis use via an online program were placed on the National Cannabis Prevention and Information Centre website, online forums, Google, university bulletin boards, in newspapers, and at community health centers.	Web-based recruiting International	Not relevant (computer-based)	Web-based	6 modules completed at intervals selected by participants	Website: Reduce Your Use: How to Break the Cannabis Habit	Self-report based on timeline followback and standardized questionnaires

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Roy-Byrne, 2014[61] Krupski, 2012[118]	A. In-person personalized feedback using a MI approach + telephone booster session: brief (30 minute) intervention in which interventionists used a MI approach and tailored the intervention to allow for flexibility as to which or how many drugs to target, as well as in how to guide the participant (e.g., specialty treatment, abstinence, harm reduction). The same interventionist attempted a followup telephone booster session within 2 weeks of the intervention (n=435) B. Enhanced usual care: participants received an illustrated handout depicting their DAST-10 drug problem severity score and list of substance abuse resources. Resembled the "notification and referral" strategy that might be implemented in high-quality usual care (n=433)	Screen-detected (screening tool NR)	Primary care 7 centers U.S.	Social workers, master's level and bachelor level interventionists Yes	Face to face followed by phone	1 30 minute personalized feedback session and 1 10-minute booster call	NR	Self-report based on standardized questionnaires; non-drug use outcome measures were assessed using Washington State administrative data (chemical dependency treatment records, inpatient hospitalizations, state patrol arrest records, death records)

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Saitz, 2014[62] Fuster, 2016[116] Kim, 2016[117] ASPIRE	A. Brief negotiated interview using some MI. Participants received a single 10- to 15-minute structured interview that included feedback, review of the "pros and cons" of use, and development of a plan for change (n=169) B. MI + telephone booster. Participants received 30 to 45 minutes of MI with an offered 20- to 30-minute booster followup session. The interview elicited possible links between drug use and health concerns, heightening discrepancies between negative drug use outcomes and valued goals, enhancing self-efficacy about behavior change, and providing options for change (n=173) C. Minimal. Participants were given information on how to contact Alcoholics Anonymous, Narcotics Anonymous, the hospital behavioral health clinic and emergency team, a state hotline, a city triage line, and websites for alcohol and drug screening (n=175)	Screen-detected (ASSIST)	Primary care Single center U.S.	A. Health educators (completed high school and had human services experience or a bachelor's degree) B. Counselors (master's degree) NR, but fidelity was assessed, so likely	A. Face to face B. Face to face C. Face to face	A. 1 10-15 minute brief negotiated interviewing session B. 1 30-45 minute MI session and 1 optional 20-30 minute booster followup session C. 1-time information	NR	Self-report based on timeline followback and standardized questionnaires Hair sample testing

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Schaub, 2015[110] Can Reduce	A. Self-help with chat, based on MI and CBT (n=114) B. Self-help without chat, based on MI and CBT (n=101) C. Waitlist control (n=93)	Press release, outpatient treatment centers, advertisements on Internet forums and prevention websites	Community recruitment (online and print media) Germany	Counselors, psychologists or psychiatrists with experience in treating cannabis-abusing patients Yes	Web	8 modules	Website	Self-report based on consumption diary (not specified as Timeline Followback) and standardized questionnaires
Stein, 2009[111]	A. MI, 4 sessions (n=97) B. Written handout of treatment resources (n=101)	Newspaper advertisement and word of mouth	Community recruitment U.S.	Therapist Yes	Face to face	4 sessions, 20-40 minutes each	No	Self-report based on standardized questionnaires
Stein, 2011[63]	A. MI: Participants received 2 45-minute MI sessions spaced 1 month apart (n=163) B. Control: assessment only (n=169)	Screen-detected (screening tool NR)	Research clinic Single center U.S.	Therapist Yes	Face to face	2 45-minute MI sessions	NR	Self-report based on timeline followback
Stephens, 2000[33]	A. Relapse Prevention Support Group: combination CBT and social support (n=117) B. Individualized Assessment and Advice: sessions with therapist feedback, MI and advice on CBT techniques (n=88) C. Delayed treatment control (n=86)	Media announcements, news stories, and paid advertisements in local newspapers and on radio stations in the greater Seattle, Washington, area promoted the Marijuana Treatment Project for adult marijuana users who wanted help quitting.	Research center Single center U.S.	Therapist (master's or doctoral level) Yes	Face to face	A. 14 2-hour sessions over 18 weeks B. 2 90-minute sessions C. NA	No	Self-report based on standardized questionnaires; days of use also verified by collaterals (e.g. spouse, partner, family, etc.)

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Stephens, 2007[112]	A. Personal feedback: therapist reviewed a personal feedback report with the participant (n=62) B. Attention control (multi-media feedback): a balanced presentation of the multiple points of view on the consequences associated with marijuana use; participants were invited to ask questions at any time but no feedback regarding the participant's use of marijuana was provided and therapists avoided using MI techniques (n=62) C. Delayed feedback: educational control condition that provided information about the latest research on marijuana delivered in an objective, stimulating, but largely didactic manner. (n=64)	Newspaper and radio advertisements, public service announcements, posted flyers and outreach at community events.	Research center Single center U.S.	Therapist (master's level) Yes	Face to face	A. 1 90-minute session B. 1 90-minute session C. NA	No	Self-report based on timeline followback and standardized questionnaires Urine testing
Tait, 2015[113]	A. MET + CBT (n=81) B. Waitlist (n=79)	Advertisements on social network sites and posters in local clinics	Community recruitment (social media and clinic posters) Australia	Not relevant (web)	Web	3 modules, completed at participants pace but suggested 1 per week	Website	Self-report based on standardized questionnaires

Appendix B10. Psychosocial Trials—Intervention Characteristics

Author, year Study	Intervention described and comparisons (A vs. B) Ns	Recruitment method	Treatment setting	Practitioner Mentions special training required?	Mode of delivery	Intensity of intervention (when and how much)	Mentions intervention materials?	Method(s) of outcome assessment
Tzilos Wernette, 2018[64]	A. Health Checkup for Expectant Moms: computerized program in a MI-consistent style (Intervention addressed both sexually transmitted infection/HIV and alcohol/drug risk). Participants interacted with a computer and were guided by an animated narrator, which engages in a MI-consistent style, can use emotionally expressive statements and empathic reflection. Participants also received brochures specifically designed to facilitate health risk behaviors during pregnancy (n=31) B. Attention control: participants interacted with the computer and were guided by the same narrator used for intervention group participants. Participants also received brochures specifically designed to facilitate health risk behaviors during pregnancy (n=19)	Screen-detected (T-ACE or SURP-P)	Obstetrics and Gynecology Clinic Single center United States	Not relevant (computer-based)	Computer-based	1 60 minute computer-delivered MI session and 1 15-minute computer-delivered booster session	NR	Self-report based on timeline followback

Appendix B10. Psychosocial Trials—Intervention Characteristics

Author, year Study	Intervention described and comparisons (A vs. B) Ns	Recruitment method	Treatment setting	Practitioner Mentions special training required?	Mode of delivery	Intensity of intervention (when and how much)	Mentions intervention materials?	Method(s) of outcome assessment
Walton, 2013[65] Project Chill	A. In-person personalized feedback using MI (The intervention, delivered by a therapist and facilitated by a computer, incorporated MI, including tailored, parallel content. The therapist used an elicit-provide-elicit framework when reviewing tailored feedback, using summaries and open-ended questions to evoke change talk (n=118) B. Computer-based personalized feedback (n=100) C. Usual care (n=110)	Screen-detected (Add Health)	Primary care 7 centers U.S.	Therapist Yes	A. Face to face B. Computer C. Face to face	1 session-minutes NR	NR	Self-report based on standardized questionnaires
Watkins, 2017[66] SUMMIT	A. Collaborative care: population-based management approach, measurement-based care, and integration of addiction expertise (n=138) B. Usual care: participants were told by the research team that the clinic provided opioid and alcohol use disorder treatment and given a number for appointment scheduling and list of community referrals; did not receive any additional outreach or contact (n=123)	Screen-detected (NIDA Quick Screen)	Primary care 2 centers U.S.	Clinician (some with waiver to prescribe buprenorphine/naltrexone), Master's level therapist (Counseling or Social Work degree), and Care Coordinators (high school degree) Yes	Face to face	Collaborative care (registry, regular assessment, adherence support) plus training for behavioral therapists and doctors for medication-assisted treatment	NR	Electronic medical records for resource utilization and self-report based on standardized questionnaires

Appendix B10. Psychosocial Trials—Intervention Characteristics

Author, year Study	Intervention described and comparisons (A vs. B) Ns	Recruitment method	Treatment setting	Practitioner Mentions special training required?	Mode of delivery	Intensity of intervention (when and how much)	Mentions intervention materials?	Method(s) of outcome assessment
Woolard, 2013[67] Project Reduce	A. MI: 2 brief interventions guided by the principles of MI. The goal of the first brief intervention was to engage the participant in reflection upon the pros and cons of alcohol and marijuana use. The focus of the second brief intervention session was to review and reinforce the change and create a change plan with those who had not made a change plan in the first session (n=206) B. Usual care: participants received routine emergency care for their presenting medical complaint and were offered information on local treatment resources for substance misuse (n= 220)	Screen-detected (published wellness questionnaire)	Emergency department, behavioral/mental health clinic Single center U.S.	PhD or master's level mental health degree interventionist Yes	Face to face	2 15-60 minute individual counseling sessions	NR	Self-report based on standardized questionnaires
Yonkers, 2012[68]	A. MET-CBT: MET, functional analysis, safe sexual behavior, communication skills, relapse prevention and problem solving skills. Research nurse therapists had the flexibility to offer additional sessions or repeat topics if there was time and need (n=92) B. Brief advice: a manualized version of standard interventions offered by obstetrical doctors and nurses (n=91)	Screen-detected (TWEAK)	Obstetrics and Gynecology Clinic 2 centers U.S.	Research nurse therapist and obstetrical doctor or nurse Yes (manualized)	Tablets	6 30 minute MET + CBT sessions	NR	Self-report based on timeline followback Urine testing

Appendix B10. Psychosocial Trials—Intervention Characteristics

Author, year Study	Intervention described and comparisons (A vs. B) Ns	Recruitment method	Treatment setting	Practitioner Mentions special training required?	Mode of delivery	Intensity of intervention (when and how much)	Mentions intervention materials?	Method(s) of outcome assessment
Zahradnik, 2009[69] Otto, 2009[120]	A. MI: Participants received 2 MI sessions. The first 30-45 minute session took place in the hospital; the second session, 4 weeks later, was conducted by phone. The intervention was based on the Transtheoretical Model of behavior change. Participants received an individualized feedback letter 8 weeks after the first intervention (n=56) B. Usual care: informational booklet about prescription drugs (n=70)	Screen-detected (SDS and other questions to assess for prescription drug use)	Hospital 2 centers Germany	Psychologist Yes	Face to face, phone, letter	1 35-minute in-person MI session, 1 phone MI session, and 1 individualized feedback letter	NR	Self-report based on standardized questionnaires

Abbreviations: ASPIRE = The Assessing Screening Plus Brief Intervention's Resulting Efficacy to Stop Drug Use study; ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; CAHL = Project Cannabis Assistance Help Line; CBT = cognitive behavioral therapy; CRAFFT = CRAFFT youth substance screening questionnaire; DAST-10 = Drug Abuse Screening Test; FRAME = Feedback, Responsibility, Advice, Menu Options, Empathy, and Self-Efficacy; GAIN-1 = Global Appraisal of Individual Needs; MAPLE = randomized controlled trial of a brief MI for young adult female marijuana users with various levels of quitting desire; MET = motivational enhancement therapy; MI = motivational interviewing; MOTI-4 = brief motivational enhancement intervention designed for young vulnerable non-treatment-seeking cannabis users; NA = not applicable; NIDA = National Institute on Drug Abuse; NR = not reported; QUIT = Quit Using Drugs Intervention Trial; SDS = Severity of Dependence Scale; SMART-ED = Screening, Motivational Assessment, Referral and Treatment in Emergency Departments; SUMMIT = Substance Use Motivation and Medication Integrated Treatment study; SURP-P = Substance Use Risk Profile-Pregnancy scale; T-ACE = screening tool for at-risk drinking developed for use in obstetrics/gynecological settings; TWEAK = five item alcohol screening tool; U.S. = United States; WIDUS = The Wayne Indirect Drug Use Screener

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Babor, 2004[30]	A. Multicomponent therapy: MET + CBT + case management (n=156) B. MET (n=146) C. Control: delayed treatment (n=148)	A vs. B vs. C Proportion still in study; 4 months: 85.3% (133/156) vs. 87.7% (128/146) vs. 92.6% (137/148)	A vs. B vs. C Proportion abstinent (self-report, random sample verified by urine testing): 22.7% (30/132) vs. 8.7% (11/127) vs. 3.6% (5/137); (A+B) vs. C: RR 4.34 (95% CI 1.75 to 10.72) Proportion of days marijuana used: 36.17% (SD 38.83) vs. 55.86% (SD 36.18) vs. 75.59% (SD 30.69)	A vs. B vs. C Marijuana Problem Scale (0 to 19): 6.02 (SD 4.85) vs. 8.35 (SD 4.06) vs. 7.77 (SD 3.90) Dependence symptoms (DSM-IV, 0 to 7): 2.47 (SD 2.34) vs. 3.70 (SD 2.26) vs. 4.36 (SD 1.92) Abuse symptoms (DSM-IV, 0 to 4): 1.03 (SD 1.02) vs. 1.38 (SD 1.10) vs. 1.63 (SD 0.91)	A vs. B vs. C ASI medical composite score: 0.22 (SD 0.30; 95% CI 0.2 to 0.3); 0.29 (SD 0.35; 95% CI 0.2 to 0.3) vs. 0.15 (SD 0.26; 95% CI 0.1 to 0.2) ASI psychiatric composite score: 0.13 (SD 0.18; 95% CI 0.1 to 0.2) vs. 0.15 (SD 0.19; 95% CI 0.1 to 0.2) vs. 0.13 (SD 0.18; 95% CI 0.1 to 0.2) ASI employment composite score: 0.20 (SD 0.19; 95% CI 0.2 to 0.2) vs. 0.22 (SD 0.22; 95% CI 0.2 to 0.3) vs. 0.20 (SD 0.17; 95% CI 0.02 to 0.02) Beck Depression Inventory score: 7.71 (SD 7.76; 95% CI 6.3 to 9.1); 10.35 (SD 8.5; 95% CI 8.9 to 11.8); 7.87 (SD 6.78; 95% CI 6.5 to 9.2) State-Trait Anxiety Inventory , State Version score: 33.35 (SD 10.13; 95% CI 31.4 to 35.3) vs. 37.5 (SD 11.61; 95% CI 35.5 to 39.5) vs. 35.5 (SD 11.21; 95% CI 33.6 to 37.4)	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Baker, 2001a[88] Baker, 2001b[89]	A. 4-session CBT: MI (Session 1) + cognitive behavioral coping strategies + relapse prevention (Sessions 2-4) + self-help booklet (n=16) B. 2-session CBT: same as Session 1 and 2 + self-help booklet (n=16) C. Control: self-help booklet only (n=32)	(A + B) vs. C Proportion completing study: 75% (24/32) vs. 87.5% (28/32)	(A + B) vs. C Proportion abstinent from amphetamines, 6 months (self-report): 58.3% (14/24) vs. 21.4% (6/28); p<0.01 Proportion abstinent from cannabis, 6 months: 6.3% (1/16) vs. 26.3% (5/19); p=NS Mean OTI amphetamine score: 1.20 (SD 1.63) vs. 0.83 (SD 1.03) at baseline, 0.18 (SD 0.52) vs. 0.39 (SD 0.62) at 6 months; mean change from baseline: 1.02 (SD 1.23) vs. 0.44 (SD 1.28); effect size 0.93 vs. 0.40; p=NS (value NR) Mean OTI cannabis score: 5.93 (SD 7.53) vs. 7.43 (SD 8.96) at baseline, 3.00 (SD 4.36) vs. 4.94 (SD 5.68) at 6 months; mean change from baseline 2.93 (SD 6.64) vs. 2.49 (SD 7.59); effect size 0.42 vs. 0.36; p=NS (value NR) Mean OTI polydrug score: 4.38 (SD 1.28) vs. 5.00 (SD 1.22) at baseline, 3.54 (SD 1.44) vs. 4.32 (SD 1.68) at 6 months; mean change from baseline 0.83 (SD 1.40) vs. 0.68 (SD 1.61); effect size 0.56 vs. 0.46; p=NS (value NR)	NR	(A + B) vs. C Narrative report of no difference between groups in OTI crime scores, OTI social functioning, or GHQ-28 scores OTI injection risk-taking score: 5.34 vs. 9.02 (SD NR); p=NS (value NR) for difference in change from baseline A vs. B vs. C OTI health scores: 12.56 vs. 21.00 vs. 19.23 (SD NR); p=NS (value NR) for difference in change from baseline	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Baker, 2005[90]	A. 4-session CBT: MI (Session 1) + cognitive behavioral coping strategies + relapse prevention (Sessions 2-4; n=66) B. 2-session CBT: same as Session 1 and 2 (n=74) C. Control (n=74)	A vs. B vs. C Proportion still in study, 6 months: 77.3% (51/66) vs. 73.0% (54/74) vs. 64.9% (48/74)	A vs. B vs. C Proportion abstinent, 6 months (ITT analysis, self-report): 37.9% (25/66) vs. 33.8% (25/74) vs. 17.6% (13/74) Mean OTI amphetamine score (ITT analysis): 1.53 (SD 1.73) vs. 1.43 (SD 1.63) vs. 1.55 (SD 1.61) at baseline; 0.68 (SD 1.09) vs. 0.94 (SD 1.78) vs. 1.00 (SD 1.37) at 6 months; effect size 0.55 vs. 0.33 vs. 0.36; p=NS (value NR) Narrative report of no difference between groups in benzodiazepine, tobacco or polydrug use	A vs. B vs. C SDS (amphetamine version): Narrative report of no difference between groups (data only reported according to number of sessions received, not by treatment allocation)	A vs. B vs. C Narrative report of no differences between groups in involvement in OTI criminal activity, injecting risk-taking behavior, or sexual risk-taking behavior Narrative report of no differences between groups in overall psychiatric distress (Brief Symptom Inventory Global Severity Index) or level of depression (Beck Depression Inventory-II)	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Bernstein, 2005[4]	A. MI + telephone booster session: Participants received a semi scripted, brief (10-45 minute) motivational interview delivered by a peer, a substance abuse outreach worker in recovery. (n=490) B. Minimal: Participants received only a handout stating that "based on your screening responses, you would benefit from help with your drug use" (n=472)	NR	A vs. B Cocaine and opiates abstinence (denominator those positive at baseline): 17.4% (70/403) vs. 12.8% (48/375), OR=1.43 (0.96 to 2.13), p=0.08 Cocaine abstinence (denominator those positive at baseline): 22.3% (84/376) vs. 16.9% (58/344), OR=1.41 (0.98 to 2.06), p=0.07 Opiates abstinence (denominator those positive at baseline): 40.2% (76/189) vs. 30.6% (49/160), OR=1.52 (0.98 to 2.38), p=0.06 Cocaine levels (Based on hair sample (units = ng/10 mg)): 436 (NR) vs. 464 (NR); between group difference NR, p=0.058 Opiate levels (Based on hair sample (units = ng/10 mg)): 18.8 (NR) vs. 22.9 (NR); between group difference NR, p=0.186	A vs. B ASI, drug subscale, reduction in score: 49% vs. 46%; p=0.06 ASI, medical subscale, reduction in score: 56% vs. 50%; p=0.055	NR	NR
Bernstein, 2009[45]	A. Brief intervention, based on a MI approach (n=47) B. Usual care (not described) (n=55)	NR	A vs. B Cannabis use, days per month, mean (SD): 11.0 (10.7) vs. 13.2 (11.7), MD -5.3 (-10.0 to -0.6), p=0.024 Cannabis abstinence (self-report): 30.9% (21/68) vs. 16.9% (12/71); RR 1.83 (95% CI 0.98 to 3.42)	NR	A vs. B Drove after cannabis use: 17% (8/47) vs. 23.6% (13/55), OR=0.60 (0.12 to 1.750, p=0.352 Rode in car with person high after cannabis use: 21.3% (10/47) vs. 23.6% (13/55), OR=0.81 (0.31 to 2.10), p=0.668	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Blow, 2017[46] Bonar, 2018[91] HealthiER You	A. Computerized brief motivational interview, targeting drug and alcohol use (n=257); A1 with (n=130) or A2 without (n=127) additional MET B. Therapist brief motivational interview, targeting drug and alcohol use (n=257); B1 with (n=127) or B2 without (n=130) additional MET C. Educational control: 3 minute review of community resources and HIV prevention (n=266); C1 with (n=136) or C2 without (n=130) additional MET Groups randomized to A, B or, C, then re-randomized to additional MET or an educational control	3 months: 81% 6 months: 85% 12 months: 87% Similar among groups	A1 vs. A2 vs. B1 vs. B2 vs. C1 vs. C2% change in mean, baseline to 12 months Days using any drug: -10.0 vs. -10.9 vs. -27.6 vs. -26.7 vs. -0.2 vs. -20.9; p<0.001 for B1, B2, and C2 Mean weighted drug days: -13.3 vs. -16.6 vs. -30.5 vs. -24.3 vs. -1.0 vs. -25.3; p<0.05 for A2 and B2; p<0.001 for B1 and C2 Days of cannabis use: -6.7 vs. -4.2 vs. -24.2 vs. -20.5 vs. 4.8 vs.-17.7; p<0.05 for C2; p<0.001 for B1	NR	HIV Risk-taking Behavior Scale coefficient (reference: C1) Computer A1: −0.94 (−2.06, 0.18) A2: 0.06 (−1.08, 1.20) Therapist B1: −1.25 (−2.38, −0.11); p<0.01 B2: −0.33 (−1.46, 0.80) Control C2: −0.03 (−1.14, 1.07)	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Bogenschutz, 2014[47] Bogenschutz, 2011[115] SMART-ED	A. Brief intervention based on MI principles + telephone booster sessions, in addition to an informational pamphlet about drug use and misuse (n=427) B. Minimal intervention: informational pamphlet about drug use and misuse, its potential consequences, and treatment options and optional referral to addiction treatment, consisting of a recommendation to seek treatment and a standardized list of available options (n=427)	NR	A vs. B Drug use days for the most frequently used drug, mean (SD): 8.6 (11.2) vs. 7.9 (11.1); between-group difference NR, p=NS (value NR) Drug use days, mean (SD): 10.7 (11.8) vs. 10.9 (12.1); between group difference NR, p=NS (value NR) Abstinence, 3 months (based on hair sample): 8.3% (46/555*) vs. 11.8% (34/287); 12 months: 17.1% (91/533*) vs. 14.9% (40/269) *Includes screening, assessment and referral to addiction treatment arm	NR	A vs. B Mortality: 1.6% (7/427) vs. 0.9% (4/427) Incarceration: 1.2% (5/427) vs. 0.5% (2/427)	NR
Copeland, 2001a[31] Copeland, 2001b[92]	A. 6CBT: intervention package incorporating motivational interview + standard relapse prevention (n=78) B. 1CBT: single session of 6CBT + self-help booklet (n=82) C. Delayed treatment control (n=69)	A vs. B vs. C Narrative report of no difference between treatment groups in likelihood of participating in follow-up	A vs. B vs. C Proportion with continuous abstinence (self-report): 15.1% (8/53) vs. 4.9% (3/61) vs. 0% (0/56) Proportion abstinent in prior month (self-report): 20.8% (11/53) vs. 17.2% (11/64) vs. 3.5% (2/56) Proportion of days abstinent at followup (self-report): 35.9% vs. 44.8% vs. 29.7%; p=NS for all comparisons Cannabis use (OTI score): 1.3 (SD 0.9) vs. 1.5 (SD 1.2) vs. 1.8 (SD 1.0); p=0.02 for A vs. C and p=0.20 B vs. C	A vs. B vs. C SDS score: 5.8 (SD 4.3) vs. 7.6 (SD 4.4) vs. 9.2 (SD 3.2); A vs. C: p<0.0001; B vs. C: p=0.008 Proportion of cannabis-related problems (Cannabis Problems Questionnaire): 23% (SD 16.8) vs. 28.4% (SD 18.6) vs. 39.1% (SD 16.6); A vs. C: p<0.0001; B vs. C: p=0.004	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
D'Amico, 2018[44]	A. CHAT, brief, 15-20 minute motivational interview delivered in primary care (n=153) B. Usual care, including a brochure with information on the effects of alcohol and drug use, how to prepare for risky situations, and online and telephone resources (n=141)	A. 7.2% (11/153) did not receive the intervention	A vs. B, 12 month followup: Past 3-month use (number of times), marijuana, mean (SD): 6.76 (8.37) vs. 5.21 (7.35),, p=0.23, effect size 0.14 On days using marijuana, number of times used, mean (SD): 1.18 (1.20) vs. 1.06 (1.16), p=0.64, effect size 0.05	A vs B, 12 month followup: Number of negative consequences experienced from marijuana use, mean (SD): 0.92 (3.26) vs. 2.36 (9.29), p=0.04, effect size -0.28	NR	NR
de Dios, 2012[93]	A. Motivational interview + mindfulness meditation (n=22) B. Control: assessment only (n=12)	NR	A vs. B Days of marijuana use at 3 months, between-group difference: -6.83 (95% CI -12.94 to -0.81) Narrative report of no difference between groups in abstinence rates	NR	NR	NR
de Gee, 2014[94]	A. Brief intervention: motivational interview-based aimed at changing adolescents' cannabis use by increasing their awareness of the possible negative consequences of cannabis use and by helping them to make informed choices about their own use (n=58) B. Control: information session (n=61)	A vs. B Proportion with followup: 77.6% (45/58) vs. 86.9% (53/61)	A vs. B Days of cannabis use/week: 4.4 (SD 2.3) vs. 4.1 (SD 2.5); MD -0.01 (95% CI -0.62 to 0.61) Mean number of joints/week: 10.4 (SD 8.4) vs. 10.1 (SD 9.7); MD 0.05 (95% CI -2.04 to 2.14)	A vs. B Mean SDS score: 3.0 (SD 2.5) vs. 3.1 (SD 2.9); MD 0.04 (95% CI -0.69 to 0.78) Mean Cannabis Use Problems Identification Test Impaired Control score: 28.9 (SD 9.4) vs. 28.6 (SD 9.6); MD 0.17 (95% CI -1.67 to 2.00) Mean Cannabis Use Problems Identification Test Problems score: 6.2 (SD 3.8) vs. 5.7 (SD 3.7); MD -0.06 (95% CI -1.11 to 0.98)	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Dembo, 2016[95]	A. Brief, 2-session youth only session, integrates MI, CBT rational-emotive therapy, and problem-solving therapy B. Brief, 2- session youth and separate 1-session parent session C. Standard truancy services plus a referral service overlay of 3 visits by a project staff member; no counseling was offered $15 was paid for completing the interviews	NR	Used auto-regressive lag model estimation Marijuana use, adolescent diagnostic interview and urine screen: A + B vs. C: Estimate -0.490, SE 0.277, p<0.05 (intervention group less likely to be involved in use) A vs. C: Estimate -0.841, SE 0.323, p<0.01 (intervention group less likely to be involved in use) B vs. C: Estimate 0.012, SE 0.390, p=NS (value NR) A vs. B: Estimate 0.790, SE 0.323, p<0.05 (those in intervention group B [family included] more likely to be involved in marijuana use than those in intervention group A)	NR	NR	NR
Dupont, 2016[96]	A. MOTI-4 (n=71) B. Usual care, 1 hour session in which the effects of cannabis on the body were discussed, including a computerized animation, followed by a quiz and receipt of information leaflet (n=60)	NR	A vs. B Mean number of cannabis joints smoked per week: ~5.8 vs. ~9.7 (estimated from figure) Multiple regression analysis Effect of gender (female) on number of cannabis joints smoked weekly: B -7.370, SE 2.415, p<0.05	NR	A vs. B Amount of Euros spent on cannabis per week: ~10 vs. ~18 (estimated from figure) Multiple regression analysis Effect of gender (female) on Euros spent on cannabis weekly: B -12.386, SE 4.253, p<0.05	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Fischer, 2012[98] Fischer, 2013[97]	A. Brief intervention: oral or written intervention consisting of short, fact-based and nonjudgmental information on cannabis-related health risks (n=72) B. Control: general health information delivered in a manner similar to the brief intervention (n=62)	A vs. B Proportion with followup, 12 months: 55.6% (40/72) vs. 51.6% (32/62)	A vs. B (among study completers n= 40 vs. 32) Days of cannabis use in the past 30 days: 23.1 (SD 7.74) vs. 23.1 (SD 7.07) at 3 months, 22.3 (SD 8.07) vs. 22.1 (SD 9.24) at 12 months Number of cannabis use episodes/day: 2.4 (SD 1.94) vs. 2.4 (SD 2.74) at 3 months, 2.6 (SD 3.39) vs. 2.2 (SD 1.30) at 12 months	NR	A vs. B Proportion who reported driving within 2 hours of cannabis use: 24% vs. 24%; p=NS	NR
Gates, 2012[99] CAHL	A. MI and CBT (n=68) B. Delayed treatment control (n=81)	A vs. B Completed 1-month (post-treatment) followup: 79% (54/68) vs. 89% (72/81)	A vs. B 28-day cannabis use frequency (days): 7.3 (SD 10.3) vs. 12.5 (SD 11.4), SMD 0.6 (95% CI 0.2 to 1.1) Cannabis use quantity per day: 5.0 (SD 13.3) vs. 6.7 (SD 10.4), SMD 0.4 (95% CI 0.0 to 0.8) Proportion of abstinent days: 73.3% (SD 36.8) vs. 55.3% (SD 40.7), SMD 0.6 (95% CI 0.2 to 1.0) 90-day illicit drug use frequency: 0.1 (SD 0.7) vs. 0.7 (SD 4.8), SMD 0 (95% CI -0.3 to 0.4)	A vs. B Cannabis Problems Questionnaire (0 to 22): 3.6 (SD 4.4) vs. 5.3 (SD 4.5), SMD 0.5 (95% CI 0.1 to 0.9) SDS (0 to 15): 3.2 (SD 3.8) vs. 5.8 (SD 4.3), SMD 0.9 (95% CI 0.5 to 1.3) ≥50% reduction in use and no problems (self-report): 38.8% (19/41) vs. 19.7% (12/61), OR 0.39 (95% CI 0.17 to 0.91)	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Gelberg, 2015[48] Baumeister, 2014[114] Project QUIT	A. Brief intervention + telephone coaching sessions: clinicians followed a paper scripted protocol; covering drug addiction as a chronic brain disease, the need to quit or reduce using drugs to prevent this disease, the physical and mental consequences of drug use, and the potential accelerated progression towards severe substance use disorders caused by poly-substance use. (n=129) B. Attention control: video doctor and information booklet on cancer screening. At study exit, participants were given all intervention materials (n=132)	NR	A vs. B Drug use days for the most frequently used drug (in the past 30 days), mean (95% CI): 7.1 (5.8 to 8.5) vs. 9.9 (95% CI 8.5 to 11.2), MD=2.68 (0.76 to 4.60), p<0.01	NR	A vs. B QOL, mental health component (As measured by SF-12 Health Survey), mean (SD): 43.71 (11.78) vs. 44.39 (12.21), MD=0.25 (SD NR), p=0.848 QOL, physical health component (As measured by SF-12 Health Survey), mean (SD): 45.07 (12.18) vs. 44.47 (12.21), MD=1.59 (SD NR), p=0.115	NR
Gelberg, 2017[49] Project QUIT (Pilot Replication)	A. Brief intervention + telephone coaching sessions. Replication of Gelberg, 2015 intervention with minor modifications. (n=23) B. Attention control. Participants received a video doctor and information booklet on cancer screening. (n=28)	NR	A vs. B Drug use days (in past 30 days) for the most frequently used drug, mean (SD): 6.61 (NR) vs. 12.93 (NR), MD= 5.28 (-0.06 to 10.63), p=0.053 Abstinence, based on urine samples: 25% (5/20) vs. 56% (12/27), RR 1.69 (95% CI 1.03 to 2.76)	NR	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Gryczynski, 2016[50]	A. Brief intervention: Computerized brief intervention consisting of a short, single-session interactive program led by an animated talking avatar. Participants' choice was emphasized throughout, and participants were free to choose which substances to focus on (up to 2) and what kinds of behavioral changes they were willing to make. The computer brief intervention included questions about substance use problems, gender-specific normative feedback messaging, rating importance to change, and rating confidence (self-efficacy) to change. Participants received tailored messages and options based on their responses. (n=40) B. Wait list: Received the allocated intervention 3 months after study enrollment (n=5/40 lost to followup at that time)	NR	A vs. B Drug positive hair tests: 68.4% (13/19) vs. 37.5% (6/16), p=0.10 Marijuana-positive hair tests: 50.0% (9/18) vs. 31.3% (5/16) p=0.32	A vs. B ASSIST, total score, mean (SE): 24.4 (4.2) vs. 27.8 (4.3) β=-2.0 (2.7), p=0.46	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Humeniuk, 2012[51]	A. Brief intervention with MI techniques: brief intervention linked to the results of the ASSIST+ a take-home guide (n=103) B. Wait list: participants were invited to contact the clinical interviewer if they had concerns about their substance use and were administered the brief intervention following the intervention period. (n=115)	NR	NR	A vs. B ASSIST, total score, mean (SD): 31.1 (19.7) vs. 31.3 (18.7), study-reported between group difference=NR, p=0.11 ASSIST, cannabis score, mean (SD): 15.1 (9.5) vs. 12.3 (7.0), study-reported between group difference=NR, p=0.08 ASSIST, stimulant score (Among those eligible for a cocaine or amphetamine-type stimulant brief intervention), mean (SD): 16.2 (11.8) vs. 13.2 (10.5), study-reported between group difference=NR, p=0.8	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Jones, 2005[100]	A. Contingency management, rewarding negative urine screens with access to the full range of counseling services; positive screens received individual 1 hour counseling sessions (n=66) B. Usual care, providing a list of referrals for aftercare options (n=64)	A vs. B In a treatment program at 1 month: 64% vs. 12%; p<0.001 In a treatment program at 3 months: 49% vs. 12%; p<0.001In a treatment program at 6 months: 39% vs. 21%; p=0.034 Retained in contingency management program, 1 month: 60% Retained in contingency management program, 3 months: 46% Retained in contingency management program, 6 months: 37%	A vs. B Abstinence at 1 month (urine testing): 42% vs. 15% at 1 month, 38% vs. 17% at 3 months, ~40% vs. ~22% at 6 months (p=NS), ~25% vs. ~23% at 12 months (p=NS) Number of clean urine samples: OR 2.23 (95% CI 1.25 to 4.00) Overall opioid abstinence: OR 2.15 (95% CI 1.16 to 4.00) Overall cocaine abstinence: OR 1.67 (95% CI 0.93 to 3.00)	NR	A vs. B Significant main effects of group condition for employment (p=0.01) and drug use (p=0.04) composite scores; mean days worked and mean legal income significantly higher for treatment group at 3 months, 6 months, and 12 months	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Lee, 2010[53]	A. Computer-based personalized feedback: In addition to brief written materials about risks associated with marijuana use and a list of community resources and adolescent treatment facilities, participants received a 20- to 30-minute structured intervention delivered by a peer educator (n=171) B. Usual Care: Participants received brief written materials about risks associated with marijuana use and a list of community resources and adolescent treatment facilities (n=170)	NR	A vs. B Cannabis use, days in past 90 days, mean, (SD): 11.0 (18.7) vs. 11.9 (19.3), between group difference NR, p=NR	A vs. B Cannabis related consequences (using Rutgers Marijuana Problem Index- how many times from 0 [never] to 4 [more than 10] each of 18 negative consequences was experienced in the last three months), mean (SD): 2.59 (3.69) vs. 2.19 (2.95); between group difference NR, p=NS (value NR)	NR	None reported

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Lee, 2013[52]	A. In-person personalized feedback: 1-hour intervention designed to provide the opportunity to discuss their cannabis use and review personalized graphic feedback. Facilitators used MI principles. (n=121) B. Control: assessment only (n=121)	NR	A vs. B Cannabis use, days in past 30 days, mean (SD), 6 months: 13.2 (10.6) vs. 11.7 (11.1), RR=1.11 (0.85 to 1.43) (negative binomial model) Mean change, 3 months: -0.6 (2.2) vs. -0.2 (2.3) Difference -0.39 (-1.04 to 0.27) Mean change, 6 months: -0.8 (2.2) vs. -0.9 (2.4) Difference 0.15 (-0.54 to 0.84) Joints smoked (Number of joints smoked during a typical week), mean (SD): 7.3 (8.4) vs. 7.5 (10.7), RR=1.46 (0.73 to 1.46) (negative binomial model)	A vs. B Cannabis-related problems, (18 items from Rutger's Marijuana Problem Index with categorical responses from 1 [never] to 5 [more than 10 times] plus 10 study-developed items unique to the physical and motivational effects of marijuana use with binary coding of 0 (not experienced) and 1 (experienced)) mean, (SD): 6.54 (5.3) vs. 6.75 (6.5), RR=1.15 (0.9 to 1.47), p=NS (value NR)	NR	None reported
Litt, 2005[103] Marijuana Treatment Project	A. MET + CBT (n=NR) B. MET (n=NR) C. Delayed treatment (n=NR)	NR	A vs. B vs. C Significantly more continuous abstinence in both treatment groups compared to control ($p<0.01$), with no difference between active treatments	NR	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Litt, 2008[101] Kadden, 2007[121]	A. MET, cognitive behavioral skills training, and contingency management (n=63) B. MET and cognitive behavioral skills training (n=61) C. Contingency management (n=54) D. Case management control (n=62)	A vs. B vs. C vs. D Attended post-treatment assessment: 94% (59/63) vs. 90% (55/61) vs. 93% (50/54) vs. 87% (54/62)	A vs. B vs. C vs. D 90-day abstinence (self-report): 23.7% vs. 21.8% vs. 18.4% vs. 13.0% at 5 months, 23.2% vs. 18.5% vs. 12.2% vs. 15.1% at 8 months, 25.3% vs. 15.4% vs. 12.5% vs. 15.4% at 11 months, and 27.6% vs. 20.4% vs. 12.5% vs. 19.2% at 14 months Narrative report of no significant treatment effect on proportion of days abstinent, joints smoked per day, cannabis Problems Scale, or the ASI	NR	NR	NR
Litt, 2013[102]	A. MET, cognitive behavioral skills training, and contingency reinforcement for completing homework assignments (n=71) B. MET, cognitive behavioral skills training, and contingency reinforcement for providing cannabis-free urine samples (n=73) C. Case management without MET or substance abuse skills training (n=71)	Retained in care: 86% (61/71) vs. 82% (60/73) vs. 86% (61/71)	Narrative report of no differences among groups in continuous abstinence, proportion of days abstinent, or Cannabis Problem Scale scores	NR	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Lozano, 2006[104]	A. CBT relapse prevention (n=117) B. MET (n=88) C. Delayed treatment control (n=86)	Retention at end of treatment (16 weeks): 86% (NR by group)	Stratified analysis by baseline treatment goals (complete abstinence, moderate use, or non-moderate use) showed that those with abstinence goals were more likely to abstain and those with moderate goals were more likely to moderate.	Significant improvement in self-reported dependence symptoms ($p<0.05$) Significant improvement in problems related to cannabis use ($p<0.01$)	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Marsden, 2006[105]	A. Brief adapted motivational intervention, manual guided, plus standard printed health risk information (n=166) B. Received printed health risk information (n=176) All received £15 plus travel expenses at recruitment and again at followup	NR	A vs. B - no significant effects Abstinence in last 90 days via Maudsley Addiction Profile (self-report, random sample verified by saliva testing) Ecstasy: 42.8% (71/166) vs. 43.8% (77/176), RR 0.98 (95% CI 0.77 to 1.25) Cocaine powder: 51.8% (86/166) vs. 44.3% (78/176), RR 1.17 (95% CI 0.94 to 1.46) Crack cocaine: 81.3% (135/166) vs. 72.7% (128/176), RR 1.12 (95% CI 0.99 to 1.26) Cannabis: no between subject differences at followup, RR 0.76 (95% CI 0.44 to 1.29) No. days used in previous 90 days (days): Ecstasy: 8.20 (SD 13.5) vs. 8.70 (SD 13.2) Cocaine powder: 5.54 (SD 11.5) vs. 7.40 (SD 12.6) Crack cocaine: 4.67 (SD 15.1) vs. 5.73 (SD 15.8) Cannabis: 52.01 (SD 36.5) vs. 57.24 (SD 36.3) Amount used in previous 90 days: Ecstasy: 1.53 vs. 1.44 tablets Cocaine powder: 0.40 vs. 0.49 grams Crack cocaine; 0.11 vs. 0.18 grams Cannabis: 3.34 vs. 3.23 grams	NR	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Martin, 2008[106]	A. "The Adolescent Cannabis Check-Up"; a brief, manualized, motivational and cognitive behavioral intervention, consisting of 2 sessions. Optional discussion of skills for quitting drug use (n=20) B. Delayed treatment control (n=20) All participants were given a $25 gift card at completion of the 3 month interview	NR	A vs. B Days of cannabis use in past 90 days: 54.3 (SD 36.1) vs. 54.5 (SD 31.6); change -19.6 (28.6) vs. -1.2 (23.3), p=0.032 Mean cones used per week, change scores: -29.0 vs. -14.0, p=0.021	A vs. B Cannabis dependence symptoms (DSM-IV, 0 to 11): 3.8 (SD 2.8) vs. 4.2 (SD 2.0); change -2.1 vs. -0.6, p=0.04 Cannabis dependence (DSM-IV): 65% vs. 80%; change -35% vs. -5%	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Martino, 2018[54]	A. In-person brief intervention based on MI. Following screening, 1 20 minute intervention based on MI to support the importance of, and a woman's confidence in, cutting down or quitting substances and obtaining treatment. (n=145) B. Computer-based brief intervention. Following screening, 1 20 minute computer-based, self-directed intervention based on MI to support the importance of, and a woman's confidence in, cutting down or quitting substances and obtaining treatment. The electronic sessions featured an interactive, 3-dimensional, mobile narrator that delivered the intervention. (n=143) C. Usual care. Received 2 minute interaction based on their ASSIST score and told about local treatments. (n=151)	NR	Substance use, days per month (Any substance use including nicotine, cannabis, alcohol, and other drugs), mean, (95% CI): A vs. C: 16.3 (14.4 to 18.5) vs. 17.9 (16.1 to 19.9), β=-0.032 (-0.115 to 0.052), p=0.461 B vs. C: 16.3 (14.3 to 18.7) vs. 17.9 (16.1 to 19.9), β=-0.016 (-0.068 to 0.100), p=0.706	NR	NR	NR
Mason, 2015[55] Mason, 2017[119]	A. Peer Network Counseling: MI guided by 5 key MI clinical issues: rapport, acceptance, collaboration, reflections, and non-confrontation. (n=59) B. Attention control (n=60)	NR	A vs. B Cannabis use, days (0-7) Cohen's d effect size: 1.17 vs. 1.33 SD and p-value NR	NR	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
McCambridge, 2004[108] McCambridge, 2005[32]	A. MI, single session adapted from work of Miller & Rollnick 1991 and Rollnick 1992 (n=105) B. Non-intervention education-as-usual control (n=95)	A vs. B Retained at 12 weeks: 92% (97/105) vs. 86% (82/95)	A vs. B, 3 months Frequency of cannabis use (per week): 5.4 vs. 16.9; change -66% vs. -27%, p<0.0001 for difference Discontinued cannabis use (self-report): 16% (16/97) vs. 5% (4/82); RR 3.38 (95% CI 1.18 to 9.72) Quantity consumed per week, MD: -1/8 of an ounce;p=0.031 Days without any cannabis use, MD: -4 days per month; p=0.008 First-time use of illicit drugs: 6% (6/97) vs. 9% (7/82) Any stimulant use: 24% vs. 41% (no difference from baseline) Other non-stimulant drug use: 11% vs. 27% (p NR for difference relative to baseline use) A (n=84) vs. B (n=78), 12 months Mean frequency of cannabis use, per week: 8.6 (SD 13.3) vs. 11.9 (SD 20.3), p>0.01 Amount of cannabis consumption, per week: 0.21 (SD 0.3) vs. 0.30 (SD 0.56), p>0.01 Number of days abstinent, per month: 17.8 (SD 10.3) vs. 13.7 (SD 11.7), p=0.02 Persons that ceased use of marijuana: 16.7% (14/84) vs. 7.7% (6/78), p=0.08 Initiated heroin use during the study period (excluded at baseline): 2.6% (2/78) vs. 7.1% (5/70)	NR	A vs. B Sold drugs to friends: 15% vs. 40%, OR 0.42, p=0.008 Sold drug to people who were not friends: 7% vs. 14%, OR 0.45, p<0.1 Parent/family problems: B=0.25, p=0.039 Interactional problems (college staff, peers, police, parents or family, local adults, partners, others): B=0.57, p=0.045	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
McCambridge, 2008[107]	A. MI (n=164) B. Control, received drug information on harm reduction and advice (n=162)	NR	A vs. B Cannabis, prevalence: 72% (118/164) vs. 78% (127/162). p=0.174 Cannabis, mean 30-day frequency: 14.6 (SD 11.7) vs. 15.9 (SD 11.6) at 3 months, difference 0.53 (95% CI -1.23 to 2.29); 13.8 (SD 11.9) vs. 14.5 (SD 11.8) at 6 months, difference -0.28 (95% CI -2.90 to 2.35), p=0.818 Drug use days, change, at 3 months: -0.7 (2.5) vs. -0.6 (2.5); Difference -0.12 (-0.67 to 0.44) Drug use days, change, at 6 months: -0.8 (2.6) vs. -0.9 (2.6); Difference 0.07 (-0.49 to 0.63) Cannabis, mean joints past week: 10.1 (SD 12.4) vs. 10.1 (SD 12.8) at 3 months, difference -0.84 (95% CI -2.33 to 0.66); 8.5 (SD 11.1) vs. 10.5 (SD 14.7) at 6 months, difference 1.33 (95% CI -1.72 to 4.38), p=0.354 Abstinent from cannabis (self-report): 21% (35/164) vs. 16% (26/162) at 3 months, RR 1.33 (95% CI 0.84 to 2.10); 28% (46/164) vs. 22% (35/162) at 6 months, RR 1.30 (95% CI 0.89 to 1.90)	A vs. B SDS (dependence): 3.4 (SD 3.0) vs. 3.5 (SD 3.2) at 3 months, difference -0.32 (95% CI -1.04 to 0.40); 3.6 (SD 3.2) vs. 3.4 (SD 3.2) at 6 months, difference -0.61 (95% CI -1.35 to 0.12), p=0.093 Cannabis, mean problems score, Cannabis Problems Questionnaire: 5.0 (SD 4.1) vs. 5.3 (SD 4.3) at 3 months, difference 0.04 (95% CI -0.61 to 0.70); 4.7 (SD 4.2) vs. 5.2 (SD 4.5) at 6 months, 0.23 (95% CI -1.11 to 1.58), p=0.708	A vs. B Cannabis, mean interactional problems score, self attributed: 0.6 (1.1) vs. 0.8 (1.3), difference 0.12 (95% CI -0.21 to 0.45), p=0.431	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Ondersma, 2007[56]	A. Computer-based brief intervention: three components based on MI and brief intervention principles: (1) feedback regarding the negative consequences of drug use that the participant reported, as well as self-reported readiness to change, and drug use as compared to that of all adult women; (2) pros and cons of drug use and related change, in which the participant chose from lists of positive and negative aspects of drug use from their perspective; and (3) a summary and query regarding the participant's interest in change, followed by optional goal-setting regarding drug use (n=55) B. None. Control group received no intervention (n=52)	NR	A vs. B Any drug use, n(%): 26 (67.6) vs. 31 (83.7), OR=2.48 (0.59 to 10.42), p=NR, NS Any cannabis use, n (%): 26 (66.1) vs. 29 (78.0), OR=2.13 (0.58 to 7.78), p=NR, NS Any other (non-cannabis) drug use, n (%): 4 (9.9) vs. 8 (21.3), OR=2.41 (0.66 to 8.83), p=NR, NS Any drug use frequency: effect size=0.46 (0.15 to 1.53), p=0.042 Cannabis use frequency (Categorical responses where 0=never, 1=once or twice, 2=monthly, 3=weekly, and 4=daily or almost daily), mean (SD): 1.91 (NR) vs. 2.08 (NR), effect size=0.39 (0.01 to 0.97), p=0.202 Other (non-cannabis) drug use frequency (Categorical responses where 0 = never, 1=once or twice, 2=monthly, 3=weekly, and 4=daily or almost daily), mean (SD): 0.11 (NR) vs. 0.34 (NR), effect size= 0.40 (0.02 to 0.78), p=0.032	NR	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Ondersma, 2014[58]	A. Computer-based personalized feedback combining CBT and MET (eCHECKUP TO GO): 6 30-minute individual behavioral therapy sessions that involved a combination of MET and CBT (n=72) B. Attention control: 1 minute of brief advice based on a manualized version of standard interventions offered by obstetrical doctors and nurses (n=71)	NR	A vs. B Abstinence (self-report and urine), 3 months: 26.4% (19/72) vs. 9.9% (7/71); RR 2.68 (95% CI 1.20 to 5.97); 6 months: 13.9% (10/72) vs. 9.9% (7/71); RR 1.41 (95% CI 0.57 to 3.49) Drug use days in the past 3 months, median: 31.6 vs. 77.2, Effect size=0.57, p=0.207	NR	NR	None reported

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Ondersma, 2018[57]	A. Computer-based brief intervention focused on parenting patterned after MI principles and was tailored to each participant. Participants received a video-based orientation ("The Parent Check-up"), tailored to their ethnic identity and religiosity. The video touched on substance use but did not focus on it exclusively. Participants received feedback and offered the option of changing in 1 of the 4 areas or ending The Parent Check-up (n=252) B. Attention control: Participants watched educational videos about infant nutrition from birth to age 1 (i.e., breastfeeding, formula feeding, when to introduce solids) with no mention of safety, emotional health, or substance use (n=248)	65.30%	A vs B, Abstinence, drug use Any in past 3 months Self-report: 46.8% (118/252) vs. 48.0% (119/248) 3 months, RR 0.98 (95% CI 0.81 to 1.17); 52.0% (131/252) vs. 50.8% (126/248) 6 months, RR 1.02 (95% CI 0.86 to 1.21) Urine: 55.2% (139/252) vs. 52.8% (131/248) 3 months and 6 months, RR 1.04 (95% CI 0.89 to 1.23) Hair: 21.8% (55/252) vs. 20.2% (50/248) 3 months, RR 1.08 (95% CI 0.77 to 1.52); 29.0% (73/252) vs. 27.8% (69/248) 6 months, RR 1.04 (95% CI 0.79 to 1.38) Cannabis in past 3 months Self-report: 48.0% (121/252) vs. 48.0% (119/248) 3 months, RR 1.00 (95% CI 0.83 to 1.20); 53.0% (134/252) vs. 52.8% (131/248) 6 months, RR 1.01 (95% CI 0.85 to 1.19) Urine: 59.1% (149/252) vs. 56.0% (139/248) 3 months, RR 1.05 (95% CI 0.91 to 1.23); 59.1% (149/252) vs. 56.8% (141/248) 6 months, RR 1.04 (95% CI 0.90 to 1.21) Hair: 42.9% (108/252) vs. 39.9% (99/248) 3 months, RR 1.07 (95% CI 0.87 to 1.32); 44.0% (111/252) vs. 41.1% (102/248) 6 months, RR 1.07 (95% CI 0.87 to 1.31)	NR	A vs. B No difference in HIV Risk-taking Behavior Scale scores at 3 months or 6 months	No serious adverse events

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Palfai, 2014[59]	A. Computer-based personalized feedback (eCHECKUP TO GO) Following assessment, participants were provided with detailed personalized feedback about their cannabis use, including costs, norms, risks, consequences, and alternative activities. (n=54) B. Attention Control: Participants were provided minimal general health feedback regarding recommended guidelines for sleep, exercise, and nutrition (n=49)	NR	A vs. B Cannabis use, days in past 90 days, mean (SD): 29.3 (29.7) vs. 37.1 (32.4), study reported between group difference: NR, p=NR, NS	A vs. B Cannabis-related consequences, (19 items from Marijuana Problem Scale with binary coding of 0 (not experienced) and 1 (experienced)), mean (SD): 2.12 (2.51) vs. 2.97 (1.72), β=0.66 (0.53), p>0.05	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Poblete, 2017[60]	A. Brief intervention based on FRAMES: ASSIST-linked brief intervention for the substance with the highest score, and the ASSIST self-help guide, with additional information regarding substances and high-risk situation management. When 2 substances had the same score, the participant had the choice to decide which substance to receive counseling for. The intervention was based on the FRAME model, which provides specific feedback, offers a menu of options, and enhances motivation to change (n=400) B. Usual care: Participants received a pamphlet of their own choosing containing broad information on substance use risk and harm (n=406)	NR	NR	A vs. B ASSIST, total score, mean (SD): 28.1 (14.4) vs. 27.9 (15.0), MD=-0.13 (-1.47 to 1.74), p=NR, NS ASSIST, cannabis score, mean (SD): 10.4 (5.4) vs. 9.8 (6.7), MD=-.021 (-1.25 to 1.66), p=NR, NS ASSIST, cocaine score, mean (SD): 11.1 (9.2) vs. 10.3 (8.5), MD=-0.11 (-3.69 to 3.48), p=NR, NS	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Rooke, 2013[109]	A. Web-based CBT + MI, 6 modules (n=119) B. Educational control, 6 modules (n=111)	A vs. B Completed followup: 54% (64/119) vs. 52% (58/111)	A vs. B Frequency of cannabis use (days in past month): 12.05 (SD 8.99) vs. 14.11 (SD 8.79); p=0.02 Quantity (standard cannabis units in past month): 36.65 (SD 44.85) vs. 39.25 (SD 39.21); p=0.16 Abstinence (self-report) 12.4% (8/64) vs. 6.6% (4/58); p=0.06	A vs. B SDS: 5.70 (SD 3.35) vs. 6.82 (SD 3.31); p=0.01 GAIN-dependence: 2.53 (SD 1.67) vs. 3.10 (SD 1.67); p=0.047 GAIN-abuse: 1.24 (SD 1.03) vs. 1.56 (SD 1.24); p=0.01* All analyses based on complier average causal effect analyses; ITT analyses were consistent except for GAIN-abuse at 6 weeks, which was NS in ITT analysis (p=0.05)	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Roy-Byrne, 2014[61] Krupski, 2012[118]	A. In-person personalized feedback using a MI approach + telephone booster session: brief (30 minute) intervention in which interventionists used a MI approach and tailored the intervention to allow for flexibility as to which or how many drugs to target, as well as in how to guide the participant (e.g., specialty treatment, abstinence, harm reduction). The same interventionist attempted a follow-up telephone booster session within 2 weeks of the intervention (n=435) B. Enhanced usual care: participants received an illustrated handout depicting their DAST-10 drug problem severity score and list of substance abuse resources. Resembled the "notification and referral" strategy that might be implemented in high-quality usual care (n=433)	NR	A vs. B Drug use days (For the most frequently used drug), mean (95% CI): 11.5 (10.3 to 12.7) vs. 10.1 (9.0 to 11.3), OR=1.20 (0.96 to 1.50) (OR calculated using negative binomial regression models), p=NS (value NR)	A vs. B Severity of disorder (ASI -Drug) (For the most frequently used drug), mean (95% CI): 0.1 (0.1 to 0.1) vs. 0.1 (0.1 to 0.1), p=NS (value not reported) Drug treatment admissions (Excluded detoxification services): 14.1% (60/426) vs. 13.5% (57/422), OR=1.16 (0.77 to 1.73), p=0.48	A vs. B All-cause mortality: 2.3% (10/500) vs. 1.6% (7/433), OR=1.42 (0.54 to 3.78), p=0.48 Consequences-medical (scale range 0-1), mean (SD): 0.54 (0.35) vs. 0.56 (0.36), β=-0.004 (-0.050 to 0.042), p=0.86 Consequences-psychiatric (scale range 0-1), mean (SD): 0.31 (0.26) vs. 0.32 (0.26), β=0.004 (-0.026 to 0.034), p=0.79 Inpatient hospitalizations: 24.9% (106/426) vs. 23.2% (98/422), OR=1.09 (0.78 to 1.51), p=0.62 Emergency department visits: 47.8% (204/426) vs. 46.9% (198/422), OR=1.04 (0.76 to 2.06), p=0.77 Outpatient visits: 94.4% (402/426) vs. 94.5% (399/422), OR=1.00 (0.53 to 1.88), p=0.99 Consequences- employment (scale range 0-1), mean (SD): 0.78 (0.24) vs. 0.78 (0.24), β=0.006 (-0.016 to 0.028), p=0.58 Consequences- family/social (scale range 0-1), mean (SD): 0.11 (0.18) vs. 0.13 (0.20), β=-0.020 (-0.046 to 0.006), p=0.14 Consequences- legal (scale range 0-1), mean (SD): 0.04 (0.10) vs. 0.04 (0.12), β=0.000 (-0.014 to 0.014), p=0.95 Felony or gross misdemeanor arrests (n (%)): 41 (9.6) vs. 37 (8.8), OR=1.21 (0.74 to 1.98), p=0.45 HIV Risk-taking Behavior Scale risk factor ≥1: OR 0.90 (0.66 to 1.25)	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Saitz, 2014[62] Fuster, 2016[116] Kim, 2016[117] ASPIRE	A. Brief negotiated interview using some features of MI; 10- to 15-minute structured interview (n=169) B. MI + telephone booster. Participants received 30 to 45 minutes of MI with an offered 20- to 30-minute booster followup session. (n=173) C. Minimal. Participants were given contact information for Alcoholics Anonymous, Narcotics Anonymous, the hospital behavioral health clinic and emergency team, a state hotline, a city triage line, and websites for alcohol and drug screening. (n=175)	NR	Drug use days using the 30-day timeline followback, mean (SD): A vs. C: 14.2 (12.5) vs. 13.8 (12.1), IRR=0.97 (0.77 to 1.22) (IRR calculated using negative binomial regression models), p=0.81 B vs. C: 14.1 (12.1) vs. 13.8 (12.1), IRR=1.05 (0.84 to 1.32) (IRR calculated using negative binomial regression models), p=0.81 Drug use days >1 time using the 30-day timeline followback, mean (SD): A vs. C: 10.8 (12.0) vs. 9.1 (11.3), IRR=1.20 (0.86 to 1.66) (IRR calculated using negative binomial regression models), p=0.31 B vs. C: 11.1 (12.2) vs. 9.1 (11.3), IRR=1.18 (0.86 to 1.65) (IRR calculated using negative binomial regression models), p=0.31 Any drug use (n (%)) Cocaine or opiates A vs. C: 150 (94.9) vs. 150 (91.5), OR=1.65 (0.65 to 4.21), p=0.57 B vs. C: 152 (93.2) vs. 150 (91.5), OR=1.29 (0.54 to 3.06), p=0.57 Abstinence, 6 months (hair testing), (A + B) vs. C: 6.3% (19/303) vs. 9.2% (14/152)	Severity of disorder (ASSIST score) Scale range 0-273, lower scores indicate better outcomes, mean (SD) A vs. C: 24.8 (17.1) vs. 25.8 (19.4), p=0.50 B vs. C: 25.9 (19.9) vs. 25.8 (19.4), p=0.50 Consequences (0-45, measured with the Short Inventory of Problems; higher score indicates worse outcome, mean [SD]) A vs. C: 12.1 (13.8) vs. 9.4 (12.1), IRR=0.95 (0.71 to 1.26), p=0.71 B vs. C: 12.7 (13.7) vs. 9.4 (12.1), IRR=1.11 (0.83 to 1.47), p=0.71 Receipt of any addiction treatment A vs. C: 17.8% (31/174) vs. 16.9% (30/178), OR=1.11 (95% CI 0.57 to 2.15), p=0.76 B vs. C: 9.6% (17/177) vs. 16.9% (30/178), OR=0.36 (0.17 to 0.78), p=0.02	Anxiety, OASIS score ≥8, A vs. C: 29% (49/169) vs. 33.7% (59/175), RR 0.86 (95% CI 0.63 to 1.18); B vs. C: 31.8% (55/173) vs. 33.7% (59/175), RR 0.94 (95% CI 0.70 to 1.27) Depression, A vs. C: 25.4% (43/169) vs. 32.6% (57/175), RR 0.78 (95% CI 0.56 to 1.09); B vs. C: 30.8% (53/173) vs. 32.6% (57/175), RR 0.94 (95% CI 0.69 to 1.28) Health-related QOL (0 to 100, higher value indicates better outcome), A vs. C: 71.5 (19.4) vs. 72.1 (20.6), study-reported group difference, p=NS (value NR), B vs. C: 68.5 (20.7) vs. 72.1 (20.6), study-reported group difference, p=NS (value NR) ED visit for addiction or mental health, A vs. C: 7.7% (13/169) vs. 9.7% (17/175), OR=0.79 (95% CI 0.36 to 1.76), B vs. C: 6.4% (11/173) vs. 9.7% (17/175), OR=0.63 (95% CI 0.27 to 1.44) Hospitalization for addiction or mental health, A vs. C: 5.9% (10/169) vs. 4.6% (8/175), OR=0.95 (95% CI 0.29 to 3.09), B vs. C: 7.0% (12/173) vs. 4.6% (8/175), OR=1.44 (95% CI 0.49 to 4.42) Specialty treatment for addiction or mental health, A vs. C: 31.4% (53/169) vs. 25.1% (44/175), OR=1.41 (95% CI 0.83 to 2.39), B vs. C: 29.5% (51/173) vs. 25.1% (44/175), OR=0.98 (95% CI 0.57 to 1.68) No difference between groups at 6 months in rates of unsafe sex	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Schaub, 2015[110] Can Reduce	A. Self-help with chat, based on MI and CBT (n=114) B. Self-help without chat, based on MI and CBT (n=101) C. Waitlist control (n=93)	A vs. B vs. C Attended followup: 33% (38/114) vs. 41% (41/101) vs. 41% (38/93)	A vs. B vs. C Cannabis use (days per week): 3.8 (SD 3.0) vs. 5.5 (SD 2.3) vs. 5.3 (SD 2.5) vs. 5.4; p=0.03 for A vs. C, p=0.87 for B vs. C Cannabis use (standardized cannabis joints): 10.9 (SD 13.8) vs. 14.2 (SD 13.3) vs. 20.7 (SD 23.7); p=0.06 for A vs. C, p=0.12 for B vs. C Abstinence (self-report): 8.8% (10/114)vs. 2.0% (2/101) vs. 4.3% (4/93); A vs. B, OR 0.21 (95% CI 0.02 to 2.33)	A vs. B vs. C Cannabis Use Disorders Identification Test, (0 to 40, >8=cannabis use disorder): 12.6 (SD 8.4) vs. 13.0 (SD 7.4) vs. 16.0 (SD 7.2) SDS: 5.3 (SD 3.8) vs. 6.0 (SD 3.3) vs. 5.9 (SD 3.8)	A vs. B vs. C Mental Health Inventory-5: 62.4 (SD 19.8) vs. 63.4 (SD 20.4) vs. 64.6 (SD 18.3)	NR
Stein, 2009[111]	A. MI, 4 sessions (n=97) B. Written handout of treatment resources (n=101)	A vs. B Completed 6 months treatment: 83% vs. 79%	A vs. B Change in cocaine days in last month: 7.6 (SD 10.9) vs. 5.6 (SD 10.9); p=0.21 Any cocaine reduction: 61.9% (60/97) vs. 56.4% (57/101); p=0.44 ≥50% cocaine reduction: 55.7% (54/97) vs. 46.5% (47/101); p=0.20 Abstinence at 6 months (self-report): 33.0% (32/97) vs. 25.7% (26/101); p=0.26 Subgroup of patients with 15+ days of cocaine use at baseline Change in cocaine days: 13.1 (SD 11.6) vs. 8.2 (SD 11.0); p=0.02 *other outcomes remained non-significant	A vs. B Any drug treatment: 17.5% (17/97) vs. 19.8% (20/101); p=0.68	SF-12 mental functioning and physical functioning components: No differences between groups (data not provided) Days employed: No difference (data not provided)	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Stein, 2011[63]	A. MI: Participants received 2 45-minute MI sessions spaced 1 month apart (n=163) B. Control: assessment only (n=169)	NR	Likelihood of marijuana use, B vs. A: OR 1.28 (95% CI 0.76 to 2.17)	A vs. B Cannabis-related consequences, 19 items from Marijuana Problem Scale with categorical responses of 0 (experiencing none), 1 (minor), or 2 (major), mean (SD): NR vs. NR, p=0.89	NR	NR
Stephens, 2000[33]	A. Relapse Prevention Support Group: combination CBT and social support (n=117) B. Individualized Assessment and Advice: sessions with therapist feedback, MI and advice on CBT techniques (n=88) C. Delayed treatment control (n=86)	A vs. B vs. C Participants still in study, 4-month followup: 81% (95/117) vs. 85% (75/88) vs. 92% (79/86)	A vs. B vs. C Cannabis use in last month (days): 6.68 (SD 9.87) vs. 7.88 (SD 10.98) vs. 17.09 (SD 10.73); A vs. C p<0.001; B vs. C p<0.001 Cannabis use, times used per day (1 to 4 scale, 4=6 or more times): 1.15 (SD 1.10) vs. 1.19 (SD 1.18) vs. 1.97 (SD 1.09); A vs. C and B vs. C, p<0.001 Abstinent during past 4 weeks (self-report): 43.6% (51/117) vs. 38.6% (34/88) vs. 17.4% (15/86); p<0.001	A vs. B vs. C Marijuana Dependence Scale (0-9): 1.96 (SD 2.73) vs. 1.94 (SD 2.71) vs. 4.63 (SD 2.59); A vs. C p<0.001; B vs. C p<0.001	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Stephens, 2007[112]	A. Personal feedback: therapist reviewed a personal feedback report with the participant (n=62) B. Attention control (multi-media feedback): a balanced presentation of the multiple points of view on the consequences associated with marijuana use; participants were invited to ask questions at any time but no feedback regarding the participant's use of marijuana was provided and therapists avoided using MI techniques (n=62) C. Delayed feedback: educational control condition that provided information about the latest research on marijuana delivered in an objective, stimulating, but largely didactic manner. (n=64)	NR	A vs. B Days of marijuana use/week, 6 months: 4.90 (SD 2.04) vs. 5.22 (SD 1.82); p=NS Days of marijuana use/week, 12 months: 4.65 (SD 1.98) vs. 5.58 (SD 2.04); p<0.05	A vs. B Dependence symptoms, 6 months (DSM-IV dependence symptoms, 0-7): 2.59 (SD 1.64) vs. 3.26 (SD 1.61); p<0.05 Dependence symptoms, 12 months: 2.43 (SD 1.29) vs. 2.88 (SD 1.32); p<0.05 Marijuana Problem Scale, 6 months (0-19): 4.06 (SD 3.16) vs. 5.46 (SD 3.08); p=NS (value NR) Marijuana Problem Scale, 12 months: 3.95 (SD 2.80) vs. 5.21 (SD 2.89); p=NS (value NR)	NR	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Tait, 2015[113]	A. MET + CBT (n=81) B. Waitlist (n=79)	A vs. B Retention at 6 months: 47% (38/71) vs. 52% (41/79); p=NS	A vs. B Abstinence from amphetamine-type stimulants at 6 months (self-report): 13.2% (5/38) vs. 19.5% (8/41) Amphetamine-type stimulants score, mean: 13.8 (SD 9.6) vs. 12.8 (SD 11.1); p=0.65 for group x time Polydrug use, mean: 4.5 (SD 2.1) vs. 4.4 (SD 1.9); p=0.68 for group x time	NR	A vs. B QOL (EUROHIS): 27.3 (SD 6.8) vs. 28.6 (SD 6.8); p=0.69 for group x time	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Tzilos Wernette, 2018[64]	A. Health Checkup for Expectant Moms: computerized program in a MI-consistent style (Intervention addressed both sexually transmitted infection/HIV and alcohol/drug risk). Participants interacted with a computer and were guided by an animated narrator, which engages in a MI-consistent style, can use emotionally expressive statements and empathic reflection. Participants also received brochures specifically designed to facilitate health risk behaviors during pregnancy (n=31) B. Attention control: participants interacted with the computer and were guided by the same narrator used for intervention group participants. Participants also received brochures specifically designed to facilitate health risk behaviors during pregnancy (n=19)	NR	A vs. B Alcohol or cannabis abstinence, by timeline follow-back self-report: 77.4% (24/31) vs. 57.9% (11/19); RR 1.34 (95% CI 0.87 to 2.05)	NR	A vs. B Condomless vaginal sex: 73% vs 95%; p=0.127	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Walton, 2013[65] Project Chill	A. In-person personalized feedback using MI (The intervention, delivered by a therapist and facilitated by a computer, incorporated MI, including tailored, parallel content. The therapist used an elicit-provide-elicit framework when reviewing tailored feedback, using summaries and open-ended questions to evoke change talk (n=118) B. Computer-based personalized feedback (n=100) C. Usual care (n=110)	NR	Cannabis use frequency (0=never, 1=1–2 days, 2=once a month or less, 3=2–3 days per month, 4=1–2 days per week, 5=3–5 days per week, and 6=every day or almost every day), mean (SD): A vs. C: 2.63 (2.20) vs. 2.14 (2.21), MD 0.15 (SE 0.14), p=0.28 B vs. C: 2.04 (2.20) vs. 2.14 (2.21), MD -0.03 (SE 0.16), p=0.85 Other drug use frequency (0=never, 1=1–2 days, 2=once a month or less, 3=2–3 days per month, 4=1–2 days per week, 5=3–5 days per week, and 6=every day or almost every day), mean (SD): A vs. C: 0.38 (1.70) vs. 0.64 (2.12), MD 0.33 (0.51), p=0.52 B vs. C: 0.48 (2.13) vs. 0.64 (2.12), MD 0.21 (0.48), p=0.66	Cannabis-related consequences (0-28; Included 23 items from the adapted version of the Rutgers Alcohol Problems Index (Marijuana Problem Inventory) and 5 items from the SDS where endorsement of an item=1 and no endorsement=0. Low value indicates better outcome), mean (SD): A vs. C: 11.1 (13.0) vs. 11.5 (14.4), MD -0.07 (0.15), p=0.62 B vs. C: 12.7 (13.8) vs. 11.5 (14.4), MD 0.08 (0.17), p=0.62	Frequency of cannabis DUI (0=never, 1=1–2 times, 2=3–5 times, 3=6–9 times, 5=10 or more times), mean (SD): A vs. C: 0.33 (0.90) vs. 0.25 (0.85), MD -0.32 (0.41), p=0.44 B vs. C: 0.45 (0.99) vs. 0.25 (0.85), MD -0.17 (0.44), p=0.70	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Watkins, 2017[66] SUMMIT	A. Collaborative care: the intervention included a population-based management approach, measurement-based care, and integration of addiction expertise through a RAND-based clinical psychologist affiliated with the MI Network of Trainers (n=138) B. Usual care: participants were told by the research team that the clinic provided opioid and/or alcohol use disorder treatment and given a number for appointment scheduling and list of community referrals. They did not receive any additional outreach or contact (n=123)	93% met with care coordinator; 69.2% followed up	A vs. B Opioid or alcohol abstinence: 32.8% (45/138) vs. 22.3% (27/123) effect size=0.12 (0.01 to 0.23), p=0.03 Opioid, any alcohol, cocaine, methamphetamine, and marijuana abstinence: 26.3% (36/138) vs. 15.6% (19/123), effect size=0.13 (0.03 to 0.23), p=0.01 Opioid abstinence: 88.7% (122/138) vs. 79.9% (98/123), effect size=0.07 (-0.07 to 0.22), p=0.33 Heroin abstinence: 93.5% (129/138) vs. 89.4% (110/123), study-reported between group difference=NR, p=NR Prescription opioid abstinence: 89.9% (124/138) vs. 93.5% (115/123), study-reported between group difference=NR, p=NR Cocaine abstinence: 87.0% (120/138) vs. 88.6% (109/123), study-reported between group difference=NR, p=NR Methamphetamine abstinence: 90.6% (125/138) vs. 81.3% (100/123), study-reported between group difference=NR, p=NR	A vs. B Consequences, scale range 0-15 as measured with the Short Inventory of Problems; higher score indicates worse outcome: 7.0 (5.9) vs. 6.2 (5.5), effect size=1.55 (-0.21 to 3.31), p=0.08 Heroin abuse or dependence with or without co-occurring alcohol or prescription opioid/heroin abuse or dependence: 24.6% (34/138) vs. 29.3% (36/123), RR 0.84 (95% CI 0.56 to 1.26) Prescription opioid use or dependence with or without co-occurring alcohol or prescription opioid/heroin abuse or dependence: 18.1% (25/138) vs. 13.8% (17/123), RR 1.31 (95% CI 0.74 to 2.31)	A vs. B Mortality: 0.7% (1/138) vs. 1.6% (2/123) Emergency department visit or hospital stay: 19.6% (27/138) vs. 22.8% (28/123), RR 0.87 (95% CI 0.55 to 1.39) QOL, mental health component (as measured by SF-12), mean (SD): 41.0 (12.4) vs. 40.8 (12.2), effect size=-1.61 (-5.61 to 2.39), p=0.43 QOL, physical health component (as measured by SF-12), mean (SD): 48.1 (11.5) vs. 46.7 (10.8), effect size=1.49 (-2.05 to 5.03), p=0.41	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Woolard, 2013[67] Project Reduce	A. MI: 2 brief interventions guided by the principles of MI. The goal of the first brief intervention was to engage the participant in reflection upon the pros and cons of alcohol and marijuana use. The focus of the second brief intervention session was to review and reinforce the change and create a change plan with those who had not made a change plan in the first session (n=206) B. Usual care: participants received routine emergency care for their presenting medical complaint and were offered information on local treatment resources for substance misuse (n= 220)	NR	A vs. B Alcohol and cannabis conjoint use in past 30 days, mean (95% CI): 1.3 (0.8 to 1.5) vs. 2.2 (1.6 to 2.9), study-reported between group difference=NR, p=0.02 Cannabis use in past 30 days, mean (95% CI): 9.4 (7.8 to 11.0) vs. 10.0 (8.4 to 11.6), study-reported between group difference=NR, p=0.83 Heavy cannabis use in past 30 days (with or without co-occurring alcohol or prescription opioid/heroin abuse or dependence), mean (95% CI): 3.2 (2.2 to 4.5) vs. 3.6 (2.5 to 5.0), study-reported between group difference=NR, p=0.30	A vs. B Negative consequences, total: 2.5 (SD 2.4) vs. 2.8 (SD 2.2) at 3 months, 2.1 (SD 2.2) vs. 2.3 (SD 2.2) at 12 months, p=NS (value NR) Negative consequences, marijuana: 1.4 (SD 1.7) vs. 1.3 (SD 1.6) at 3 months, 1.0 (SD 1.61) vs. 0.97 (SD 1.4) at 12 months, p=NS (value NR)	A vs. B Cannabis-related injuries: 1.7 vs. 1.5, study-reported between group difference=NR, p=NS (value NR)	NR

Appendix B11. Psychosocial Trials—Results

Author, year Study	Intervention described and comparisons Ns	Retention in care	Drug use abstinence/frequency	Drug use severity	Clinical health, social or legal outcomes	Adverse events
Yonkers, 2012[68]	A. MET-CBT: MET, functional analysis, safe sexual behavior, communication skills, relapse prevention and problem solving skills. Research nurse therapists had the flexibility to offeradditional sessions or repeat topics if there was time and need (n=92) B. Brief advice: a manualized version of standard interventions offered by obstetricaldoctors and nurses (n=91)	NR	A vs. B % of days using drugs or alcohol, mean (SD), at 3 month followup: 13 (SD 24) vs. 14 (SD 25); At delivery: 7 (SD 22) vs. 6 (SD 17) Abstinence from alcohol and drugs (self-report and urine): 32.8% (21/64) vs. 34.4% (22/64) Abstinence from drugs (urine): 59.4% (38/64) vs. 51.6% (33/64) Abstinence from alcohol and drugs (self-report): 40.8% (29/64) vs. 37.5% (27/64)	NR	NR	NR
Zahradnik, 2009[69] Otto, 2009[120]	A. MI: Participants received 2 MI sessions. The first 30-45 minute session took place in the hospital; the second session, 4 weeks later, was conducted by phone. The intervention was based on the Transtheoretical Model of behavior change. Participants received an individualized feedback letter 8 weeks after the first intervention. which was sent to study participants 8 weeks after the first intervention (n=56) B. Usual care: informational booklet about prescription drugs (n=70)	NR	A vs. B Prescription drug abstinence (based on hair sample), 3 months: 17.9% (10/56) vs. 8.6% (6/70); RR 2.08 (95% CI 0.81 to 5.38); 12 months: 25% (14/56) vs. 20% (14/70); RR 1.25 (95% CI 0.65 to 2.40)	NR	A vs. B Mortality: 1.8% (1/56) vs. 0% (0/70)	NR

Appendix B11. Psychosocial Trials—Results

Abbreviations: ASI = Addiction Severity Index; ASPIRE = The Assessing Screening Plus Brief Intervention's Resulting Efficacy to Stop Drug Use study; ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; CAHL = Project Cannabis Assistance Help Line; CBT = cognitive behavioral therapy; CI = confidence interval; DAST-10 = Drug Abuse Screening Test; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; DUI = driving under the influence; EUROHIS = EUROHIS quality of life 8-item index; FRAME = Feedback, Responsibility, Advice, Menu Options, Empathy, and Self-Efficacy; GAIN = Global Appraisal of Individual Needs; GHQ-28 = 28-item General Health Questionnaire; IRR = incidence rate ratio; ITT = intention to treat; MD = mean difference; MET = motivational enhancement therapy; MI = motivational interviewing; MOTI-4 = brief motivational enhancement intervention designed for young vulnerable non-treatment-seeking cannabis users; NR = not reported; NS = not significant; OASIS = Overall Anxiety Severity and Impairment Scale; OR = odds ratio; OTI = Opioid Treatment Index; QOL = quality of life; QUIT = Quit Using Drugs Intervention Trial; RAND = RAND (Research and Development) Corporation; RR = risk ratio; SD = standard deviation; SDS = Severity of Dependence Scale; SE = standard error; SF-12 = 12-Item Short Form Health Survey; SMART-ED = Screening, Motivational Assessment, Referral and Treatment in Emergency Departments; SMD = standardized mean difference; SUMMIT = Substance Use Motivation and Medication Integrated Treatment study.

Appendix B12. Psychosocial Trials—Quality Assessment

Author, year	Valid random assignment/ random sequence generation methods	Allocation concealment	Balance in baseline characteristics	Fidelity to intervention protocol	Low risk of contamination between groups	Participants analyzed as originally allocated	No, or minimal, post-randomization exclusions	Outcome data reasonably complete and comparable between groups
Babor, 2004[30]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Baker, 2001a[88] Baker, 2001b[89]	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Baker, 2005[90]	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Bernstein, 2005[4]	Yes	Yes	No, and no adjustments	Yes	Yes	Yes	Yes	No
Bernstein, 2009[45]	Yes	Yes	No, but accounted for	Yes	Yes	Yes	Yes	Yes
Blow, 2017[46] Bonar, 2018[91]	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes
Bogenschutz, 2014[47] Bogenschutz, 2011[115]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Copeland, 2001a[31] Copeland, 2001b[92]	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes
D'Amico, 2018[44]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
de Dios, 2012[93]	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
de Gee, 2014[94]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Dembo, 2016[95]	Unclear	Unclear	Yes	Yes, likely	Yes	Unclear	Unclear	Unclear
Dupont, 2016[96]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Fischer, 2012[98] Fischer, 2013[97]	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes
Gates, 2012[99]	Unclear	Unclear	Yes	Yes	Yes	No	No; 11 participants excluded post-randomization	Yes
Gelberg, 2015[48] Baumeister, 2014[114]	Yes	NR	Unclear	Yes	Yes	Yes	Yes	Yes
Gelberg, 2017[49]	Yes	NR	Yes	Yes	Yes	Yes	Yes	No
Gryczynski, 2016[50]	Yes	Yes	No; not ASSIST global drug score	NR	Yes	Yes	Yes	Yes
Humeniuk, 2012[51]	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes
Jones, 2005[100]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Lee, 2010[53]	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear
Lee, 2013[52]	Yes	Unclear	Yes	No	Yes	Yes	Yes	Yes
Litt, 2005[103]	Yes; urn	Yes; central	No; not Addiction Severity Index or Beck Depression Inventory	Yes	Yes	Yes	Yes	Yes

Appendix B12. Psychosocial Trials—Quality Assessment

Author, year	Valid random assignment/ random sequence generation methods	Allocation concealment	Balance in baseline characteristics	Fidelity to intervention protocol	Low risk of contamination between groups	Participants analyzed as originally allocated	No, or minimal, post-randomization exclusions	Outcome data reasonably complete and comparable between groups
Litt, 2008[101] Kadden, 2007[121]	Yes; urn	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Litt, 2013[102]	Yes; urn	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Lozano, 2006[104]	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes; 6/291 excluded post-randomization	Yes
Marsden, 2006[105]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Martin, 2008[106]	Yes	Yes	No, treatment group reported more days of cannabis use in the past 90 than control group, p<0.019	Yes	Yes	Yes	Yes	Yes
Martino, 2018[54]	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes
Mason, 2015[55] Mason, 2017[119]	Yes	Unclear	No, but accounted for in analysis	Yes	Unclear	Yes	Yes	Yes
McCambridge, 2004[108] McCambridge, 2005[32]	Unclear	Yes	No; not dependence on illegal drugs, interactional problems with friends and family, and others	Yes	Yes	Yes	Yes	Yes
McCambridge, 2008[107]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ondersma, 2007[56]	Yes	Yes		Yes	Yes	Yes	Yes	Yes
Ondersma, 2014[58]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ondersma, 2018[57]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Palfai, 2014[59]	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	Unclear
Poblete, 2017[60]	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	No
Rooke, 2013[109]	No; drawing 1 of 2 tokens from a box	Unclear	Yes	No; nearly half lost	Yes	Yes	Yes	No
Roy-Byrne, 2014[61] Krupski, 2012[118]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Saitz, 2014[62] Fuster, 2016[116] Kim, 2016[117]	Yes	Unclear	No, but accounted for in analysis	Yes	Yes	Yes	Yes	Yes
Schaub, 2015[110]	Yes	Unclear	Yes	No; ~25% of the "chat" group received chat	Yes	Yes	Yes	No
Stein, 2009[111]	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Stein, 2011[63]	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes

Appendix B12. Psychosocial Trials—Quality Assessment

Author, year	Valid random assignment/ random sequence generation methods	Allocation concealment	Balance in baseline characteristics	Fidelity to intervention protocol	Low risk of contamination between groups	Participants analyzed as originally allocated	No, or minimal, post-randomization exclusions	Outcome data reasonably complete and comparable between groups
Stephens, 2000[33]	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes
Stephens, 2007[112]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Tait, 2015[113]	Yes; centralized	Yes	Yes; except for actual help seeking	No; about half lost	Yes	Yes	Yes	Yes
Tzilos Wernette, 2018[64]	Yes; computer	Unclear	No, but accounted for in analysis	Yes	Yes	Yes	Yes	Yes
Walton, 2013[65]	Yes; computer	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes
Watkins, 2017[66]	Yes; random number generator	Yes	No, but accounted for in analysis	Yes	Unclear	Yes	Yes	Yes (some data imputed)
Woolard, 2013[67]	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes
Yonkers, 2012[68]	Yes; computer	Yes	Unclear	Yes	Yes	Yes	Yes	Yes
Zahradnik, 2009[69] Otto, 2009[120]	Unclear	Unclear	No, and not adjusted	Yes	Yes	Yes	Yes	Yes

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Appendix B12. Psychosocial Trials—Quality Assessment

Author, year	Time point and follow-up	Reasons for missing data similar across groups	Missing data unlikely to bias results	Blinding of outcome assessors	Outcomes measured using consistent and appropriate procedures and instruments across treatment groups	No evidence of biased use of inferential statistics	No evidence that measures, analyses, or subgroup analyses selectively reported	Quality Rating
Babor, 2004[30]	4 months; 92.9% (415/450)	Yes	Yes	Yes	Yes	Yes	Yes	Good
Baker, 2001a[88] Baker, 2001b[89]	6 months; 71.4% (153/214)	Yes	Yes	Yes	Unclear	Unclear	Unclear	Fair
Baker, 2005[90]	6 months; 82.2% (60/73)	Yes	Yes	Unclear	Unclear	Unclear	Unclear	Fair
Bernstein, 2005[4]	12 months 73.4% (102/139)	Unclear	Yes: adequate handling	Unclear	Yes	Yes	Yes	Fair
Bernstein, 2009[45]	6 months: 81.9% (962/1175) 66.2% (778/1175) with data for analysis (based on confirmation of use)	Unclear	Yes: adequate handling	Yes	Yes	Yes	Yes	Fair
Blow, 2017[46] Bonar, 2018[91]	12 months: 87% (679/870)	Yes	Yes: adequate handling	Yes	Yes	Yes	Yes	Good
Bogenschutz, 2014[47] Bogenschutz, 2011[115]	12 months Total: 81.2% (1043/1285) IG1: 79.2% IG2: 81.4% CG: 82.8%	Yes	Yes: adequate handling	Yes	Yes	Yes	Yes	Fair
Copeland, 2001a[31] Copeland, 2001b[92]	6 months; 74.2% (170/229)	Yes	Yes	Yes	Yes	Yes	Yes	Fair
D'Amico, 2018[44]	12 months: 80%	Yes	Yes	Unclear	Yes	Yes	Yes	Fair
de Dios, 2012[93]	3 months; 73.5% (25/34)	Yes	Yes	Yes	Yes	Yes	Yes	Fair
de Gee, 2014[94]	3 months; 82.4% (98/119)	Yes	Yes	Unclear	Yes	Yes	Yes	Good
Dembo, 2016[95]	72%. 18 months	Unclear	Unclear	Unclear	Yes	Unclear - used modeling	Yes	Fair
Dupont, 2016[96]	83% and 73% 6 months	Yes	Yes	Unclear	Yes	Yes	Yes	Fair
Fischer, 2012[98] Fischer, 2013[97]	12 months; 53.7% (72/134)	Yes	Yes	No	Yes	Yes	Yes	Fair

Appendix B12. Psychosocial Trials—Quality Assessment

Author, year	Time point and follow-up	Reasons for missing data similar across groups	Missing data unlikely to bias results	Blinding of outcome assessors	Outcomes measured using consistent and appropriate procedures and instruments across treatment groups	No evidence of biased use of inferential statistics	No evidence that measures, analyses, or subgroup analyses selectively reported	Quality Rating
Gates, 2012[99]	4 weeks: 79% (54/68) vs. 89% (72/81)	No; more non-contactable participants in intervention group	Unclear	No	Yes	Yes	Yes	Fair
Gelberg, 2015[48] Baumeister, 2014[114]	3 months: Total: 78.1% (261/334) IG: 75.4% (129/171) CG: 83.4% (136/163)	Yes	Yes: adequate handling	Not applicable: no assessment staff involved	Yes	Yes	Yes	Fair
Gelberg, 2017[49]	3 months Total: 78.5% (51/65) IG: 71.9% (23/32) CG: 84.8% (28/33)	Unclear	Yes: adequate handling	Not applicable: no assessment staff involved	Yes	Yes	Yes	Fair
Gryczynski, 2016[50]	3 months: 89% 6 months: 84%	Yes	Yes	NR	Yes	Yes	Yes	Fair
Humeniuk, 2012[51]	3 months: 87% vs. 86%	Unclear	Yes	No	Yes	Yes	Yes	Fair
Jones, 2005[100]	26 weeks: not reported	Unclear	No; high and differential attrition	No	Yes	Yes	Yes	Fair
Lee, 2010[53]	3 months: 95% 6 months: 94%	Yes	Yes	No	Yes	Yes	Yes	Fair
Lee, 2013[52]	3 months: 85% 6 months: 83%	Unclear	Yes	No	Yes	Yes	Yes	Fair
Litt, 2005[103]	4 months: 89% 9 months: 87% 15 months: 83%	Unclear	Yes	No	Yes	Yes	Yes	Fair
Litt, 2008[101] Kadden, 2007[121]	9 weeks: 94% (59/63) vs. 90% (55/61) vs. 93% (50/54) vs. 87% (54/62)	Yes	Yes	No	Yes	Yes	Yes	Fair
Litt, 2013[102]	9 weeks: 86% (61/71) vs. 82% (60/73) vs. 86% (61/71)	Yes	Yes; low attrition	No	Yes	Yes	Yes	Fair
Lozano, 2006[104]	16 weeks: 86%	Unclear	Unclear	No	Yes	Yes	Yes	Fair
Marsden, 2006[105]	87% and 88% 6 months	Yes	Yes	Unclear	Yes	Yes	Yes	Good

Appendix B12. Psychosocial Trials—Quality Assessment

Author, year	Time point and follow-up	Reasons for missing data similar across groups	Missing data unlikely to bias results	Blinding of outcome assessors	Outcomes measured using consistent and appropriate procedures and instruments across treatment groups	No evidence of biased use of inferential statistics	No evidence that measures, analyses, or subgroup analyses selectively reported	Quality Rating
Martin, 2008[106]	80% and 80% 3 months	Yes	Yes	Unclear	Yes	Yes	Yes	Fair
Martino, 2018[54]	3 months: 97% vs. 97% vs. 96% 6 months: 89% vs. 89% vs. 86%	Yes	Yes	No	Yes	Yes	Yes	Good
Mason, 2015[55] Mason, 2017[119]	6 months: 97% vs. 100%	Yes	Yes	Not applicable: no assessment staff involved	Yes	Yes	Yes	Fair
McCambridge, 2004[108] McCambridge, 2005[32]	12 weeks: 92% (97/105) vs. 86% (82/95)	Unclear	Yes; low attrition	No	Yes	Yes	Yes	Fair
McCambridge, 2008[107]	80% and 81% 6 months	Yes	Yes	Unclear	Yes	Yes	Yes	Fair
Ondersma, 2007[56]	6 months; 69%	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Ondersma, 2014[58]	6 months; 66%	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Ondersma, 2018[57]	6 months; 65%	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Palfai, 2014[59]	6 months: 83.7% (103/123) (IG and CG NR, but says no differences)	Unclear	Yes: adequate handling	NA: no assessment staff involved	Yes	No, but within-group statistics are available	Unclear	Fair
Poblete, 2017[60]	3 months Total: 61.7% (497/806) IG: 64.8% (259/400) CG: 58.6% (238/406)	Unclear	Yes: adequate handling	Yes	Yes	Yes	Yes	Fair
Rooke, 2013[109]	12 weeks: 54% (64/119) vs. 52% (58/111)	Unclear	No; high attrition	NA; automated outcome collection	Yes	Yes	Yes	Fair
Roy-Byrne, 2014[61] Krupski, 2012[118]	6 months: 88.4% 12 months: 89.5% (777/89.5) (IG: 88.5%, CG: 90.5%)	No	Yes: good handling/low attrition	Yes	Yes	Yes	Yes	Good

Appendix B12. Psychosocial Trials—Quality Assessment

Author, year	Time point and follow-up	Reasons for missing data similar across groups	Missing data unlikely to bias results	Blinding of outcome assessors	Outcomes measured using consistent and appropriate procedures and instruments across treatment groups	No evidence of biased use of inferential statistics	No evidence that measures, analyses, or subgroup analyses selectively reported	Quality Rating
Saitz, 2014[62] Fuster, 2016[116] Kim, 2016[117]	6 months: 97.9% (517/528) (IG1: 97.1%, IG2: 97.7%, CG: 98.9%)	Yes	Yes: good handling/low attrition	NR	Yes	Yes	Yes	Good
Schaub, 2015[110]	Attended followup: 33% (38/114) vs. 41% (41/101) vs. 41% (38/93)	Yes	Unclear	No	Yes	Yes	Yes	Fair
Stein, 2009[111]	Completed 6 months treatment: 83% vs. 79%	Unclear	Yes; low attrition	No	Yes	Yes	Yes	Fair
Stein, 2011[63]	6 months; 78.9% (262/332)	Yes	Yes	Yes	Yes	No	No	Fair
Stephens, 2000[33]	4 months; 85.6% (249/291)	Yes	Yes	Unclear	Yes	Yes	Yes	Fair
Stephens, 2007[112]	12 months; 80.6% (groups A and B only; 100/124)	Yes	Yes	Yes	Yes	Yes	Yes	Good
Tait, 2015[113]	6 months: 47% (38/71) vs. 52% (41/79)	Unclear	Unclear	No	Yes	Yes	Yes	Fair
Tzilos Wernette, 2018[64]	4 months; 97% (30/31) vs. 100% (19/19)	Yes	Yes	Unclear	Yes	Yes	Yes	Fair
Walton, 2013[65]	1 year; 77% (77/100) vs. 88% (104/118)	Unclear	Yes	Yes	Yes	Yes	Yes	Fair
Watkins, 2017[66]	6 months; 74% (138/187) vs. 65% (123/190)	Unclear	Yes	Yes	Yes	Yes	Yes	Fair
Woolard, 2013[67]	12 months; 83% (206/249) vs. 83% (220/266)	Unclear	Yes	Yes	Yes	Yes	Yes	Fair
Yonkers, 2012[68]	3 months post-delivery; 95% (86/91) vs. 89% (82/92)	Yes	Yes	Unclear	Yes	Yes	Yes	Fair
Zahradnik, 2009[69] Otto, 2009[120]	12 months; 89% (50/56) vs. 89% (62/70)	Yes	Yes	Yes	Yes	Yes	Yes	Fair

Abbreviations: ASSIST = Alcohol, Smoking, and Substance Involvement Screening Test; CG = control group; IG = intervention group.

Appendix C1. Outcome Measures and Scoring

Abbreviation	Full name of outcome measure	Scale	Direction
ADI	Adolescent Diagnostic Interview	Varies according to subscale/domain	Higher score=worse outcomes
ARI	AIDS Risk Inventory	Varies according to subscale/domain	Lower score=lower risk of acquiring AIDS
ASI	Addiction Severity Index	0 to 9	Lower score=better outcomes
ASSIST	Alcohol, Smoking, and Substance Involvement Screening Test	0-39 for individual drug categories and alcohol; total score range 0-414	Higher score=higher risk of problematic drug use
BDI	Beck Depression Inventory	0 to 63	Higher score=more severe depressive symptoms
BPRS	Brief Psychiatric Rating Scale	0 to 126	Higher score=more severe psychiatric condition
CGI	Clinical Global Impressions	1 to 7	Higher score=more severe illness
COWS	Clinical Opiate Withdrawal Scale	Varies according to subscale/domain	Higher score=more severe symptoms
CPQ	Cannabis Problems Questionnaire	0 to 22	Higher score=more problems
CUDIT	Cannabis Use Disorders Identification Test	0 to 40	Higher score=more severe cannabis use disorder
CUPIT	Cannabis Use Problems Identification Test	0 to 58 and 0 to 24	Higher score=more problems and/or less control over cannabis use
DSM-IV CPS	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Compendium of Pharmaceuticals and Specialties	0 to 11	Higher score=worse mental disorder
EUROHIS	EUROHIS-QOL 8-item index	0 to 40	Higher score=better quality of life
GAIN	Global Appraisal of Individual Needs	Varies according to subscale/domain	Higher score=greater need for referral
GHQ-28	28-Item General Health Questionnaire	0 to 84	Lower score=better health
HRQOL	Health-Related Quality of Life	0 to 100	Higher score=better outcome
MAP	Maudsley Addiction Profile	0 to 240	Higher score=greater addiction severity
MDS	Marijuana Dependence Scale	0 to 9	Higher score=greater dependence on marijuana
MHI-5	Mental Health Inventory-5	0 to 100	Lower score=greater emotional functioning
MMPI	Minnesota Multifactoral Personality Inventory	Varies according to subscale/domain	Higher score=worse depression
MPS	Marijuana Problem Scale	0 to 38	Higher score=more cannabis use consequences
NIP	Noteworthy Index of Problems	0 to 19	Higher score=greater frequency of drug or alcohol use events
OASIS	Overall Anxiety Severity and Impairment Scale	0 to 20	Higher score=more severe anxiety severity and impairment
OTI	Opioid Treatment Index	Varies according to subscale/domain	Higher score=greater dysfunction
RAPI	Rutgers Alcohol Problems Index	0 to 69	Higher score=more instances of negative problems related to alcohol drinking in the past year
RMPI	Rutgers Marijuana Problem Index	Varies according to subscale/domain	Higher score=more instances of negative consequences related to drug use experienced in the last 3 months
SCL-5	Symptom Checklist-5	0 to 4	Higher score=worse anxiety and depression

Appendix C1. Outcome Measures and Scoring

Abbreviation	Full name of outcome measure	Scale	Direction
SDS	Severity of Dependence Scale	0 to 15	Higher score=higher level of dependence
SF-12	12-Item Short Form Health Survey	0 to 100	Higher score=better health
SIP-R	Short Inventory of Problems	0 to 45	Higher score=worse outcome
SOWS	Subjective Opiate Withdrawal Scale	0 to 4	Higher score=more severe symptoms
SSAI	Spielberger State-Anxiety Inventory	20 to 80	Higher score=greater anxiety
STAI	State-Trait Anxiety Inventory	0 to 160	Higher score=greater anxiety
TSLS	Temporal Satisfaction with Life Scale	0 to 7	Higher score =worse overall life satisfaction
VAS	Visual Analog Scale	0 to 10	Lower score=greater subjective wellbeing
YSR	Youth Self-Report	0 to 62 and 0 to 64	Higher score=more problems and/or fewer social competencies