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Screening in Primary Care Settings for Illicit Drug Use: Staged Systematic Review for the United States Preventive Services Task Force

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Structured Abstract

Background. Illicit drug use and abuse are serious problems among adolescents, adults, and pregnant women in the United States, and approximately 3.2% of the population age 12 and over meet criteria for a drug use disorder. Many individuals with drug use disorders have co-existing mental and physical health conditions.

Purpose. To update the 1996 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for drug misuse in primary care. The USPSTF previously concluded there was insufficient evidence to recommend for or against routine screening for drug misuse. This report describes a staged, systematic review that assessed whether the evidence for selected critical key questions is now sufficient for the USPSTF to make a recommendation on this topic.

Data sources. Ovid MEDLINE, PsycINFO, and the Cochrane Database of Systematic Reviews, from 1994 through April 2006. Literature searches were supplemented with materials recommended by experts in the field and from reference lists in included articles.

Study Selection. We developed an analytic framework and identified five critical key questions (KQ) to examine evidence sufficiency in a causal chain linking primary care screening for drug misuse to treatment outcomes and longer-term health benefits of reductions in illicit drug use. We focused on the most prevalent and/or harmful substances: illicit opiates, cocaine, and cannabis. Using inclusion/exclusion criteria specific to each critical KQ, we reviewed a total of 4587 abstracts for all key questions and 41 full-text articles for inclusion regarding direct evidence of health benefits of drug screening programs in primary care, 127 articles for inclusion regarding drug misuse treatment outcomes in primary care-screened populations, and 79 articles for inclusion regarding improvements in health or mortality following reduction in or cessation of illicit drug use. Inclusion criteria for drug misuse treatment articles required randomized controlled or controlled trial designs comparing a treatment to placebo or minimal treatment control; comparative effectiveness trials were excluded. Using USPSTF and other published methods, we critically appraised studies using quality criteria specific to their design. We listed studies excluded from analysis and rationales for their exclusion.

Data Extraction. We abstracted, critically appraised, and synthesized 28 articles meeting our criteria for all critical KQs. Abstracted elements were arrayed in evidence tables, using abstraction criteria specific to each KQ.

Data Synthesis and Results. We qualitatively summarized the findings, with an emphasis on the best available evidence for each critical KQ and the overall coherence of the evidence. We found no evidence addressing the effects on health outcomes of screening in primary care settings to identify and treat drug misuse among asymptomatic individuals. We found no evidence that drug misuse treatment affects health outcomes among individuals screened in primary care, and found little qualifying evidence in non-screened (treatment-seeking) populations. We found fair to good evidence that various drug misuse treatments—including pharmacotherapies and behavioral interventions—effectively reduce opiate, cocaine, or marijuana misuse. All but one of the 17 included drug misuse treatment trials were conducted among treatment-seeking, instead of primary-care-screened populations. The exception was a brief motivational intervention that reduced cocaine and opiate use among primary care patients

identified through screening for use of these substances. We found less consistent evidence of drug misuse treatment effects on social and legal outcomes, although behavioral counseling interventions for cannabis misuse appear to reduce cannabis-related problems. We found fair evidence that stopping or reducing drug misuse is related to reduced mortality and morbidity, although none of this evidence was derived from individuals screened for drug misuse in primary care settings.

Conclusions. Although many advances in drug misuse treatment have occurred during the past decade, the vast majority of trials have been conducted among treatment-seeking populations, and thus the relevance of outcomes from such studies is of uncertain applicability to asymptomatic primary care populations that could be screened for drug misuse. Evidence that reducing or stopping drug misuse is associated with improved health outcomes similarly derives from non-screened or treatment-seeking populations, and the generalizability of these findings to general primary care populations may be limited.

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I. Introduction

This report is a staged systematic review to update the 1996 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for drug misuse.[1] The USPSTF previously concluded there was insufficient evidence to recommend for or against routine screening for drug misuse in primary care. This report examines whether the evidence for the critical key questions is now sufficient for the USPSTF to make a recommendation on this topic.

Background

Prevalence and burden of disease

Illicit drug use and abuse are serious problems among adolescents, adults, and pregnant women in the United States. Substance Abuse and Mental Health Services Administration (SAMHSA) recently reported epidemiological data on drug use in its 2004 National Survey on Drug Use and Health (NSDUH).[2] Among persons age 12 and older in 2004, 7.9% (19.1 million) reported using illicit drugs during the past 30 days, which is essentially unchanged since 2002. However, among adolescents age 12-17 rates of illicit drug use declined slightly from 11.6% in 2002, to 10.6% in 2004. Marijuana remains the most commonly used illicit drug in the US, with 14.6 million past-month users (6.1% of those age 12 and older). Rates of use have remained stable over the past decade.[3] Among the 19.1 million past-month illicit drug users in 2004, 56.8% used marijuana only, 19.7% used marijuana with some other drug, and less than one-quarter (23.6%) used one or more illicit drugs other than marijuana.[2] While cocaine is the second most commonly used single drug, it is used by less than 1% of the population (0.8%). Although other illicit substances are similarly used by a small minority—hallucinogens (0.4%), inhalants (0.3%), heroin (0.1%)—the potential for abuse or dependence is quite high. Among past-year heroin users, 67.8% met criteria for drug abuse or dependence.[2]

Peak illicit drug use in the US occurs between the ages of 18 and 20 years, with 21.7% of people in this age range having used drugs within the last month. Percentages of the population who use drugs monthly decrease steadily with age, down to 0.6% for those aged 65 or older. Rates of illicit drug use vary significantly across racial/ethnic groups, with persons reporting more than one race having the highest rates (13.3%), followed by American Indians or Alaska Natives (12.3%), African Americans (8.7%), whites (8.1%), and Hispanics (7.2%). Men are more likely to engage in drug use than women (9.9% vs. 6.1%), but adolescent rates (age 12 to 17) of current illicit drug use are similar for boys and girls (10.6% for both).

In 2004, 4.6% of pregnant women aged 15 to 44 years reported using illicit drugs within the last month, compared to 10.2% of women in the same age range who were not pregnant.[2] A number of studies have found poor pregnancy, neonatal, and childhood outcomes among women who used illicit drugs during pregnancy.[4]

No significant changes over the past few years are reported in estimates of the percentage of the US population with dependence on or abuse of illicit drugs (3.2%). Among individuals with dependence or abuse diagnoses for any illicit drug in 2004, 61.2% were dependent upon or abused marijuana. Among past-year illicit drug users, the proportion classified with illicit drug dependence or abuse varies by specific drug: 67.8% among heroin users, 27.8% of cocaine

users, and 17.6% of marijuana users, with lower percentages for other substances, including alcohol.[2]

Burden of preventable illness/natural history

Illicit drugs, tobacco, and alcohol are responsible for more deaths, illness, and disabilities than from any other preventable condition.[5] The World Health Organization Report 2002[6] includes illicit drug use among the 10 leading preventable risk factors for years of healthy life lost and disability in developed countries.

Adverse health effects of drug use vary greatly depending on the type of drug used. These effects can range from acute cardiovascular complications, such as those seen with cocaine use, to the more controversial respiratory or amotivational syndrome seen with marijuana.[7] One study compared the prevalence of medical conditions among 747 substance abuse patients with 3,690 demographically-matched controls from the same health maintenance organization.[8] Approximately one third of the medical conditions examined were more common among substance abuse patients than among the matched controls, and several of the conditions were among the most costly. Illicit drug use can adversely affect both mother and fetus in multiple ways, including decreasing the likelihood of seeking adequate prenatal care, and reducing gestational length and birth weight.[9]

The economic cost of drug abuse in the US was $67 billion in 1990.[5] Most of the total costs of drug misuse are primarily related to costs of crime loss and incarceration. Deaths and illness account for only 17 percent of total costs, and medical costs are less than 5 percent. The costs associated with AIDS, however, represent almost 10 percent of the total and will likely continue to increase, given the role that drug misuse (e.g., needle sharing and unsafe sexual practices among IV drug users) plays in the AIDS epidemic.[5]

In addition to negative physical outcomes and economic costs, drug misuse also increases the risk for child abuse and family violence. Living with someone who abuses drugs during childhood is associated with negative long-term outcomes, including increased likelihood of illicit drug use.[10] The justice system expends enormous resources working with individuals who have been arrested for illicit-drug possession, drug trafficking, and other crimes committed while under the influence of drugs. Workplaces also suffer from reduced productivity.

The age at which drug use was initiated predicts subsequent abuse and dependence, with higher rates observed among persons who initiate use at younger ages. This trend has been observed in all demographic groups.[2]

Drug misuse is often characterized as a chronic illness, with similar issues to other chronic conditions, such as treatment adherence, relapse,[11] and potentially long-term treatment. The life course of narcotics misuse often includes light drug use, heavy drug use, abstinence, treatment engagement, methadone maintenance, incarceration, and death. Hser and colleagues conducted longitudinal research with male addicts over a 33-year period. At follow-up, 49% had died (most commonly from accidental poisoning or drug overdose), 23% were abstinent, 13% were active opiate users, and 6% were incarcerated (9% were not interviewed).[12] Less is known about the natural history for drugs other than heroin.

Condition definition

The term “drug abuse” is ambiguous, having a general meaning in the US that includes a large range of illicit substance use and associated problems, and a specific definition within the Diagnostic and Statistical Manual (DSM IV-TR).[13] For this review, we use the phrase “drug misuse” when referring to the wider range of illicit substance use, and reserve “drug abuse” for the DSM-IV-TR diagnostic designation (defined below).

Within the DSM-IV-TR, specific drug use disorders are defined within two categories: substance abuse disorders and substance dependence disorders. Criteria for these two clinical diagnoses are defined in the DSM IV-TR as follows:

Substance abuse.

A) A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12-month period:

1. Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)
2. Recurrent substance use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by substance use)
3. Recurrent substance-related legal problems (e.g., arrests for substance-related disorderly conduct)
4. Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with spouse about consequences of intoxication, physical fights)

B) The symptoms have never met the criteria for Substance Dependence for this class of substance.[13]

Substance dependence. A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring any time in the same 12-month period:

1. Tolerance, as defined by either of the following: a need for markedly increased amounts of the substance to achieve intoxication or desired effect markedly diminished effect with continued use of the same amount of the substance
2. Withdrawal, as manifested by either of the following: the characteristic withdrawal syndrome for the substance the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms
3. The substance is often taken in larger amounts or over a longer period than was intended
4. There is a persistent desire or unsuccessful efforts to cut down or control substance use
5. A great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects

6. Important social, occupational, or recreational activities are given up or reduced because of substance use
7. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption)[13]

In DSM-IV-TR, substance use includes alcohol, illicit drugs, nicotine, and caffeine. While the work presented here excludes alcohol, nicotine, and caffeine, there remains a wide range of substances included under the definition of drug misuse (see Table 1). This updated review focuses on the misuse of marijuana, cocaine, heroin, or multiple substances. These conditions were chosen based on overall prevalence of use and prevalence of problematic use as indicated by the proportion of users meeting diagnostic criteria for abuse or dependence.

Previous USPSTF recommendations

In 1996, the USPSTF concluded there is insufficient evidence to recommend for or against routine screening for drug abuse with standardized questionnaires or biologic assays (C recommendation).[1] The 1996 Task Force review addressed the following substances: illicit drugs (e.g., cocaine, heroin, phencyclidine, methaqualone, hallucinogen, marijuana), legal drugs not prescribed by a physician (e.g., amphetamines, benzodiazepines, barbiturates, and anabolic steroids), and inhalants (amyl and butyl nitrite, gasoline, nitrous oxide, glue, other solvents). The Task Force addressed three separate populations for drug misuse screening: adolescents, adults, and pregnant women.

Staged systematic review

To update this topic, we utilized an analytic framework (Figure 1) with eight Key Questions (KQs):

KQ 1. Is there direct evidence that screening for drug misuse reduces morbidity and/or mortality?
KQ 2. Do screening tests accurately detect drug misuse?
KQ 3. Does screening for drug misuse result in adverse effects?
KQ 4. Does treatment for drug misuse among individuals identified through screening improve morbidity and/or mortality?
KQ 5. Does treatment for drug misuse among individuals identified through screening result in decreased drug misuse?
KQ 5a. Does treatment for drug misuse reduce risk behaviors or improve social and legal outcomes?
KQ 6. Does treatment for drug misuse result in adverse effects?
KQ 7. Is decreased use or abstinence following drug misuse reliably associated with reduced morbidity and mortality?

For this report, we used a staged review approach that focused first on the evidence for the following five critical key questions oriented toward the health benefits of treatment and on

an overarching question determining whether there is direct evidence of benefit from screening to identify patients for treatment.

Critical key questions

KQ 1. Is there direct evidence that screening for drug misuse reduces morbidity and/or mortality?
KQ 4. Does treatment for drug misuse among individuals identified through screening improve morbidity and/or mortality?
KQ 5. Does treatment for drug misuse among individuals identified through screening result in decreased drug misuse?
KQ 5a. Does treatment for drug misuse reduce risk behaviors or improve social and legal outcomes?
KQ 7. Is decreased use or abstinence following drug misuse reliably associated with reduced morbidity and mortality?

In the logic of the staged review, if the evidence for these critical key questions is insufficient to establish the links between drug misuse identification through screening, treatment, and clinically-meaningful health benefits, further systematic review to include the other key questions in the analytic framework is unwarranted. Insufficiency of evidence for these critical key questions indicates that the overall body of evidence is insufficient for a USPSTF recommendation for drug misuse screening as a clinical preventive service in primary care. Indication of sufficient evidence for critical key questions 4, 5, 5a, and 7 indicates that a full systematic review of all key questions would be warranted.

II. Methods

Literature search and strategy

This staged review is intended to update the previous USPSTF report on drug misuse, which was based on an authoritative, but non-systematic, research review.[1] Consequently, we conducted literature searches to systematically locate relevant literature for our critical key questions as follows (see Appendix A – Search Strategies).

For key question 1, we searched Ovid MEDLINE for the time period 1994-April 2006. Randomized controlled trials (RCTs), controlled clinical trials, and longitudinal cohort studies were included. We identified no relevant articles for this key question.

For key questions 4, 5, and 5a, we conducted a two-stage literature search to locate high-quality, relevant systematic reviews, supplemented by bridge searches as necessary. We also retrieved all potentially relevant treatment research or trials cited in the previous 1996 USPSTF report. Relevant systematic reviews were identified from four distinct searches of Ovid MEDLINE, the Cochrane Database of Systematic Reviews (CDSR), the Database of Abstracts of

Reviews of Effectiveness (DARE), and PsycINFO for the time frame 1994-January 2006. We identified 14 high-quality systematic reviews that addressed treatment for one or more of the illicit drugs addressed in this report (heroin, cocaine, marijuana, multiple drugs). We used those systematic reviews as sources of relevant trials for this review, supplemented by a two additional searches for randomized or controlled clinical trials in Ovid MEDLINE and PsycINFO from 2001-April 2006. Additional articles were obtained from comparing reference lists of related reviews, studies, editorials, reports, websites, and by consulting experts. We identified 17 relevant articles for these key questions.

For key question 7, we searched Ovid MEDLINE for the time period 1994-April 2006. Randomized controlled trials (RCTs), controlled clinical trials, and longitudinal, cohort studies were included. We also retrieved all potentially relevant articles cited in the 1996 USPSTF report. We identified eleven relevant articles for this key question.

All studies were managed in an electronic database (Reference Manager®).

Inclusion and exclusion criteria

Two investigators reviewed identified abstracts for potential relevance to all critical key questions and determined eligibility by applying inclusion and exclusion criteria specific to each critical key question (Appendix B – Inclusion and Exclusion Criteria). Full-text articles for included abstracts, articles from the previous USPSTF report, and articles located from existing systematic reviews were examined for relevance. Eligible studies provided data relevant to the critical key questions for marijuana, cocaine, opiates, or multiple substances, and were English-language, primary care feasible or referable (defined in Appendix B), conducted in a US (or applicable country), and examined adolescents/teens ages 12-17, young adults ages 18-25, adults ages 26+, or pregnant women. Studies of detoxification/withdrawal, comparative treatment effectiveness, and animal studies were not included.

For KQ 1, randomized controlled trials (RCTs), controlled clinical trials, and longitudinal cohort studies were included. For KQs 4, 5, and 5a**,** RCTs and controlled clinical trials were included. For KQ7, we included RCTs, controlled clinical trials, and longitudinal cohort studies.

Data abstraction and critical appraisal

Data were extracted from each paper, entered into evidence tables, and for key questions 4, 5, and 5a, the main findings were highlighted in a summary table, with trials categorized by population, drug, and treatment type. Information abstracted in an evidence table for trials of drug treatment included: target population, whether the population was screened/not screened in primary care, total number of patients, patient inclusion/exclusion criteria, type of drug(s) treated, treatment and control conditions, treatment duration and longest follow-up, results (by key question), whether results differed at short follow-up(s), and reviewer comment. For key question 7, the following information was abstracted: study design, target population, whether the population was screened or not screened in primary care, total number of patients, inclusion

criteria and sample description, exclusion criteria, type of drug(s), groups analyzed, length of follow-up(s), type of data analysis, outcome(s), results, and reviewer comment. A second investigator reviewed or abstracted studies if the initial investigator required confirmation of exclusion or inclusion criteria or data abstraction elements.

The quality of studies, including systematic reviews, was rated using design-specific criteria developed by the USPSTF (Appendix C)[14] and others (Appendix D)[15,16](Appendix E).[17] Each study's overall rating is a combination of internal and external validity ratings. Throughout the literature review and data abstraction process, when reviewers disagreed, a final rating was reached through consensus.

Size of literature reviewed

A total of 4587 unique citations were identified, 4459 by the literature searches and 128 from reference lists, suggested by experts, etc. (Appendix F – Search and Selection of the Literature). Six hundred and twenty seven abstracts were dual-reviewed (independently reviewed by two investigators) for papers showing direct evidence of screening related to reduced morbidity and/or mortality. None of these met the inclusion criteria (KQ 1). Three thousand four hundred and fifty nine abstracts were dual-reviewed for randomized controlled trials, controlled trials, systematic reviews or meta-analysis reports showing evidence that treatment improves morbidity and mortality, results in decreased drug misuse, or improves social and legal outcomes. Of these, 17 met the inclusion criteria (KQs 4, 5, 5a). One thousand eight hundred and fifteen abstracts were dual-reviewed from a search addressing whether decreased use or abstinence following drug misuse is reliably associated with reduced morbidity and mortality. Of these, 11 met the inclusion criteria (KQ 7).

Literature synthesis

Since this staged review's primary purpose was to determine evidence sufficiency, we did not undertake quantitative data synthesis such as meta-analysis. These techniques are used to provide summary effect sizes or explore heterogeneity in systematic reviews of treatment. Instead, we qualitatively summarized our findings, with an emphasis on the best available evidence for each critical key question and the overall coherence of the evidence. This level of synthesis was appropriate to the decision being made by the USPSTF using this review.

External review process

The USPSTF appointed liaisons to advise the Oregon Evidence-based Practice Center in formulating and reporting this focused systematic review. An additional set of outside experts provided advice in the review formulation stage and commented on a draft version of the evidence synthesis.

III. Results

Drug misuse screening and health outcomes (Key Question 1)

We found no evidence addressing the effects on health outcomes of screening to identify and treat drug misuse among asymptomatic individuals in primary care settings. It should be noted that evidence relevant to this key question would require comparing screened versus unscreened individuals. Evidence derived from a context of universal screening comparing individuals who screened positive for drug misuse with individuals who screened negative would not be considered applicable to this key question.

Drug misuse treatment: Overview (Key Questions 4/5/5a)

Table 2 summarizes the more detailed evidence in Table 3 about the 17 fair- or good-quality trials that were included in Key Question 4, 5, or 5a. Trials are listed alphabetically by first author, within drug categories defined by the main drug being treated: opiates, opiates and cocaine, cocaine, and cannabis. Some trials reported outcomes for drugs in addition to the main drug under which they are categorized. The 6 trials examining treatments for opiate misuse[18,19-23] were conducted among a total of 906 patients, primarily addicted to heroin. All were conducted among young adult or adult populations, with the exception of Guo 2001[21], which included some adolescents. Five of the six opiates treatments were prescription drugs. One treatment was a comprehensive, intensive psychosocial intervention.[20] One trial (Bernstein 2005)[24] evaluated a counseling intervention to decrease opiate and cocaine use among 1175 primary care patients. Among the six trials of cocaine misuse in 650 patients,[25-30] five tested prescription drug treatments and one[26] examined an acupuncture treatment. All were conducted among young adult or adult populations. The four trials of cannabis misuse in 1170 patients[31-34] all involved counseling interventions. All were among young adults and adults, except McCambridge (2004, 2005)[33], which included adolescents. Follow-up periods ranged from immediate post-treatment assessments to 1-year post-intake, but were less than six months in duration in 12 of the 17 trials. None of the trials was conducted among pregnant women. With the important exception of Bernstein et al.,[24] none was conducted among asymptomatic individuals identified through screening for drug misuse in primary care settings.

Drug misuse treatment and health outcomes (Key Question 4)

Fewer than half of the trials in Table 2 reported mental or physical health outcomes after drug misuse treatment. Two of these were opiate trials,[18,20] three were cocaine trials[25,27,29] and two were cannabis trials (Table 2, column 5). Follow-up periods were 4 months or less, and health outcomes were measured by indices of mental or physical health symptoms, rather than diagnosed health conditions. Assadi et al.,[18] in a trial of baclofen treatment of opiate dependence, found a significant reduction in depression symptoms in the treatment group at 3 months (although there was no difference in opiate use). Gruber et al.[20] found that a comprehensive psychosocial

intervention reduced depressive symptoms, but not anxiety symptoms, a general index of psychiatric severity, or a general index of physical health at 3-month follow-up. Trials of cocaine misuse treatments reported mostly non-significant results for health outcomes. While desipramine was shown in one trial[25] to improve two indices of psychiatric severity, it did not improve depressive symptoms or cocaine use. Of the two cannabis trials, one reported an improvement in anxiety, but not other psychiatric or medical symptoms, using a motivational enhancement counseling intervention,[32] and the other reported no effect of combined cognitive-behavioral and motivational counseling on a general index of psychiatric symptoms.[31]

Summary of Key Question 4. The evidence summarized in Table 2 provides little indication that drug misuse treatment improves health outcomes. Most trials did not report health outcomes. None of the evidence came from trials of asymptomatic individuals who were identified through screening for drug misuse in primary care. There was no representation of adolescent or pregnant female populations.

Drug misuse treatment, drug use, and social or legal outcomes (Key Questions 5/5a)

All of the trials in Table 2 reported drug use outcomes, often including both self-reported and biochemical (usually urinalysis) measures of use. These trials provide good evidence that several drugs (methadone, buprenorphine, and naltrexone) reduce opiate use, at least in the short-term. One intensive, psychosocial intervention also reduced heroin use at 3-month follow-up according to self-reports, but not according to urinalysis. Auricular acupuncture[26] and desipramine[28] reduced cocaine use when measured by urinalysis at post-treatment assessments, while disulfiram[30]reduced self-reported, but not biochemically-verified, cocaine use. The three cannabis treatment trials among young adults or adults reduced multiple self-reported measures of cannabis use. Results from the one cannabis trial including adolescents[33] were inconsistent, but nonetheless found significantly more days abstinent in the treatment group. None of the cannabis trials reported separate biochemical measures of drug use outcomes, although some reported high levels of agreement between self-report and urinalysis results (e.g., Marijuana Treatment Project[32]). The largest single trial[24] tested a motivational counseling intervention conducted by former drug users to reduce opiate and/or cocaine use among 1175 patients in an outpatient medical clinic. Based on analyses of hair samples, the intervention reduced cocaine use and opiate use at 6-month follow-up. Results for combined cocaine and opiate use were marginally non-significant (p=0.052). Bernstein et al. recruited participants by screening asymptomatic primary care patients for opiate or cocaine use, making this trial unique among those in our review.

Only six trials reported intermediate social and legal outcomes. Gruber et al.[20] reported no effects of their psychosocial intervention for opiate misuse on any of several measures of employment, illegal activity, or social functioning at 3-month follow-up. Interim methadone treatment (i.e., during a waiting period before slots in existing methadone treatment programs were available) did significantly reduce illegal activity and the amount of money spent on drugs during a 4-month follow-up period. One cocaine trial (of desipramine treatment) found null results on indicators of employment, illegal activity, and social functioning.[25] Three of the cannabis trials reported significant improvements in cannabis-related problems,[31,32,34] and one of these also reported improvement in an employment index.[32]

Summary of Key Questions 5/5a. Overall, the evidence in Table 2 indicates that various drug misuse treatments—including pharmacotherapies and behavioral interventions—effectively reduce opiate, cocaine, or marijuana misuse (KQ5). Follow-up periods were typically short, however, rarely being longer than 6 months after intake. All trials were conducted among treatment-seeking, instead of screened, populations, with one exception[24] in which a brief intervention reduced cocaine and opiate use among primary care patients identified through screening for use of these substances. Evidence of treatment effects on other intermediate outcomes was sparser and less consistent, although behavioral counseling interventions for cannabis misuse appear to reduce cannabis-related problems.

Health benefits of decreasing or ceasing drug misuse (Key Question 7)

Nine of the eleven studies which were identified as relevant to the health benefits of cessation or reduced drug use examined opiate, cocaine, or multiple drug misuse among young adult or adult populations, while two addressed cocaine or cannabis misuse among pregnant women (see Table 4). None directly studied adolescent populations. Among the nine studies of young adults or adults, follow-up periods ranged from 6 months (two studies) to 33 years (one study). Injecting drugs was a frequent route of administration (five studies; route not reported or in four studies). Health outcomes in these studies included mortality, indices of physical and/or mental health and functioning, participation in highly active anti-retroviral therapy (HAART), and HIV disease progression in HAART patients. None of the studies was conducted among screened primary care populations.

Among young-adult and adult populations, the strongest evidence for health benefits comes from evaluations of the association between stopping opiate (usually heroin) misuse and mortality. In a 15-year follow-up study of 188 persons treated for opiate dependence in a Danish community, Sorensen et al.[35] interviewed the sample 5 years following treatment, identifying groups that had either quit using opiates entirely, still used occasionally, or continued to use daily. The risk of mortality (hazard rate) over the succeeding 10 years (post-interview) was about half as high in the group who had quit, compared to the group who continued daily use [hazard ratio (95% CI): 0.45 (0.2, 0.8)]. These results were adjusted for age, gender, and number of mental health hospitalizations. Mortality progressively increased between those who had become abstinent at 5-year follow-up, those who occasionally used illegal drugs, and those who used illegal drugs daily. Compared to the general Danish population, mortality remained significantly elevated, however, even in the group that had become abstinent [Standard Mortality Ratio (95% CI): 7 (2.4, 17.0) among women, 8 (6.7, 21.6) among men]. The mortality evidence from Sorensen et al. may be considered stronger or more applicable to Key Question 7 than that from most other included studies because the longitudinal data covered three observation points—during treatment, 5 years post-treatment, and 15-years post-treatment—allowing clear temporal ordering between reported reduction of drug misuse and mortality over the succeeding 10 years. Two other studies in adults also observed samples over at least three time points.[12,36] Hser et al.[12] conducted a 33-year follow-up of 581 male, criminal offender heroin addicts receiving mandatory treatment in a California criminal justice setting in the period 1962 to 1964. Interviews were conducted in 1974-75, 1985-86, and 1996-97. Mortality was ascertained as of the latter two periods, at approximately 22 and 33 years after intake. There was no significant

improvement in mortality in current non-users of heroin, compared with current users, at either the 22- or 33-year follow-ups. Cross-sectional analyses at the 1996-97 interview showed that non-users had significantly less disability, depression, and anxiety symptoms than current users, but there was no difference between these groups in proportions with hepatitis, HIV, or STDs. Although the sample of male heroin addicts in the Hser et al. study[12] was selected from a criminal justice-related population, reducing its generalizeability to primary care populations, the study was included here because of the value of its unusually long follow-up period. Fridell and Hesse[36] identified 125 "drug abusers," two-thirds of whom reported injection drug use, who sought inpatient treatment in Sweden in 1988-89. Among ninety persons interviewed at 5 years post treatment, mortality was ascertained over the next 10 years. Survival analyses showed no significant association between length of time abstinent at 5-year follow-up and mortality. Cross-sectional analyses at the 5-year follow-up revealed higher global functioning and lower global psychiatric severity in persons who had been abstinent for 6 or more months compared with all others. In summary, across the three studies that examined mortality outcomes, only Sorensen[35] showed a reliable longitudinal association between cessation of opiate use and reduced mortality. Cross-sectional results were mixed, with some evidence of better functioning among drug misusers who were abstinent at the time of assessment, compared with continuing drug users.

Four studies[37-40]examined changes in drug misuse or injection practices in relation to adherence to needed medical treatment, to disease progression, or to mortality, among individuals in treatment for HIV. Lucas et al.[37] identified groups of former heroin or cocaine users (no use in past 6 months), never users, and current users among 764 persons who met criteria for HAART. In general, current users were significantly more likely than never users to have never used HAART. Among those taking HAART, current users were less likely to adhere to the medication regimen and had poorer responses to HAART. Former users were more similar to never users than to current users. In a later report from the same study site, Lucas et al.[39] compared the development of new opportunistic conditions among 1851 HIV patients using HAART across groups of non-drug users, intermittent drug users during abstinent periods, intermittent drug users during active use periods, and persistent drug users. During abstinent periods, intermittent users were not significantly more likely to develop new conditions compared to nonusers, but during active drug use periods, intermittent users had significantly higher risk of developing new conditions (about double that of nonusers). Mortality among intermittent users was intermediate between that of nonusers and persistent users.

Bouhnik et al.[38] followed 144 drug-injecting HIV patients over 18 months, finding that those who had quit injecting drugs for at least 12 months were significantly less likely to be depressed (symptom score) than those who continued to inject, although HAART participation and responses to treatment did not consistently differ. Moatti et al.[40] examined short-term HAART adherence among 164 HIV-positive injecting drug users, finding that adherence among individuals who had quit injecting drugs for the past 6 months or more was not significantly different from adherence among patients on buprenorphine maintenance treatment; in contrast, adherence among active injecting drug users was significantly lower than among patients in treatment. In a sample of 393 individuals who had injected drugs in the past 10 years, Knowlton et al.[41] found significantly lower odds of having depressive symptoms at 1-year follow-up among those who had stopped using all drugs versus those who continued to use. Gossop et al.[42] took a different approach in conducting cluster analyses of factors at intake among 478 persons beginning methadone treatment who participated in 1-year follow-up. Four clusters were

identified based on drug use patterns both at intake and follow-up; the two clusters showing improved drug use patterns tended to have improved physical and mental health index scores at 1 year relative to the non-changing clusters. In summary, these six studies all found some associations between reduction or cessation of drug misuse and a variety of health outcomes. All but one of the studies[39] were limited by analyses of behavioral changes between only two time points, producing essentially cross-sectional results in which the timing of changes in drug use were contemporaneous with changes in health indicators.

Two studies assessing health outcomes associated with cocaine misuse were conducted among pregnant women. Shankaran et al.[43] examined patterns of cocaine and marijuana use (separately) during pregnancy in relation to weight, length, and head circumference of infants at birth. Patterns of drug use were identified by mothers' reports following live birth, based on reported drug use during two six-month time periods: the 3 months before pregnancy and the first trimester, and the second and third trimesters. Five patterns were examined across the two time periods: consistently high, consistently moderate, consistently low use, increasing use, and decreasing use. A group-matched comparison group of non-users of cocaine or opiates was identified. Results showed that no marijuana use pattern was related to any of the birth outcomes, compared to non-drug users. Consistently low cocaine use was associated with lower birth weight, and consistently moderate cocaine use was associated with smaller head circumference, compared to non-drug users, but no dose-response relationship was apparent, and decreasing cocaine use was not related to any of the three outcomes. In an earlier, smaller study (N=115), Chasnoff et al.[44] compared pregnancy complications and birth outcomes among women who were: a) exposed to cocaine in the first trimester only; b) exposed to cocaine throughout pregnancy; or c) not exposed to drugs or alcohol during pregnancy. Cocaine exposure throughout pregnancy was associated with more preterm deliveries, lower birth weights, being small for gestational age, and placental abruption than cocaine exposure limited to the first trimester exposure or no exposure. Neonatal weight and length were significantly lower among those who used cocaine throughout pregnancy compared to non-users, but were not significantly different for first trimester-only users. Both cocaine-exposed groups tended to have worse scores on a neonatal behavioral assessment scale than the non-exposed infants. In summary, evidence from these studies is limited to two small studies and mixed with regard to benefits of reducing or quitting drug use during pregnancy, with Shankaran et al.[43] finding little association between drug use patterns and birth outcomes, and Chasnoff et al.[44] finding that stopping cocaine use after the first trimester is associated with improvement in some outcomes, but not others, compared to a continuously exposed group.

IV. Discussion

Limitations of the Literature Review

This review was not intended to be a comprehensive, cumulative review of evidence regarding drug misuse screening and treatment. It was designed, rather, to address whether there still is insufficient evidence available to answer critical key questions required for the USPSTF to make a recommendation on this topic as a clinical preventive service in primary care. Our review was limited to the defined scope of work as a staged review to update a previous USPSTF recommendation.

One limitation in this review was our focus on the most prevalently misused substances and those most likely to be associated with abuse or dependence. While the misuse of prescription-type drugs is fairly prevalent (2.5% of persons age 12 and over),[2] this category represents at least four different types of medications (pain relievers, tranquilizers, stimulants – including methamphetamine – and sedatives), and multiple individual medications (see Table 1). These different substances represent different misuse profiles, including different average ages of initiation, sources of drug, trends in the number of users, and annual incidence of new users. Misuse of prescription medications is likely to be a growing public health problem and should be considered in future USPSTF updates for this topic.

Drug Misuse Treatment (Key Questions 4/5/5a)

The drug misuse treatment literature is voluminous and heterogeneous with regard to types of drugs, types of drug treatments, and types of study designs. We applied a series of inclusion and exclusion criteria to identify the most relevant and valid research. A clear understanding of these criteria, listed in Appendix B, is necessary to judge the adequacy and applicability of our findings. After reviewing much of this literature, we focused our review on treatment for the four categories of drugs (opiates, cocaine, cannabis, and mixed drugs) that represent the most prevalent and addictive illicit drugs in the US. Also, in order to efficiently examine the evidence regarding the efficacy of drug misuse treatment, we first reviewed existing systematic and authoritative reviews which included evidence from RCTs or from controlled trials comparing drug misuse treatment to placebo or no (minimal) treatment. We created bridge searches (as necessary) to fill the gaps in the literature. Many studies were excluded after careful review, mostly due to design (uncontrolled studies, comparative effectiveness studies, or studies not reporting outcomes designated a priori in our analytic framework). Excluded studies are identified in Appendix G.

Two of the exclusion criteria we applied to the drug misuse treatment literature (key questions 4, 5, and 5a) markedly reduced the volume of included evidence: detoxification/withdrawal studies and studies of comparative treatment effectiveness. We excluded detoxification/withdrawal studies because we conceptualized detoxification as an intermediate step with short-term outcomes designed to stabilize individuals and prepare them for drug misuse treatment, rather than as "treatment" itself. We excluded comparative effectiveness studies (e.g., medication plus counseling versus placebo plus counseling, or

medication dosage comparisons) because they did not provide evidence relevant to establishing the efficacy of treatment versus no treatment. This decision has been criticized by some drug misuse treatment researchers, who feel that it is unethical to conduct trials in which treatment-seeking individuals are assigned to no-or-minimal-treatment control conditions, because they believe the efficacy of drug misuse treatment is established. Both detoxification and comparative effectiveness were frequently addressed in systematic reviews and individual trials.

A potential limitation of our review of health outcomes following drug misuse treatment is that by limiting the treatment literature to RCTs and CCTs, which tend to have relatively short follow-up periods, we may have reduced the likelihood of finding studies documenting long-term improvements in morbidity and mortality. We searched explicitly, however, for cohort studies of health effects associated with changes in drug use and believe we would have located most longer-term follow-up trials reviewed for our treatment benefit questions if these trials were available.

The treatments tested in the 17 trials included in our review are relatively heterogeneous. All but one of the treatments for opiate misuse, and all but one of the treatments for cocaine misuse, are medications, whereas all four treatments for cannabis misuse, and the one trial for opiate and cocaine use, are counseling interventions. A common theme is that the studies were conducted among non-screened populations (with one exception, Bernstein 2005[24]). Participants were frequently recruited through advertisements or as they sought treatment at an existing drug treatment agency. Because it is an exception to this norm, the Bernstein trial deserves special comment. Bernstein (2005) was the only trial in which participants were recruited by screening an asymptomatic, outpatient medical clinic population for drug use. The Bernstein population may not have had levels of internal or external motivation to reduce drug use similar to those in the treatment-seeking populations examined in the other studies. The Bermstein trial was also unique in that participants reported sub-diagnostic levels of drug use. These participants may not have met diagnostic criteria for drug misuse (i.e., abuse or dependence criteria from the DSM-IV). It thus differs from the other trials along two dimensions—motivation and addiction severity.

Linking Changes in Drug Misuse to Health Outcomes (Key Question 7)

We identified eleven relevant longitudinal studies that linked reduction in, or cessation of, drug misuse to morbidity or mortality. Results were mixed among studies of young adults or adults, with perhaps the strongest evidence of benefit coming from a Danish study that found the risk of mortality over a 10-year period was reduced by 55% among former opiate addicts who had become abstinent, relative to continuing daily drug users.[35] Two other long-term studies of mortality, however, did not find reduced risks among former opiate or injection drug users. Other outcomes at 6-12 months generally support benefit through improvement in compliance with or response to necessary medical care (HAART), improvement in depressive and anxiety symptoms, or improvement in physical health measures, with reduced use or abstinence among injection drug users (of opiates or cocaine) compared to ongoing users. Factors that differentiated those who reduced or stopped drug misuse and those who continued to use may explain some of these differences. Also, these studies frequently examined only two time points, showing cross-sectional correlations between contemporaneous changes in drug misuse and morbidity outcomes, rather

than linking reductions in drug misuse with subsequent improvements in health. The two studies of cocaine and cannabis use among pregnant women provided inconsistent results, with one study[43] finding no reliable evidence that cocaine or cannabis use during pregnancy was associated with poorer birth outcomes, and one[44] finding that stopping cocaine use early in pregnancy was associated with some improvements in birth outcomes relative to continuing users.

Conclusions

The central goal of the staged review process is to establish the sufficiency of evidence for answering critical key questions about drug misuse screening as a clinical preventive service in primary care. The following details our provisional conclusions about this evidence, organized by critical key question (Table 5).

Key Question 1

We found no studies addressing whether drug misuse screening programs in primary care reduce morbidity or mortality in any of the four population subgroups we examined, and therefore provisionally conclude there is insufficient evidence for this key question.

Key Questions 4/5/5a

Among screened individuals. We found one trial by Bernstein 2005[24] providing evidence that drug misuse treatment decreases drug misuse *in screened, asymptomatic individuals* (key question 5). No studies in screened individuals addressed morbidity or mortality (key question 4), or intermediate social or legal outcomes (key question 5a), in any of the four populations.

We, therefore, provisionally conclude that there is there is some evidence that drug misuse treatment reduces drug misuse in screened, asymptomatic individuals. There is insufficient evidence, however, that drug misuse treatment in such individuals improves morbidity or mortality, or intermediate social and legal outcomes.

Among treatment-seeking individuals. All but one of the treatment studies we examined reported on treatment-seeking individuals who may have presented for treatment as a result of internal motivators, external motivators, or a combination of both. Because our inclusion criteria (Appendix B) set a high threshold for study design and quality, we expect that our results represent the strongest evidence available for the health, drug, and intermediate outcomes we considered. This evidence is very limited for health outcomes, since most studies did not report health outcomes. Among those that did, only three reported significant treatment effects on symptoms of depression or anxiety, and two of these reported multiple non-significant effects on other psychiatric measures.

The evidence supporting the efficacy of drug misuse treatment on drug use intermediate outcomes was more robust, with at least one trial showing significant improvements in drug use behaviors in each of the drug categories of opioids, cocaine, and cannabis. Social and legal intermediate outcomes, however, were not frequently reported in the evidence. One opiate treatment trial reported significant treatment effects on legal outcomes, and one cannabis trial

reported mixed results on an employment measure (although three found improvements in cannabis-related problems).

We provisionally conclude: a) there is insufficient evidence that drug misuse treatment in treatment-seeking individuals improves morbidity or mortality (key question 4); b) there is good evidence that drug misuse treatment in treatment-seeking individuals reliably reduces drug misuse (key question 5); and c) that there is insufficient evidence that drug misuse treatment in treatment-seeking individuals improves intermediate social and legal outcomes.

Key Question 7

Given the dearth of evidence from the drug misuse treatment studies on outcomes other than drug misuse behaviors, the evidence link between these intermediate outcomes and health outcomes becomes quite important. While the evidence we identified from eleven studies is mixed, there is evidence that stopping heroin addiction is associated with reduced mortality risk, and that stopping injection drug use is associated with better adherence and response to medical treatment (among individuals with HIV) and with better mental and physical health functioning. We provisionally conclude that there is fair evidence that reducing or stopping drug misuse is associated with some health outcomes, in some populations. The generalizability of these studies to general primary care populations may be limited.

Overall

Our provisional conclusions for each of the critical key questions reviewed suggest the state of the evidence regarding drug misuse screening in primary care essentially has not changed since the previous USPSTF review of drug abuse screening.[1] Although many advances in drug misuse treatment have occurred during the past decade, the vast majority of studies are conducted in treatment-seeking populations, and thus the relevance of outcomes from such studies is of uncertain applicability to asymptomatic primary care populations that could be screened for drug misuse. The Bernstein trial of a brief, motivational counseling intervention to reduce opiate and cocaine use in a screened, outpatient clinic population may herald a new generation of drug misuse treatment research that will provide evidence more applicable to primary care populations**.**

Our finding of continuing evidence insufficiency is also consistent with the perspective described in recently initiated research by the National Quality Forum.[45] The project, "Evidence-based Practices to Treat Substance Use Disorders" funded by the Robert Wood Johnson Foundation, is attempting to achieve national consensus on effective practices for treating substance use disorders. Seven practice categories were defined in an expert workshop and the project is seeking input about specific practices within each area. The workshop panel concluded that the evidence on opportunistic screening for drugs in health care settings was not strong enough or general enough to warrant inclusion as a general best practice. In contrast, opportunistic screening for alcohol use disorders in health care settings was included.

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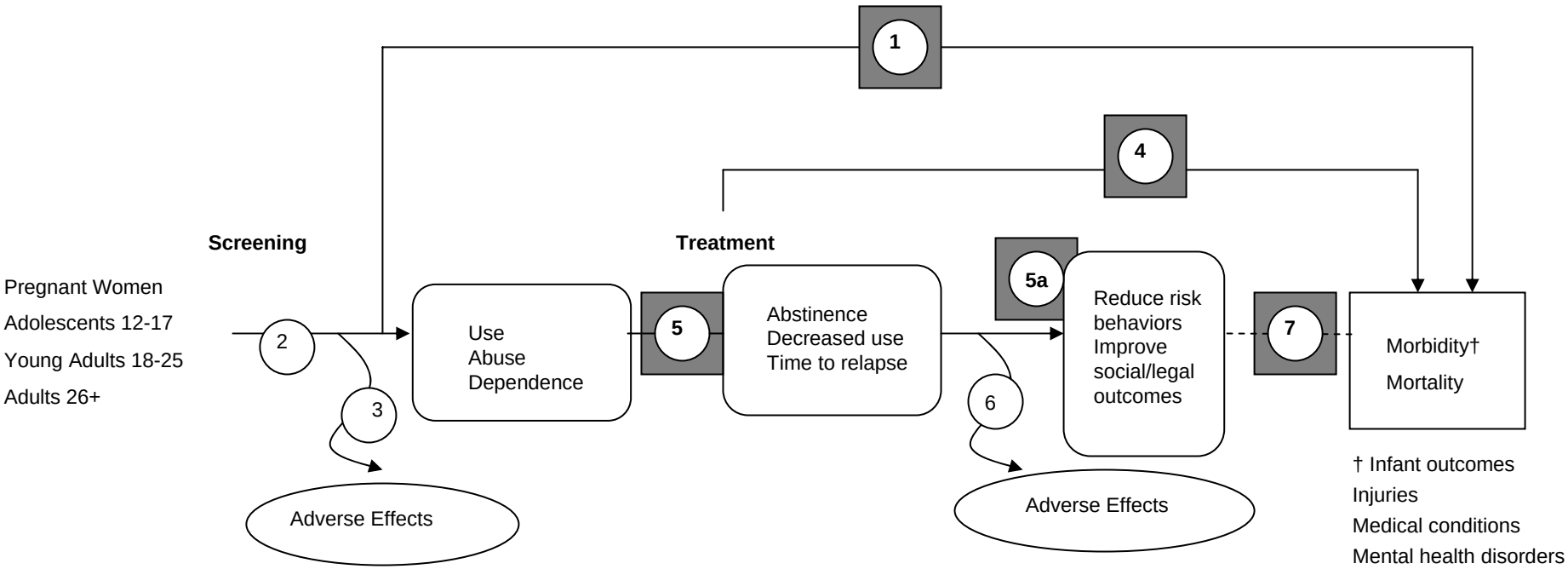
Figure 1. Drug* Misuse Analytic Framework and Key Questions



KQ 1 Is there direct evidence that screening for drug misuse reduces morbidity and/or mortality?
KQ 2 Do screening tests accurately detect drug misuse?
KQ 3 Does screening for drug misuse result in adverse effects?
KQ 4 Does treatment for drug misuse among individuals identified through screening improve morbidity and/or mortality?
KQ 5 Does treatment for drug misuse among individuals identified through screening result in decreased drug misuse?
KQ 5a Does treatment for drug misuse reduce risk behaviors/improve social/legal outcomes?
KQ 6 Does treatment for drug misuse result in adverse effects?
KQ 7 Is decreased use or abstinence following drug misuse reliably associated with reduced morbidity and/or mortality?

Grey box = critical key question

Drugs included are opiates, cocaine, marijuana, and mixed drugs

Table 1. Categories of Drugs Used Illicitly*

Included in Review

Category	Examples
Marijuana	Hashish
Cocaine	Crack
Opioids	Heroin

Not included in Review

Category	Examples
Hallucinogens	LSD, PCP, peyote, mescaline, mushrooms, "Ecstasy" (MDMA)
Inhalants	Amyl nitrite, cleaning fluids, gasoline, paint, glue
Pain relievers†	Oxycodone (OxyContin), propoxyphene (Darvon), hydrocodone (Vicodin)
Tranquilizers†	Diazepam (Valium), alprazolam (Xanax)
Stimulants†	Dextroamphetamine (Dexedrine), methylphenidate (Ritalin), methamphetamine
Sedatives†	Methaqualone (Quaalude), pentobarbital sodium (Nembutal),

*Nine categories based on Substance Abuse and Mental Health Services Administration; 2004 National Survey on Drug Use and Health (NSDUH). Available online at: http://www.oas.samhsa.gov/NSDUH.htm#NSDUHinfo. Accessed January 8, 2008

†Prescription type, non-medical use (psychotherapeutics); over-the-counter medications are excluded.

Table 2. Summary Table - Randomized Controlled Trials of Drug Treatment (Opiates, Cocaine, and Cannabis) for Young Adults and Adults (KQ 4/5/5a)

Author/Year Quality	N	Intervention	Follow-up (weeks)	Outcomes			
				Health (KQ 4)	Drug Use (KQ 5)		Social/Legal (KQ 5a)
					Self-report	*Biochemical*	
Opiates							
Assadi 2003[18] Fair	40	Baclofen	12	S (depression)	NS (days used)	NS (UA)	*
Fudala 2003[19] Fair/good	296	Buprenorphine, Buprenorphine+naloxone	4 (post-tx)	*	*	S (UA)	*
Gruber 2000[20] Fair	52	Comprehensive psycho-social including CBT	12	S (depression), NS (anxiety), NS (ASI psych), NS (ASI medical)	S (time to first use), S (ASI drug), S (days used heroin), NS (days used cocaine)	NS (UA heroin), NS (UA cocaine), NS (UA both)	NS (ASI employment), NS (currently employed), NS (days paid work), NS (ASI legal), NS (days illegal activity), NS (ASI family/social)
Guo 2001[†21] Fair	49	Naltrexone	24	*	S (abstinent), S (average months abstinent)	S (UA)	*
Johnson 1995[22] Fair-	150	Buprenorphine	2	*	*	S (UA, males), NS (UA, females)	*
Schwartz 2006[23] Fair	319	Methadone (interim)	16	*	S (days used heroin)	S (UA heroin), NS (UA cocaine)	S (ASI legal), S (amount illegal income), S (money spent on drugs)
Opiates and Cocaine							
Bernstein 2005[‡24] Good	1175	MI	24	*	*	NS (hair, cocaine & opiates), S (hair, cocaine), S (hair, opiates)[§]	*
Cocaine							
Arndt 1992[25] Fair	79	Desipramine	12 (post-tx)	NS (ASI medical), NS (days medical problems), S (ASI psych), S (days psych problems), NS (BDI)	NS (ASI drug), NS (days used)	Significant—but favors control (UA)	NS (ASI employment), NS (ASI legal), NS (ASI family/social)
Avants 2000[26] Fair	82	Auricular acupuncture	8 (post-tx)	*	*	S (UA)	*
Batki 1996[27] Fair	32	Fluoxetine	2	NS (depression), NS (anxiety)	NS (days used)	NS (UA), NS (plasma)	*
Feingold 2002[28] Fair	180	Desipramine	26	*	*	S (UA)	*

Table 2. Summary Table - Randomized Controlled Trials of Drug Treatment (Opiates, Cocaine, and Cannabis) for Young Adults and Adults (KQ 4/5/5a) (continued)

Author/Year Quality	N	Intervention	Follow-up (weeks)	Outcomes			
				Health (KQ 4)	Drug Use (KQ 5)		Social/Legal (KQ 5a)
					Self-report	*Biochemical*	
Cocaine							
Passos 2005[29] Fair-	210	Nefazodone	10 (post-tx)	NS (depression)	NS (abstinence), NS (days to first relapse)	*	*
Petrakis 2000[30] Fair	67	Disulfiram	12 (post-tx)	*	S (frequency), S (quantity)	NS (UA)	*
Cannabis							
Copeland 2001[31] Good-	229	CBT + MI, 1 or 6 sessions	32	NS (psychiatric symptoms)	NS (days abstinent), S (abstinent past month), S (daily quantity), S (SDS score)	*	S (cannabis-related problems)
Marijuana Treatment Project 2004[32] Fair	450	MET 2 sessions, MET 9 sessions + CBT+ case management	16	NS (depression), NS (ASI medical), NS (ASI psych), S (anxiety)	S (% days used), S (period smoked daily), S (amount daily), S (abstinent), S (dependence sx), S (abuse sx)	*	S (ASI employment, only 1 Tx group), S (cannabis-related problems)
McCambridge 2005[†33] Fair	200	MI	52	*	NS (freq./wk), NS (quant./wk), S (abstinent days/mo.)	*	*
Stephens 2000[34] Fair	291	RPT 28 hours+, other psychosocial 3 hours	16	*	S (abstinent past month), S (days used past month), S (frequency daily), S (dependence sx)	*	S (cannabis-related problems)

*This outcome is not reported for this trial
[†]Includes teen-aged adolescents
[‡]Screened medical clinic population
[§]p-values = 0.052, 0.045, 0.050 respectively
+Additional therapy may have been given to treatment group

ASI=Addiction Severity Index; CBT=Cognitive Behavioral Therapy; MET=Motivational Enhancement Therapy; MI=Motivational Interviewing; NS=Not significant; RPT=Relapse Prevention Therapy; S=Significant difference, favors treatment group; Sx=symptoms; Tx=treatment; UA=Urinalysis

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a)

Author, Year Quality Rating	Key Question	Target Population (T, Y, A, P)*	Screened Population (Y/N)	Total Number of Patients	Inclusion Criteria	Exclusion Criteria	Type of Drug(s) Being Treated	Treatment/ Intervention (I) & Control (C) Conditions
Bernstein 2005[24] Good	5	Y, A	Y (23,669 screened, 5% pos.)	1,175	Medical visit at "episodic" care center; Speak English or one of 3 other languages; Able to complete basic cognitive function tasks for consent; Self-report cocaine or heroin use in past 30 days	In drug abuse tx; In protective custody	Cocaine Opiates	I: Motivational interview, active referrals, written handout of treatment sources, 10-day follow-up call C: Handout of treatment sources
Batki 1996[27] Fair	4, 5	Y, A	N	32	In specific outpatient tx program for $\geq$ 2 weeks; Using cocaine	None	Cocaine	I: Fluoxetine C: Placebo

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Treatment Duration, Longest Follow-up (All Follow-ups)	Results for Health Outcomes† (KQ4)	Results for Drug Use Outcomes† (KQ5)	Results for Social/legal Outcomes† (KQ5a)	Did Outcomes Differ at Earlier Follow-ups? (Y/N)	Comments
Bernstein 2005[24] Good	6-mos (3-, 6-mos)	None	Abstinence (average % negative hair analysis tests, among those positive at intake): Cocaine: I: 22.3% C: 16.9% Adjusted OR=1.51 (1.01, 2.24), p=.045 Opiates: I: 40.2% C: 30.6% Adjusted OR=1.57 (1.00, 2.47) p=.050 Both: I: 17.4% C: 12.8% Adjusted OR=1.51 (0.98, 2.26), p=.052	None	NA	Peer-counselor - PC-referable? Patient sample based on "use" rather than diagnoses of abuse or dependence
Batki 1996[27] Fair	Tx: 12 weeks Follow-up: took average of weeks 1-6 of tx	HAM-D ns HAM-Anxiety ns	Biochemical: Urine ns Plasma ns Mean (SD) days used/week: I: 1.6 (0.4) C: 1.4 (0.3) Ns	None	N	Says 12-week trial, but results only cover first 6 weeks of treatment

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Key Question	Target Population (T, Y, A, P)*	Screened Population (Y/N)	Total Number of Patients	Inclusion Criteria	Exclusion Criteria	Type of Drug(s) Being Treated	Treatment/ Intervention (I) & Control (C) Conditions
Copeland 2001[31] Good	4, 5, 5a	Y, A	N	229	Age 18+; English-literate; Desire to quit cannabis	Weekly use of drugs other than cannabis; AUDIT > 15 plus alcohol-related social problems; Cannabis tx past 3 mos; Current tx for other substance use problems	Cannabis	I1: 1-session manual-based CBT+MI I2: 6-session manual-based CBT-MI C: Wait-list
Johnson 1995[22] Fair	5	Y, A	N	150	Urine negative for methadone and positive for opiates; Age 18-50; Negative pregnancy test; No major medical illness; No chronic conditions; No history of serious psychological illness; Met federal guidelines for methadone tx; DSM-III-R criteria for opioid dependence; No prior drug abuse tx with buprenophine; 3 mos since last tx at clinic	None	Opiates	I1: 2-mg buprenorphine I2: 8-mg buprenorphine C: Placebo

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Treatment Duration, Longest Follow-up (All Follow-ups)	Results for Health Outcomes† (KQ4)	Results for Drug Use Outcomes† (KQ5)	Results for Social/legal Outcomes† (KQ5a)	Did Outcomes Differ at Earlier Follow-ups? (Y/N)	Comments
Copeland 2001[31] Good	Tx: 1-6 weeks Longest follow-up: average 8 mos	GSI from SCL-90-R Mean (SD): I1: 0.5 (0.4) I2: 0.6 (0.3) C: 0.6 (0.4) NS, adjusted pairwise p=.2, .6	% days abstinent: I1: 44.8% I2: 35.9% C: 29.7% NS (p=.09) % complete abstinent prior month: I1: 17.2% I2: 20.8% C: 3.6% I1, I2>C, adjusted pairwise p: .05, .05 Daily amount cannabis use Mean (SD) I1: 1.5 (1.2) I2: 1.3 (0.9) C: 1.8 (1.0) I1 vs. C, NS; I2<C adjusted p=.02 SDS score Mean (SD) I1: 7.6 (4.4) I2: 5.8 (4.3) C: 9.2 (3.2) I1, I2<C adjusted p=.01	% cannabis-related problems endorsed among large list Mean (SD) I1: 28.4 (18.6) I2: 23.0 (16.8) C: 39.1 (16.6) I1, I2<C Adjusted p=.004, <.001	N	
Johnson 1995[22] Fair	Tx: This study takes place after 2 weeks of tx 2 weeks	None	% of positive urines Males: I1: ~70% I2: ~65% C: ~95% I1, I2< C, P<.05 Female: I1: 90% I2: ~88% C: 99% P= ns	None	N	Only have outcomes at end of 2nd week of treatment

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Key Question	Target Population (T, Y, A, P)*	Screened Population (Y/N)	Total Number of Patients	Inclusion Criteria	Exclusion Criteria	Type of Drug(s) Being Treated	Treatment/ Intervention (I) & Control (C) Conditions
Gruber 2000[20] Fair	4, 5, 5a	Y, A	N	52	Positive opiate toxicology screen at detox admission; Ages 18-50; Unemployed or employment that would not interfere with tx schedule	History of psychotic sx; Reporting risk of suicide; Medical problems that would interfere with program participation; Enrolled in methodone or other outpatient drug-free tx program; Pregnant women	Opiates	I: Needs assessment, drug-free housing if needed; 2-wk daily 6-hr tx schedule including 1-on-1 CBT counseling, social skills training, job club, recreational activity; approximately $400 per patient in abstinence-contingent support for housing, food, transportation; Abstinence-contingent participation in therapeutic social and recreational activities C: Referral to community tx resource

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Treatment Duration, Longest Follow-up (All Follow-ups)	Results for Health Outcomes† (KQ4)	Results for Drug Use Outcomes† (KQ5)	Results for Social/legal Outcomes† (KQ5a)	Did Outcomes Differ at Earlier Follow-ups? (Y/N)	Comments
Gruber 2000[20] Fair	Tx: 3-mos Assessment: 3-mos post-intake	BDI: I: 12.9 C: 17.3 p=.05 for repeated-measures group effect, P=ns for group x time interaction State-Trait Anxiety Index: I: 37.6 C: 43.2 P=ns ASI-Psychological: I: .04 C: .01 P=ns ASI-Medical: I: 0.19 C: 0.31 P=ns	Days to first use of either heroin or cocaine: I: longer time to first use than C, survival analysis p=.05 ASI-Drug composite score: I: 0.14 C: 0.20 Group effect p=.05, Group*time interaction p=.02 Days heroin use, past mo: I: 8.6 C: 11.3 Group effect p=.05 Days cocaine use past mo: I: 5.7 C: 4.4 ns %Abstinent, SR verified by UA, past 30 days: Heroin: I: 32% C: 21%, p=ns Cocaine: I: 29% C: 17% p=ns Both: I: 29% C: 12.5%, p=ns	ASI-Employ: I: .78 C: .85 P=ns Curr employed: I: 39% C: 21% P=ns Days paid work: I: 8.3 C: 7.1 P=ns ASI-Legal: I: 0.12 C: 0.12 P=ns Days illegal activity: I: 5.1 C: 1.0 P=ns ASI: Family-social I: 0.08 C: 0.06 P=ns	Y Heroin use I<C at 1 mo	Small N and unable to randomly assign 5 patients, post-tx assessment; but otherwise good quality study

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Key Question	Target Population (T, Y, A, P)*	Screened Population (Y/N)	Total Number of Patients	Inclusion Criteria	Exclusion Criteria	Type of Drug(s) Being Treated	Treatment/ Intervention (I) & Control (C) Conditions
Stephens 2000[34] Fair	5, 5a	Y, A	N	291	Used cannabis ≥ 50 times in past 90 days	Alcohol or other drug abuse; Severe psychological distress; Involved in other formal tx for cannabis abuse	Cannabis	I1: 14 2-hr relapse prevention group plus optional 4-session group for support ppl I2: 2 90-min session modeled after Miller's Drinker's Check-up, invited to bring support person to 2nd session C: Delayed tx
Arndt 1992 RM 7800 Fair	4, 5, 5a	Y, A	N	79	Stable condition in VA MMT; Urine sample positive for cocaine; Age 20-50; DMS-III diagnosis of cocaine abuse last ≥ 3 mos	Medical condition contra-indicating desipramine	Cocaine	I: MMT with extensive services plus desipramine C: MMT with extensive services plus placebo

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Treatment Duration, Longest Follow-up (All Follow-ups)	Results for Health Outcomes† (KQ4)	Results for Drug Use Outcomes† (KQ5)	Results for Social/legal Outcomes† (KQ5a)	Did Outcomes Differ at Earlier Follow-ups? (Y/N)	Comments
Stephens 2000[34] Fair	4-mo (longest w control group) (1,4 mos)	None	% Abstinent past month: I1: 37% I2: 37% C: 9% I1, I2>C, p<.001 Days of use/month: Mean (SD) I1: 6.7 (9.9) I2: 7.9 (11.0) C: 17.1 (10.7) I1,I2<C p<.001 Times/day (ordinal scale): I1: 1.2 (1.1) I2: 1.2 (1.2) C: 2.0 (1.1) I1, I2<C P<.001 # Dependence-related symptoms: I1:2.0 (2.7) I2: 1.9 (2.7) C: 4.6 (2.6) I1, I2<C, P<.001	# Cannabis-related problems: I1: 3.5 (4.2) I2: 3.3 (4.0) C: 7.9 (4.2) I1, I2,C p=.001	N	Used 4-month outcomes because no control group after that
Arndt 1992[46] Fair	Tx: 12 weeks Follow-up: 6 mos	ANCOVA (Group differences): ASI-medical, days medical problems, ns; ASI psychiatric, s; # days psych problems, s; BDI, ns	ANCOVA (Group differences): ASI drug, ns; % Cocaine positive, UA: I: 78% C: 36% P<0.05 *favoring control*	ANCOVA (Group differences): ASI employment, ns; ASI legal, ns; ASI family/social, ns	Y – 2 psychological symptom measures favored I at 3-mos follow-up	Male only, in MMT

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Key Question	Target Population (T, Y, A, P)*	Screened Population (Y/N)	Total Number of Patients	Inclusion Criteria	Exclusion Criteria	Type of Drug(s) Being Treated	Treatment/ Intervention (I) & Control (C) Conditions
Feingold 2002[28] Fair	5	Y, A	N	109	Age 20-53; opiate-dependent; used cocaine ≥ 1 time in past week plus positive urine test in past month; completed ≥ 16 weeks treatment	History of psychosis; current alcohol or sedative dependence; currently suicidal; current use of prescribed psychoactive medications; significant medical condition; illiteracy; prior buprenorphine tx	Cocaine	I1: Maintained on methadone I2: Maintained on buprenorphine In each group, half received desipramine for 7 weeks, and then placebo for 7 weeks
Passos 2005[29] Fair	4,5	Y, A	N	210	Age 18-65; DSM-IV or ICD-10 diagnosis of cocaine dependence	Psychotic/ cognitive impairment diagnosis; external contingencies that could influence reliability of self-report (e.g., probation); health condition that precluded nefazodone; woman of child-bearing age not on birth control; using terfenadine or astemizole; suicidal ideation; epilepsy; used MAO-Is or other psychotropic medications in past 15 days; crack or injectable cocaine users	Cocaine	I: Nefazodone (plus other tx modalities offered) C: Placebo (plus other tx modalities offered)

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Treatment Duration, Longest Follow-up (All Follow-ups)	Results for Health Outcomes† (KQ4)	Results for Drug Use Outcomes† (KQ5)	Results for Social/legal Outcomes† (KQ5a)	Did Outcomes Differ at Earlier Follow-ups? (Y/N)	Comments
Feingold 2002[28] Fair	26-weeks	None	Main effect of desipramine significant (p<.001) Possible carry-over effects (group getting desipramine first may have maintained when switched to placebo)	None	N	Sample of people in MMT or BMT
Passos 2005[47] Fair	NR Did "comparison of end-points", presumably covering 10-week treatment period, most of which dropped out before 10 weeks	≥ 50% reduction on HAM-D: I: 60.7% C: 50.8% (p=.14)	≥ 3 weeks abstinence: I=49.5% C=45.7% p=.58 Days to first relapse: I=28.9 (2.4) C=25.6 (2.4) p=.39	None	N	Brazil

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Key Question	Target Population (T, Y, A, P)*	Screened Population (Y/N)	Total Number of Patients	Inclusion Criteria	Exclusion Criteria	Type of Drug(s) Being Treated	Treatment/ Intervention (I) & Control (C) Conditions
Marijuana Treatment Project 2004[32] Fair	4, 5, 5a	Y, A	N	450	Age 18+, DSM-IV diagnosis current marijuana dependence, used cannabis 40 of past 90 days	Unwilling to accept random assignment; legal status might have interfered with tx; current DMS-IV diagnosis of dependence on another drug or alcohol; need for immediate medical or psychological tx that precluded randomization; currently in tx or self-help group; inability to provider contact person	Cannabis	I1: 2-session MET I2: 9-session MET+CBT+Case management C: Delayed tx

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Treatment Duration, Longest Follow-up (All Follow-ups)	Results for Health Outcomes† (KQ4)	Results for Drug Use Outcomes† (KQ5)	Results for Social/legal Outcomes† (KQ5a)	Did Outcomes Differ at Earlier Follow-ups? (Y/N)	Comments
Marijuana Treatment Project 2004[32] Fair	Tx: 5 weeks or 9 weeks Follow-up: 4-mos (4-, 9-, 15-mo follow-up, but only 4 had control condition)	BDI, ASI-Med, ASI-Psych all ns; State-Trait Anxiety Inventory-State Form I2< I1, C, p<.01	% Days smoking, Mean (sd): I1: 55.9 (36.2) I2: 36.2 (38.8) C: 75.6 (30.9) p<.001 Periods smoked/day, Mean (sd): I1: 1.4 (0.9) I2: 1.0 (1.1) C: 2.0 (1.1) P<.001 Joints per day I1: 1.5 (1.6) I2: 1.0 (1.7) C: 2.0 (1.9) p<.05 % Abstinent past 90 days: I1: 8.6% I2: 22.6% C: 3.6% P<.001 Dependence symptoms, Mean (sd): I1: 3.7 (2.3) I2: 2.5 (2.3) C: 4.4 (1.9) p<.001 Abuse symptoms, Mean (sd): I1: 1.4 (1.1) I2: 1.0 (1.0) C: 1.6 (1.0) p<.001	ASI-Employment I2< I1, C, p<.05 Marijuana Problems Scale, I1, I2 < C, p<.001	N	Variety of recruitment sources, including self-referral, referral from medical doctors, social services, etc.

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Key Question	Target Population (T, Y, A, P)*	Screened Population (Y/N)	Total Number of Patients	Inclusion Criteria	Exclusion Criteria	Type of Drug(s) Being Treated	Treatment/ Intervention (I) & Control (C) Conditions
McCambridge 2004, 2005[33,48] Fair	5	T, Y	N	200	Age 16-20; weekly cannabis or stimulant use within previous 3mos	Opiate use; injecting drug use	Cannabis	I: Motivational interview C: "Education as usual," no study-provided information or tx
Assadi 2003[18] Fair	4, 5	Y, A	N	40	Age 18-60; opiate dependence per DSM-IV; detoxed at specified facility	Pregnant or lactating; clinically serious unstable medical condition; receiving other medications; history of psychosis, mania, or severe depression; concurrent dependency on alcohol, cocaine, hallucinogens; diagnosis of antisocial personality disorder; mentally retarded	Opiate	I: Baclofen C: Placebo

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Treatment Duration, Longest Follow-up (All Follow-ups)	Results for Health Outcomes† (KQ4)	Results for Drug Use Outcomes† (KQ5)	Results for Social/legal Outcomes† (KQ5a)	Did Outcomes Differ at Earlier Follow-ups? (Y/N)	Comments
McCambridge 2004, 2005[33,48] Fair	Tx 1-session Follow-up 12-mo (3-, 12-mo)	None	Frequency of use/week (95% CI): I: 8.6 (5.8, 11.5) C: 11.9 (7.4, 16.4), p= ns Quantity of use/week (95% CI): I: 0.21 (0.14, 0.27) C:0.30 (0.17, 0.42) p=ns Abstinent days/mo (95% CI): I: 17.8 (15.6, 20.0) C: 13.7 (11.1, 16.3), p=.025	None	Y, cannabis use significantly lower in tx group at 3-mo	Mainly peer recruitment
Assadi 2003[18] Fair	Tx: 12-weeks Follow-up: 12 weeks max	I-group showed greater improvement in HAM-D (p<.001)	No differences on % opiate-positive urine samples (I=76.9%, C=75.8%) Also no differences on days/week using opiates, opiate craving score, opiate withdrawal score	None	N	Conducted in Iran, also only included those seeking detox at specific facility

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Key Question	Target Population (T, Y, A, P)*	Screened Population (Y/N)	Total Number of Patients	Inclusion Criteria	Exclusion Criteria	Type of Drug(s) Being Treated	Treatment/ Intervention (I) & Control (C) Conditions
Avants 2000[26] Fair	5	Y, A	N	82	Age 18+; Enrolled in MMT; DSM-IV diagnosis of cocaine dependence; evidence of recent cocaine use (positive urine screen or self-report)	Dependence on any other substance than opiates, cocaine, or nicotine; current tx for cocaine dependence; current use of psychotropic medications unless used for > 90 days; use of acupuncture in past 30 days; actively suicidal or psychotic	Cocaine	I1: Auricular acupuncture C1: Needle-insertion control C2: Relaxation training (no needles)

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Treatment Duration, Longest Follow-up (All Follow-ups)	Results for Health Outcomes† (KQ4)	Results for Drug Use Outcomes† (KQ5)	Results for Social/legal Outcomes† (KQ5a)	Did Outcomes Differ at Earlier Follow-ups? (Y/N)	Comments
Avants 2000[26] Fair	Tx: 8 weeks Follow-up: up to 8 weeks	None	% Positive urine samples per week, analyzed longitudinally: I1 fewer pos samples than C1 or C2 (p=.01 for repeated measures test of similarity of intercept and slope, p=.01 for I vs C1, p=.05 for I vs C2	None	N	Only included ITT analysis because those dropping out had higher prop of positive urine tests, so completers are a biased group.

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Key Question	Target Population (T, Y, A, P)*	Screened Population (Y/N)	Total Number of Patients	Inclusion Criteria	Exclusion Criteria	Type of Drug(s) Being Treated	Treatment/ Intervention (I) & Control (C) Conditions
Fudala 2003[19] Fair	5	Y, A	N	296	Ages 18-59; DSM-IV diagnosis opiate dependence; seeking opiate-substitution pharmaco-therapy	Pregnant or nursing; medical condition making participation hazardous; aspartate or alanine aminotransferase levels > 3 times upper limit of normal; current primary Axis I DSM-IV diagnosis other than opiate, caffeine, or nicotine dependence; use of methadone, levomethadyl acetate, or naltrexone within 14 days of enrollment	Opiates	I1: Buprenorphine alone I2: Buprenorphine + naloxone C: Placebo
Schwartz 2006[23] Fair	5, 5a	A	N	319	1 year of meeting DSM-IV criteria for opiate dependence	Pregnant; acute medical or psychiatric illness	Opiates	I: Interim tx while awaiting admission to MTP; orientation to MTP, physical exam, methadone under direct observation for up to 120 days C: Wait list for study MTP, plus information on access to other MTPs in area

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Treatment Duration, Longest Follow-up (All Follow-ups)	Results for Health Outcomes† (KQ4)	Results for Drug Use Outcomes† (KQ5)	Results for Social/legal Outcomes† (KQ5a)	Did Outcomes Differ at Earlier Follow-ups? (Y/N)	Comments
Fudala 2003[19] Fair	Tx: 4-week Followup: 4-week	None	% Negative urine tests: I1: 20.7% I2: 17.8% C: 5.8% I1, I2 > C, p<.001 Clinician rating of patient functioning: I1, I2>C, p<.001	None	N	Recruited from ppl seeking opiate-substitution pharmacotherapy
Schwartz 2006[23] Fair	Tx: up to 4 mos Follow-up: up to 4 mos	None	% with urine tests positive for opiates: I: 57% C: 79% p<.001 # days used heroin, past 30 days: I: 4.2 (8.6) C: 26.4 (8.8) p<.001 % with urine tests positive for cocaine: I: 62% C: 63% p=.85	ASI-legal, group x time interaction (p<.001) Amount of money spent on drugs, past 30 days I: $76 C: $560 (p<.001) Amount of illegal income in past 30 days I: $36 C: $412 (p<.02)	N	Recruited from people seeking methadone tx at community tx program

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Key Question	Target Population (T, Y, A, P)*	Screened Population (Y/N)	Total Number of Patients	Inclusion Criteria	Exclusion Criteria	Type of Drug(s) Being Treated	Treatment/ Intervention (I) & Control (C) Conditions
Guo 2001[21] Fair	5	T, Y, A	N	49	DSM-IV diagnosis of opiate dependence; successfully completed detox for ≥ 7 days; urine test negative for morphine; patients had "strong desire to abstain from opiates"; accept naltrexone as tx; had relative or friend who guaranteed to supervise patients tx	Receiving tx for opiates; acute withdrawal diagnosis; apparent withdrawal after naloxone challenge test; allergic to naltrexone; severe physical or mental disease	Opiates	I: Naltrexone C: Placebo
Petrakis 2000[30] Fair	5	A	N	67	Enrolled in MMT for opiate dependence for ≥ 3 mos.; cocaine dependence; current use of cocaine	Psychotic or bipolar disorders, serious psychiatric symptoms, medical problems that would contraindicate disulfiram; pregnant	Cocaine	I: Disulfiram 250 mg/day (n=36) C: Placebo (n=31) (Both medications dissolved in methadone dose)

Table 3. Evidence Table - Individual Articles Pertaining to Drug Misuse Treatment (KQ 4/5/5a) (continued)

Author, Year Quality Rating	Treatment Duration, Longest Follow-up (All Follow-ups)	Results for Health Outcomes† (KQ4)	Results for Drug Use Outcomes† (KQ5)	Results for Social/legal Outcomes† (KQ5a)	Did Outcomes Differ at Earlier Follow-ups? (Y/N)	Comments
Guo 2001[21] Fair	Tx: 6 mos Follow-up: 6 mos (1-, 2-, 3-, 4-, 5-, 6-mo)	None	% Abstinent at 6-mo: I: 31.4% C: 7.1% p<.05 Average mos abstinent: I: 3.3 (2.3) C: 2.1 (1.6) p<.05 % Positive urine samples: I: 24.4% C: 40.5% p<.05	None	N	Set in China, required relative/friend to supervise taking medications
Petrakis 2000[30] Fair	Tx: 3-mos; Folow-up at post-tx only	None	Random effects regression: Group x time, frequency of cocaine use (p=0.04); quantity of cocaine use (p=0.02) based on self-report; results NS when based on UA. Self-reported days cocaine use in past 30, mean (SD): Pre-tx: I: 19.65 (9.86) C: 16.74 (9.78) Post-tx: I: 4.96 (7.50) C: 6.68 (7.03) Self-reported grams cocaine used weekly in past 30 days, mean (SD): Pre-tx: I: 3.16 (5.07) C: 1.46 (1.92) Post-tx: 0.59 (1.28) 0.41 (0.51)	None	NA	Small sample, MMT patients; 52% female increases generalizability among this population, but no follow-up interval after treatment end, and results NS when based on urinalysis

*Populations include: T, Teens; Y, Young adults; A, Adults; P, Pregnant Women.
†Results at longest follow-up assessment
ASI=Addiction Severity Index; AUDIT=Alcohol Use Disorders Identification Test; CBT=Cognitive Behavioral Therapy; GSI=General Severity Index; SCL-90-R=Symptom Checklist- 90-Revised; HAM-D=Hamilton Depression Rating Scale; MI=Motivational Interviewing; MET=Motivational Enhancement Therapy; MTP=Methadone Treatment Program; NR=Not reported; Ns=Not significant; RBT=Reinforcement-based Intensive Outpatient Treatment; RPT=Relapse Prevention Therapy; S=Significant; SDS=Severity of Dependence Scale;
Sx,=Symptoms; Tx=Treatment; UA=Urinalysis.

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7)

Author, Year Quality Rating	Study Design	Target Pop. (T,Y,A,P)	Screened Pop.? (Y/N)	Total Number of Patients	Inclusion Criteria, Sample Description	Exclusion Criteria	Type of Drug(s)
Sorensen 2005[35] Fair	Prospective Cohort	A	N	300 at intake; 188 interviewed in 1984	Copenhagen, Denmark. Treated for opioid addiction in 1973	Died before 1984 (n=78), non-response to interview attempt in 1984 (n=34)	Opiates (Heroin, morphine)

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Groups Analyzed	Length of Follow-up	Type of Analysis	Outcome(s)	Results[†]	Reviewer Comment
Sorensen 2005[35] Fair	Based on drug status in 1984: 1. Stable drug-free abstinent (n=87); 2. Occasional illegal drug use or in MMT (n=53); 3. Daily (illegal) drug use or daily injection drug use (may have also included alcohol or other drug use) (n=48)	15 yr (1984-99)	1. Survival analysis (Cox proportional hazards) 2. Comparison with sex-specific standard mortality ratios (SMR) for Danish population	Mortality, SMR	1. Hazard rate (95% CI): Group 1: 0.45 (0.2, 0.8); Group 2: 0.74 (0.4, 1.4) Group 3: ref. (adjusted for age, gender, psychosis hospitalization) 2. Sex-specific SMRs (95% CI): Women Group 1: 7 (2.4, 17.0) Group 2: 22 (8.2, 48.8) Group 3: 34 (15.7, 65.1) Men Group 1: 8 (4.6, 13.6) Group 2: 11 (5.9, 19.0) Group 3: 13 (6.7, 21.6)	3 time points, allows inference from drug misuse cessation to subsequent reduction in mortality

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year	Quality Rating	Study Design	Target Pop. (T,Y,A,P)	Screened Pop.? (Y/N)	Total Number of Patients	Inclusion Criteria, Sample Description	Exclusion Criteria	Type of Drug(s)
Hser 2001[12]	Fair	Prospective cohort, some cross-sectional analyses	Y, A	N	581 at intake; 242 interviewed in 1996-97: 284 dead, 31 refused, 24 lost to fup	Male criminal offenders, mandated to opioid treatment in 1962-64	NR	Heroin

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Groups Analyzed	Length of Follow-up	Type of Analysis	Outcome(s)	Results[†]	Reviewer Comment
Hser 2001[12] Fair	1. For mortality analysis: Current heroin users vs. non-users, at 2 interview points: 1974-75 & 1985-86 2. For health outcomes among 242 interviewed in 1996-97: persons abstinent >= past 5 yr (n=113) vs. current users or abstinent < past 5 yr (n=129)	For mortality: 2 10-yr intervals (at 1996-97 and 1985-86 fups) Cross-sectional for other health outcomes	Multiple logistic regression: 1974-75 & 1985-86 heroin use status to predict mortality by 1985-86 & 1996-97, respectively. Adj. for race, age, disability status, cigarette smoking, heavy alcohol use, years since first heroin use, arrests since previous interview	1. Mortality 2. Physical & mental health status: a) disability b) hepatitis c) HIV d) STD's e) depression f) anxiety g) somatization disorder h) OCD i) interpersonal sensitivity	1. Active heroin status (yes vs. no): 1974-75 to 1985-86 (n=439): Adj. OR (95% CI) = 1.32 (0.75-2.35) 1985-86 to 1996-97 (n=345): 1.38 (0.76-2.50) 2. Abstinent vs. other: Physical health: a) disability: 33.0% vs. 53.1%, p=** b) hepatitis: 41.6% vs. 41.7%, p=NS c) HIV: 0.9% vs. 1.6%, p=NS d) STDs: 24.1% vs. 30.5%, p= NS Mental health, mean, (sd): e) depression: 1.32 (0.38) vs. 1.54 (0.58), p=** f) anxiety: 1.19 (0.28) vs. 1.40 (0.48) p=** g) 1.39 (0.34) vs. 1.56 (0.49) p=** h) OCD: 1.51 (0.46) vs. 1.66 (0.59), p=* i) interpersonal sensitivity: 1.32 (0.35) vs. 1.50 (0.48), p=**	Long-term fup, 3 time points are strengths; criminally-involved, male sample limits generalizability; cross-sectional results for morbidity outcomes

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year	Quality Rating	Study Design	Target Pop. (T,Y,A,P)	Screened Pop.? (Y/N)	Total Number of Patients	Inclusion Criteria, Sample Description	Exclusion Criteria	Type of Drug(s)
Fridell 2006[36]	Good	Prospective cohort, some cross-sectional analyses	A	N	125 at intake; 90 at fup	"Drug abusers" admitted to detoxification & rehabilitation inpatient unit in Lund, Sweden, in 1988-89	NR	Mixed: amphetamines (39%), opiates (28%), cannabis (18%), tranquilizers (11%); 67% "some" IDU

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Groups Analyzed	Length of Follow-up	Type of Analysis	Outcome(s)	Results[†]	Reviewer Comment
Fridell 2006[36] Good	1) Abstinence, ascertained at 5 yr fup, defined as no use of illegal drugs & no abuse of alcohol vs. other (42% abstinent for past 6 mos.) 2) Length of time abstinent at 5 yr fup	10 yr (5yr fup to 15 yr fup); (5 yr: intake to 5 yr fup)	Survival analysis (15 yr mortality); Cross-sectional (5 yr fup)	Mortality (24% at 15 yr fup) GAF, GSI (at 5 yr fup only)	Coefficient for time abstinent at 5 yr fup: -0.30, Wald statistic = 1.88, p=NS (n=90) GAF reported only for 5 yr fup (cross-sectional, n=90): Abstinent = 75 Other = 64, p=*** GSI at 5 yr fup: Abstinent = 54 Other = 60, p=*	3 time points, strengthens (null) mortality findings; small sample, cross-sectional analysis of 5-yr data limits inferences

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year	Quality Rating	Study Design	Target Pop. (T,Y,A,P)	Screened Pop.? (Y/N)	Total Number of Patients	Inclusion Criteria, Sample Description	Exclusion Criteria	Type of Drug(s)
Lucas 2001[37]	Fair	Prospective cohort, with cross-sectional analyses	A	N	764	Attendees at an HIV-1 specialty clinic in Baltimore, MD who consented, completed an interview, and met criteria for HAART	NR	Heroin or cocaine

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Groups Analyzed	Length of Follow-up	Type of Analysis	Outcome(s)	Results[†]	Reviewer Comment
Lucas 2001[37] Fair	Drug use categories, based on self-report: *Never*: never used drugs (n=189); *Former*: past use of heroin or cocaine, but not in 6 mos. Before interview (n=376); *Active*: used heroin or cocaine in past 6 mos. (n= 199);	Essentially 6 mos. (retrospective report of drug use history)	Multivariate logistic & linear regr	1. Never vs. ever used HAART (full sample); 2. Medication nonadherence (n=127) vs. adherence (n=431) among subsample taking HAART, (n=558); 3. Virologic & immunologic responses to HAART, among subsample taking HAART, (n=558)	1. Never vs. ever used HAART, Adj. OR (CI): Never (ref) Former = 1.6 (1.0-2.7) Active = 4.8 (2.8-8.3) 2. % medication nonadherence: Never = 24% Former = 17% (p=NS compared to Never) Active = 34% (p=0.05 compared to Never; p=*** compared to Former) 3. Median reduction in HIV-1 RNA level: Never vs. Former (p=NS); Never vs. Active (p=***); Former vs. Active (p=***); Median increase in CD4+ lymphocyte count: Never vs. Active (p=**); Former vs. Active (p=**)	Limited by ascertainment of drug use status at only one time point, lack of adjustment for tobacco use or psychiatric conditions (e.g., depression)

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year	Quality Rating	Study Design	Target Pop. (T,Y,A,P)	Screened Pop.? (Y/N)	Total Number of Patients	Inclusion Criteria, Sample Description	Exclusion Criteria	Type of Drug(s)
Bouhnik 2004[38]	Fair	Prospective cohort, with cross-sectional analyses	A	N	144	Among HIV-positive patients enrolled in a larger cohort study, those who self-reported as IDU's at enrollment, and reported cessation of IDU ≥12 mo or continued IDU at 18 mo. fup	Missed more than 1 visit between enrollment & 18 mo. fup (n=33); IDU cessation < 12 mo. at 18 mo. fup (n=20)	NR (injected drugs, likely heroin or cocaine)

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Groups Analyzed	Length of Follow-up	Type of Analysis	Outcome(s)	Results[†]	Reviewer Comment
Bouhnik 2004[38] Fair	IDUs (n=54) vs. Ex-IDUs (n=90)	Essentially 12-mos. (retrospective report of recent IDU)	Cross-sectional; univariate logistic regression	CES-D (depressive symptoms) >= 16; Immunologic (CD4 cell count) & virologic (plasma viral load) indicators of HIV progression; HAART participation (y/n); Inconsistent condom use (y/n)	CES-D: IDU= 40.7% Ex-IDU= 20.0%, p=**; OR=0.36 (0.17-0.77) CD4 cell count: IDU=456 Ex-IDU=397, p=0.052, OR=0.85 (0.73-1.00); Plasma viral load (log copies/ml): IDU=3.40 Ex-IDU=3.24, p=ns, OR= 0.90 (0.64-1.27) HAART participation: IDU=66.7% Ex-IDU=80.0%, p=ns, OR=2.00 (0.93-4.30) Inconsistent condom use: IDU=40.7% Ex-IDU=20.0%, p=**, OR=0.36 (0.17-0.77)	2 time points, with retrospective ascertainment of IDU cessation. Analyses unclear regarding adjustment for covariates.

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Study Design	Target Pop. (T,Y,A,P)	Screened Pop.? (Y/N)	Total Number of Patients	Inclusion Criteria, Sample Description	Exclusion Criteria	Type of Drug(s)
Knowlton 2001[41] Fair	Prospective cohort, with cross-sectional analyses	Y, A	N	503 at intake; 393 at fup	Subset from larger study (ALIVE), initial criteria age >= 18, injected drugs in past 10 yrs	NR	Heroin & cocaine

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Groups Analyzed	Length of Follow-up	Type of Analysis	Outcome(s)	Results[†]	Reviewer Comment
Knowlton 2001[41] Fair	Former drug users (stopped b/n baseline & fup) compared to continuing users	1 yr	Multiple logistic regr	High (>=16) vs. lower CES-D score	Adj. OR = 0.40** (Beta=-0.92, SE=0.35) (adjusted for baseline drug use, functional limitations, perceived social support, depressive symptoms; plus declining physical function measured at fup	2 time points, correlational results; lack of adjustment for tobacco use limits interpretation of association between stopping drug use & depression

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year

Quality Rating	Study Design	Target Pop. (T,Y,A,P)	Screened Pop.? (Y/N)	Total Number of Patients	Inclusion Criteria, Sample Description	Exclusion Criteria	Type of Drug(s)
Gossop 2000[42] Fair	Prospective cohort, with cross-sectional analyses	A	N	667 at intake; 478 at fup	Problem drug users beginning a new methadone treatment episode during March-July 1995; able to provide address in the UK	Primary diagnosis of alcohol dependence, previous	Opioids (heroin, illicit methadone), benzodiazepines, cocaine, amphetamines

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Groups Analyzed	Length of Follow-up	Type of Analysis	Outcome(s)	Results[†]	Reviewer Comment
Gossop 2000[42] Fair	4 groups, based on cluster analysis of drug use at baseline and fup: *Group 1 (improved response #1,* n=121, 25%): high frequency opiate users at baseline, greatly reduced opiate, stimulant, and benzodiazepine use at fup; *Group 2 (improved response #2*, n=162, 34%): Mainly used opiates at baseline, decreased opiate use significantly, but slightly increased benzodiazepine use; Group 3 (*poor response,* n=88*,* 18%*)*: No change in opiate or stimulant use, slight increase in benzodiazepine use; Group 4 (*low rate use,* n=107, 22%): Relatively low use of opiates, stimulants & benzodiazepines at baseline, reduction in benzodiazepines.	1 yr	Repeated measures ANCOVA	Physical health index; anxiety & depression index (not described in article)	Physical health, mean (sd) at intake & fup: Group 1: 16.8 (7.8), 11.5 (6.9) Group 2: 16.2 (8.3), 12.0 (8.2) Group 3: 18.2 (8.6), 17.6 (8.1) Group 4: 12.9 (7.1), 11.1 (7.9) Group diff. F (3,470)= 10.46, p=*** Anxiety & depr, mean (sd) at intake & fup: Group 1: 3.0 (1.8), 2.6 (1.8) Group 2: 3.1 (1.8), 2.7 (2.1) Group 3: 3.2 (2.1), 3.7 (2.0) Group 4: 3.3 (1.9), 2.5 (2.0) Group diff. F (3, 470)=8.99, P=***	Useful groupings of longitudinal drug use patterns. 2 time points, correlational results. Some concern about adequacy of adjustment for baseline differences between analysis groups

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Study Design	Target Pop. (T,Y,A,P)	Screened Pop.? (Y/N)	Total Number of Patients	Inclusion Criteria, Sample Description	Exclusion Criteria	Type of Drug(s)
Moatti 2000[40] Fair	Prospective cohort, with retrospective analyses	Y, A	N	164	HIV patients infected through injecting drug use. Age 18+; CD4 cell counts >= 300 x 10^6 / l in last visit before enrollment; no opportunistic infections	NR	NR (injected drugs, likely heroin or cocaine)

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Groups Analyzed	Length of Follow-up	Type of Analysis	Outcome(s)	Results[†]	Reviewer Comment
Moatti 2000[40] Fair	Group 1. On buprenorphine drug maintenance treatment (n=32); Group 2. Ex-IDU, stopped >= 6 mos. Ago (n=113) Group 3. Active IDU, not on Buprenorphine drug maintenance treatment (n=19)	Essentially 6 mos. (retrospective report of recent drug use)	Univariate comparisons of medians (Mann-Whitney test), logistic regression	Short-term adherence to antiretroviral drug therapy, based on self-report to nurse examiner and self-administered questionnaire. "Non-adherence" defined as reporting less than 80% of total dose of antiretroviral drug, or reporting not being "totally adherent" with HAART, during prior week.	Adherent, n (%): Group 1: 25 (78.1) Group 2: 74 (65.5) Group 3: 8 (42.1) Adj OR (CI): Group 1 (ref) Group 2: 2.32 (0.83-6.48) Group 3: 5.09 (1.29-20.13) Adjusted for sex, age, education, employment, alcohol consumption, index of negative life events, social support, clinical stage, # HIV symptoms, # HAART prescribed pills, prior antiretroviral treatment, time since initiated HAART, specific protease inhibitors used	HIV clinic patients, small samples in analysis groups, limit generalizeability

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Study Design	Target Pop. (T,Y,A,P)	Screened Pop.? (Y/N)	Total Number of Patients	Inclusion Criteria, Sample Description	Exclusion Criteria	Type of Drug(s)
Lucas 2006[39] Fair	Prospective cohort	Y, A	N	1851 persons; 5,486 surveys 65% of participants completed >1 survey	Attendees at an HIV-1 specialty clinic in Baltimore, MD who consented, completed >=1 interview, and met criteria for HAART	NR	Heroin or cocaine

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Groups Analyzed	Length of Follow-up	Type of Analysis	Outcome(s)	Results[†]	Reviewer Comment
Lucas 2006[39] Fair	Based on reported drug use: Group 1: nonusers (n=1028) Group 2: intermittent users, abstinent during past 6 mos. (time dependent); Group 3: intermittent users, active during past 6 mos. (time dependent; n=588 for groups 2 + 3, NR separately); Group 4: persistent users (n=235)	Up to 5 years	For primary outcome: Joint longitudinal-survival model with time-dependent variables For secondary outcome: Cox survival analysis	Primary: Development of new "opportunistic conditions" related to HIV disease progression; coded 1 if any present during a 6-mo. period Secondary: mortality, over 3-yr period	Primary (OR, 95% CI): Group 1 (ref) Group 2 = 1.4 (1.0, 1.9) Group 3 = 2.3 (1.5, 3.0) Group 4 = 2.1 (1.4, 3.1) Adjusted for age, sex, race, peak HIV-1 RNA, nadir CD4 cell count, at-risk alcohol use Secondary (hazard ratio, 95% CI): Group 1 (ref) Groups 2+3 = 1.9 (1.4, 2.4) Group 4 = 2.9 (2.1, 4.1) Adjusted for age, sex, race, peak HIV-1 RNA, nadir CD4 cell count	Strong within-person analyses; HIV clinic patient sample limits generalizeability

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Study Design	Target Pop. (T,Y,A,P)	Screened Pop.? (Y/N)	Total Number of Patients	Inclusion Criteria, Sample Description	Exclusion Criteria	Type of Drug(s)
Shankaran 2004[43] Fair	Retrospective cohort	P	N	651	Age 18+; delivery in participating hospital; birth weight ,1500 g OR >=1500 g plus birth occurred during specified recruitment hours	Birth outside catchment area for fup; multiple gestation; maternal psychosis	Cocaine, cannabis

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Groups Analyzed	Length of Follow-up	Type of Analysis	Outcome(s)	Results[†]	Reviewer Comment
Shankaran 2004[43] Fair	All who self-reported drug use during pregancy AND confirmed by baby's meconium; Divided into 5 groups, for each drug: consistently high use, consistently moderate use, consistently low use, increasing use, decreasing use (change in use based on use in 3-mos before pregnancy & first trimester with use during trimesters 2 & 3) Group-matched with comparison group not exposed to cocaine or opiates	NA; mothers interviewed at 1-mo. well-baby check	Multivariate linear regression; covariates included patterns of use of other substances, clinic, maternal race, maternal age, parity, prepregnancy weight, gestational age, infant gender, socioeconomic status	Birthweight, length at birth, head circumference at birth	Among 15 comparisons for each drug (5 groups x 3 outcomes): Cocaine: All NS except 2: low users' birthweight < non-users' ; moderate users' head circumf. < non-users' Cannabis: All NS	90/745 (12.1%) with meconium positive for cocaine or opiates denied use and were dropped from analysis. Likely bias as a result. 2 significant associations with cocaine use not consistent with dose-response relationship

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Study Design	Target Pop. (T,Y,A,P)	Screened Pop.? (Y/N)	Total Number of Patients	Inclusion Criteria, Sample Description	Exclusion Criteria	Type of Drug(s)
Chasnoff 1989[44] Fair	Retrospective cohort	P	N	115 (94, 89 for some analyses)	Cocaine-exposed groups attended clinic that provided substance abuse and perinatal care, 1986-early 1988, used cocaine during pregnancy; comparison group with no drug use history received perinatal care at same hospital.	Opiate use during pregnancy; 34 whose temporal patterns of cocaine use during pregnancy differed from those of 2 cocaine-exposed study groups	Cocaine

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Groups Analyzed	Length of Follow-up	Type of Analysis	Outcome(s)	Results[†]	Reviewer Comment
Chasnoff 1989[44] Fair	Group 1: used cocaine during first trimester only (n=23); Group 2: used cocaine throughout pregnancy (n=52); Group 3: did not use any drugs or alcohol throughout pregnancy (n=40)	NA; through childbirth	Chi-square, ANOVA	Perinatal complications; neonatal growth parameters (full-term infants only, among 94 mothers); Neonatal Behavioral Assessment Scale (7 dimensions)	Complications, %: preterm delivery: Group 1, 17% Group 2, 31% Group 3, 3% (p=**) low birth weight: Group 1, 0% Group 2, 25% Group 3, 5% (p=**) small for gestational age: Group 1, 0% Group 2, 19% Group 3, 3% (p=*) abruptio placentae: Group 1, 9% Group 2, 15% Group 3, 0% (p=*) Neonatal growth, mean (sd): Weight, g: Group 1, 3160 (453) Group 2, 2829 (708) Group 3, 3436 (628). Group 1 vs. Group 3, p=NS. Group 2 vs. Group 3, p=** Length, cm: Group 1, 49.3 (2.5) Group 2, 48.0 (3.6) Group 3, 51.1 (2.9). Group 1 vs. Group 3, p=NS. Group 2 vs. Group 3, p=** Head circum., cm: Group 1, 33.4 (2.2) Group 2, 32.7 (2.3)	Small, highly selected samples limit inferences & generalizeability. Few direct comparisons between cocaine-exposed groups; group-matching may not adequately adjust for baseline differences between groups

Table 4. Evidence Table - Relationships Between Stopping or Reducing Drug Misuse and Morbidity or Mortality Outcomes (KQ 7) (continued)

Author, Year Quality Rating	Groups Analyzed	Length of Follow-up	Type of Analysis	Outcome(s)	Results[†]	Reviewer Comment
					Group 3, 34.6 (1.6). Group 1 vs. Group 3, p=NS. Group 2 vs. Group 3, p=** Neonatal Behavioral Assessment Scale: Groups 1 & 2 had worse scores than Group 3 on 4 of 7 dimensions (p=*)	

*p<0.05, **p<0.01, ***p<0.001

[†]Results at longest follow-up assessment

ANCOVA= Analysis of covariance; A =Adults (26+); CI=95% confidence interval; Fup= Follow-up; GAF=Global Assessment of Functioning; GSI=Global Severity Index; HAART=Highly active antiretroviral therapy; IDU=Injection drug use(r); MMT=Methadone maintenance treatment NA=Not applicable; NR=Not reported; NS=Not significant (p>0.05); OR=Odds ratio; P=Pregnant females; Sd=standard deviation; STD=sexually transmitted disease; T=Teen/Adolescents (12-17); Y=Young adults (18-25)

Table 5. Summary of Evidence Quality by Key Question and Population

Critical Key Question	Overall USPSTF Quality	Reviewed Evidence/Comment
KQ1. Is there direct evidence that screening for drug misuse reduces morbidity and/or mortality? Populations: Pregnant women Adolescents 12-17 y Young adults 18-25 y Adults 26+ y	Poor, all populations	RCTs or CCTs; Cohort or longitudinal studies No evidence found
KQ4. Does treatment for drug misuse among individuals identified through screening improve morbidity and/or mortality? Populations: Same as KQ1	In screened individuals: Poor, all populations In non-screened individuals: Poor, in pregnant women and adolescents	RCTs or CCTs No evidence found No evidence found
	Fair, in young adults and adults	7 of 16 trials reported health outcomes 2 trials of treatments for opiate dependence reported treatment improved depressive symptoms at post-treatment assessment (Assadi 2003[18]; Gruber 2000[20]) Of 3 trials of treatments for cocaine dependence, 1reported desipramine treatment reduced psychiatric problems post-treatment (but cocaine use was not reduced in this trial) (Arndt 1992[25]); 2 reported no effects of fluoxetine or nefazodone, respectively, on psychiatric symptoms (Bakti 1996[27]; Passos 2005[29]) Of 2 trials of counseling treatments for cannabis dependence reporting health outcomes, 1 found no effect on psychiatric symptoms (Copeland 2001[31]), and 1 found treatment improved anxiety symptoms (but not 3 other psychiatric or physical health indicators) (Marijuana Treatment Project 2004[32])

Table 5. Summary of Evidence Quality by Key Question and Population

Critical Key Question	Overall USPSTF Quality	Reviewed Evidence/Comment
KQ5. Does treatment for drug misuse among individuals identified through screening result in decreased drug misuse? Populations: Same as KQ1	In screened individuals: **Fair**, among young adults and adults;	RCTs or CCTs 1 good quality trial showed that brief behavioral counseling significantly reduced cocaine and opiate use in an outpatient clinic population (Bernstein 2005[24])
	Poor, among adolescents and pregnant women	No evidence found
	In non-screened individuals: Poor, in pregnant women	No evidence found
	Fair, in adolescents **Good**, in young adults and adults	16 trials of pharmaco- or psycho-social treatments reported drug use outcomes: 3 pharmaco treatments (Fudala 2003[49]; Guo 2001[21]; Schwartz 2006[23]) and 1 psycho-social intervention (Gruber 2000[20]) significantly reduced opiate use 1 acupuncture (Avants 2000[26]) and 1 pharmaco treatment (Feingold 2002[28]) reduced cocaine use 4 psycho-social treatments for cannabis dependence reported reductions cannabis use (Copeland 2001[31]; Marijuana Treatment Project 2004[32]; McCambridge 2005[33]; Stephens 2000[34]) 2 of these trials included adolescents (Guo 2001[21]; McCambridge 2005[33]) No or inconsistent treatment effects were reported in 6 trials: Assadi 2003[18]; Johnson 1995[22]; Arndt 1992[25]; Bakti 1996[27]; Passos 2005[29]; Petrakis 2000[30])
KQ5a. Does treatment for drug misuse reduce risk behaviors/improve social/legal outcomes? Populations: Same as KQ1	In screened individuals: Poor, all populations	RCTs or CCTs No evidence found
	In non-screened individuals: Poor, in adolescents and pregnant women	No evidence found
	Fair, in young adults and adults	6 studies reported social/legal outcomes: 1 pharmaco-therapy (methadone) for opiate dependence reported reduced illegal activity

Table 5. Summary of Evidence Quality by Key Question and Population

Critical Key Question	Overall USPSTF Quality	Reviewed Evidence/Comment
		3 psycho-social intervention for cannabis dependence reported improvements in cannabis-related social problems (Copeland 2001[31]; Marijuana treatment Project 2004[32]; Stephens 2000[34]) 1 psycho-social intervention for opiate dependence (Gruber 2000[20]) and 1 pharmcotherapy for cocaine dependence (Arndt 1992[25]) reported no effects on multiple indicators of employment and social functioning
KQ7. Is decreased use or abstinence following drug misuse reliably associated with reduced morbidity and/or mortality? Populations: Same as KQ1		RCTs or CCTs; cohort or longitudinal studies
	In screened individuals: Poor, all populations	No evidence found
	In non-screened individuals: Poor, in adolescents	No evidence found
	Fair, among non-screened individuals, in young adults, adults, and pregnant women	In young adults and adults: 1 study showed risk of death over 10 years reduced by 55% among former opiate addicts who became abstinent (Sorensen 2005[35]) 5 studies showed associations between stopping opiate use and better psycho-social functioning (Hser 2001[12]; Fridell 2006[36]; Gossop 2000[42]) or fewer depressive symptoms (Knowlton 2001[41]; Bouhnik 2004[38]) 1 study showed association between stopping heroin and cocaine use and better adherence to and responses to HAART (Lucas 2001[37]) 1 study showed decreased risk of HIV disease progression among intermittent drug users during periods of abstinence (Lucas 2006[39]) 1 study showed association between stopping injecting drug use and short-term adherence to HAART(Moatti 2000[40] In pregnant women: 1 study showed stopping cocaine use in first trimester was associated with some reduction in pregnancy complications and better neonatal outcomes compared to continuing cocaine users (Chasnoff 1989[44]) 1 study showed no clear association between patterns of cocaine or cannabis use during pregnancy with neonatal outcomes (Shankaran 2004[43])

Appendix A. Search Strategies

KQ1 Screening
Database: Ovid MEDLINE®
1994 to April 21, 2006
1 Substance Abuse Detection/
2 substance-related disorders/ or amphetamine-related disorders/ or cocaine-related disorders/ or marijuana abuse/ or opioid-related disorders/ or heroin dependence/ or morphine dependence/ or phencyclidine abuse/ or substance abuse, intravenous/
3 Mass Screening/
4 2 and 3
5 1 or 4
6 health outcome$.ti,ab.
7 health consequences.ti,ab.
8 functional status.ti,ab.
9 health status/
10 health status indicators/
11 "Outcome Assessment (Health Care)"/
12 mo.fs.
13 mortality/
14 quality of life/
15 exp arrhythmia/
16 exp myocardial infarction/
17 cerebral hemorrhage/
18 seizures/
19 exp respiratory tract diseases/
20 depression/
21 exp hepatitis/
22 exp endocarditis, bacterial/
23 exp glomerulonephritis/
24 pulmonary embolism/
25 suicide/
26 suicide, attempted/
27 homicide/
28 pregnancy outcome/
29 pregnancy complications/
30 abruptio placentae/
31 Infant, Premature/
32 Labor, Premature/
33 Premature Birth/
34 fetal growth retardation/
35 weight gain/ and pregnancy/
36 Abnormalities, Drug-Induced/
37 Neonatal Abstinence Syndrome/
38 exp accidents/
39 in.fs.
40 exp "wounds and injuries"/
41 asphyxia/
42 exp "Attention Deficit and Disruptive Behavior Disorders"/
43 exp schizophrenia/
44 exp psychotic disorders/
45 exp mood disorders/
46 exp anxiety disorders/
47 exp personality disorders/
48 exp BRAIN/de, gd [Drug Effects, Growth & Development]
49 exp brain diseases/
50 exp Sexually Transmitted Diseases/
51 Fetal Alcohol Syndrome/
52 exp Sex Offenses/
53 Pregnancy, Unplanned/
54 unplanned pregnanc$.ti,ab.
55 unintended pregnanc$.ti,ab.
56 exp HOMELESS PERSONS/
57 exp Educational Measurement/

58 ACHIEVEMENT/
59 UNDERACHIEVEMENT/
60 Student Dropouts/
61 or/6-60
62 5 and 61
63 limit 62 to english language
64 limit 63 to animals
65 limit 63 to humans
66 64 not 65
67 63 not 66
68 limit 67 to yr="1994 - 2006"
69 from 68 keep 1-500

KQs 4, 5, & 5a Treatment -- Systematic Review Search

Database: Ovid MEDLINE(R); CDSR; DARE; PsycINFO
1994 to November 17, 2005

1 Substance-Related Disorders/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
2 Amphetamine-Related Disorders/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
3 Cocaine-Related Disorders/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
4 Marijuana Abuse/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
5 Opioid-Related Disorders/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
6 Heroin Dependence/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
7 Morphine Dependence/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
8 Phencyclidine Abuse/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
9 Substance Abuse, Intravenous/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
10 Behavior, Addictive/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
11 Substance Abuse Treatment Centers/
12 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13 systematic review$.mp.
14 systematic literature review$.mp.
15 meta-analysis.pt.
16 meta-analysis.ti.
17 meta-analyses.ti.
18 metaanalysis.ti.
19 Evidence-Based Medicine/
20 (evidence-based and (guideline$ or recommendation$)).mp.
21 (evidenced-based and (guideline$ or recommendation$)).mp.
22 consensus development conference.pt.
23 health planning guidelines/
24 "cochrane database of systematic reviews".jn.
25 acp journal club.jn.
26 health technology assessment winchester england.jn.
27 evidence report technology assessment summary.jn.
28 (evidence based dentistry or evidence based mental health or evidence based nursing).jn.
29 clinical evidence.jn.
30 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31 12 and 30
32 limit 31 to yr="1994 - 2006"
33 limit 32 to english language

KQs 4, 5, & 5a Treatment -- Bridge Search, Individual Articles

Databases: Ovid MEDLINE(R); PsycINFO
2001 to April 7, 2006

Database: Ovid MEDLINE(R)
Search Strategy:
---

1 Substance-Related Disorders/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
2 Cocaine-Related Disorders/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]

3 Marijuana Abuse/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
4 Opioid-Related Disorders/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
5 Heroin Dependence/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
6 Morphine Dependence/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
7 Substance Abuse Treatment Centers/
8 Behavior, Addictive/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
9 Substance Abuse, Intravenous/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
10 Substance Withdrawal Syndrome/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12 Substance-Related Disorders/pc [Prevention & Control]
13 Cocaine-Related Disorders/pc [Prevention & Control]
14 Marijuana Abuse/pc [Prevention & Control]
15 Opioid-Related Disorders/pc [Prevention & Control]
16 Heroin Dependence/pc [Prevention & Control]
17 Morphine Dependence/pc [Prevention & Control]
18 Substance Abuse, Intravenous/pc [Prevention & Control]
19 Behavior, Addictive/pc [Prevention & Control]
20 Substance Withdrawal Syndrome/pc [Prevention & Control]
21 Crack Cocaine/
22 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23 cocaine.ti,ab.
24 marijuana.ti,ab.
25 marihuana.ti,ab.
26 cannabis.ti,ab.
27 opioid.ti,ab.
28 opioids.ti,ab.
29 opiate.ti,ab.
30 opiates.ti,ab.
31 narcotic.ti,ab.
32 narcotics.ti,ab.
33 morphine.ti,ab.
34 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33
35 misus$.ti,ab.
36 abus$.ti,ab.
37 addict$.ti,ab.
38 dependent$.ti,ab.
39 dependence.ti,ab.
40 35 or 36 or 37 or 38 or 39
41 ((cocaine or marijuana or marihuana or cannabis or opioid or opioids or opiate or opiates or narcotic or narcotics or morphine) adj25 (misus$ or abus$ or addict$ or dependent$ or dependence)).ti,ab.
42 22 or 41
43 treat.ti,ab,hw.
44 treated.ti,ab,hw.
45 treating.ti,ab,hw.
46 treatment$.ti,ab,hw.
47 therapy.ti,ab,hw.
48 therapies.ti,ab,hw.
49 43 or 44 or 45 or 46 or 47 or 48
50 42 and 49
51 11 or 50
52 limit 51 to (clinical trial or controlled clinical trial or randomized controlled trial)
53 clinical trials/ or controlled clinical trials/ or randomized controlled trials/
54 double-blind method/ or random allocation/ or single-blind method/
55 random$.ti,ab.
56 53 or 54 or 55
57 51 and 56
58 52 or 57
59 limit 58 to english language
60 limit 59 to humans
61 limit 59 to animals
62 61 not 60
63 59 not 62

64 limit 63 to yr="2001 - 2006"

Database: EBM Reviews - Cochrane Central Register of Controlled Trials
Search Strategy:
---
1 Substance-Related Disorders/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
2 Cocaine-Related Disorders/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
3 Marijuana Abuse/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
4 Opioid-Related Disorders/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
5 Heroin Dependence/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
6 Morphine Dependence/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
7 Substance Abuse Treatment Centers/
8 Behavior, Addictive/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
9 Substance Abuse, Intravenous/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
10 Substance Withdrawal Syndrome/dt, rh, th [Drug Therapy, Rehabilitation, Therapy]
11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12 Substance-Related Disorders/pc [Prevention & Control]
13 Cocaine-Related Disorders/pc [Prevention & Control]
14 Marijuana Abuse/pc [Prevention & Control]
15 Opioid-Related Disorders/pc [Prevention & Control]
16 Heroin Dependence/pc [Prevention & Control]
17 Morphine Dependence/pc [Prevention & Control]
18 Substance Abuse, Intravenous/pc [Prevention & Control]
19 Behavior, Addictive/pc [Prevention & Control]
20 Substance Withdrawal Syndrome/pc [Prevention & Control]
21 Crack Cocaine/
22 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23 cocaine.ti,ab.
24 marijuana.ti,ab.
25 marihuana.ti,ab.
26 cannabis.ti,ab.
27 opioid.ti,ab.
28 opioids.ti,ab.
29 opiate.ti,ab.
30 opiates.ti,ab.
31 narcotic.ti,ab.
32 narcotics.ti,ab.
33 morphine.ti,ab.
34 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33
35 misus$.ti,ab.
36 abus$.ti,ab.
37 addict$.ti,ab.
38 dependent$.ti,ab.
39 dependence.ti,ab.
40 35 or 36 or 37 or 38 or 39
41 ((cocaine or marijuana or marihuana or cannabis or opioid or opioids or opiate or opiates or narcotic or narcotics or morphine) adj25 (misus$ or abus$ or addict$ or dependent$ or dependence)).ti,ab.
42 22 or 41
43 treat.ti,ab,hw.
44 treated.ti,ab,hw.
45 treating.ti,ab,hw.
46 treatment$.ti,ab,hw.
47 therapy.ti,ab,hw.
48 therapies.ti,ab,hw.
49 43 or 44 or 45 or 46 or 47 or 48
50 42 and 49
51 11 or 50
52 limit 51 to yr="2001 - 2005"

Database: PsycINFO
Search Strategy:
---

1 Drug Addiction/
2 Drug Abuse/
3 Drug Dependency/
4 Heroin Addiction/
5 Polydrug Abuse/
6 Intravenous Drug Usage/
7 Methadone Maintenance/
8 Drug Withdrawal/
9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10 exp TREATMENT/
11 9 and 10
12 Drug Rehabilitation/
13 cocaine.ti,ab,id,hw.
14 marijuana.ti,ab,id,hw.
15 marihuana.ti,ab,id,hw.
16 cannabis.ti,ab,id,hw.
17 opioid.ti,ab,id,hw.
18 opioids.ti,ab,id,hw.
19 opiate.ti,ab,id,hw.
20 opiates.ti,ab,id,hw.
21 narcotic.ti,ab,id,hw.
22 narcotics.ti,ab,id,hw.
23 morphine.ti,ab,id,hw.
24 heroin.ti,ab,id,hw.
25 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
26 misus$.ti,ab,id,hw.
27 abus$.ti,ab,id,hw.
28 addict$.ti,ab,id,hw.
29 dependent$.ti,ab,id,hw.
30 dependence.ti,ab,id,hw.
31 26 or 27 or 28 or 29 or 30
32 treat$.ti,ab,id,hw.
33 therapy.ti,ab,id,hw.
34 therapies.ti,ab,id,hw.
35 32 or 33 or 34
36 25 and 31 and 35
37 11 or 12 or 36
38 random$.ti,ab,id,hw.
39 clinical trial$.ti,ab,id,hw.
40 controlled trial$.ti,ab,id,hw.
41 38 or 39 or 40
42 37 and 41
43 limit 42 to english language
44 limit 43 to yr="2001 - 2006"

KQ7 Reduction/cessation of drug misuse and health outcomes

Database: Ovid MEDLINE®
1994 to April 14, 2006

1 substance-related disorders/ or amphetamine-related disorders/ or cocaine-related disorders/ or marijuana abuse/ or opioid-related disorders/ or heroin dependence/ or morphine dependence/ or phencyclidine abuse/ or substance abuse, intravenous/
2 health outcome$.ti,ab.
3 health consequences.ti,ab.
4 functional status.ti,ab.
5 health status/
6 health status indicators/
7 "Outcome Assessment (Health Care)"/

8 mo.fs.
9 mortality/
10 quality of life/
11 exp arrhythmia/
12 exp myocardial infarction/
13 cerebral hemorrhage/
14 seizures/
15 exp respiratory tract diseases/
16 depression/
17 exp hepatitis/
18 exp endocarditis, bacterial/
19 exp glomerulonephritis/
20 pulmonary embolism/
21 suicide/
22 suicide, attempted/
23 homicide/
24 pregnancy outcome/
25 pregnancy complications/
26 abruptio placentae/
27 Infant, Premature/
28 Labor, Premature/
29 Premature Birth/
30 fetal growth retardation/
31 weight gain/ and pregnancy/
32 Abnormalities, Drug-Induced/
33 Neonatal Abstinence Syndrome/
34 exp accidents/
35 in.fs.
36 exp "wounds and injuries"/
37 asphyxia/
38 exp "Attention Deficit and Disruptive Behavior Disorders"/
39 exp schizophrenia/
40 exp psychotic disorders/
41 exp mood disorders/
42 exp anxiety disorders/
43 exp personality disorders/
44 exp BRAIN/de, gd [Drug Effects, Growth & Development]
45 exp brain diseases/
46 exp Sexually Transmitted Diseases/
47 Fetal Alcohol Syndrome/
48 exp Sex Offenses/
49 Pregnancy, Unplanned/
50 unplanned pregnanc$.ti,ab.
51 unintended pregnanc$.ti,ab.
52 exp HOMELESS PERSONS/
53 exp Educational Measurement/
54 ACHIEVEMENT/
55 UNDERACHIEVEMENT/
56 Student Dropouts/
57 or/2-56
58 quit$.ti,ab.
59 reduc$.ti,ab.
60 recover$.ti,ab.
61 decreas$.ti,ab.
62 abstinen$.ti,ab.
63 abstain$.ti,ab.
64 58 or 59 or 60 or 61 or 62 or 63
65 1 and 57 and 64
66 risk$.mp.
67 cohort studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/ (547819)
68 between group$.mp.
69 66 or 67 or 68

70 65 and 69
71 limit 70 to english language
72 limit 71 to animals
73 limit 71 to humans
74 72 not 73
75 71 not 74
76 limit 75 to yr="1994 - 2006"

Appendix B. Inclusion and Exclusion Criteria

Key Question 1. Is there direct evidence that screening for drug misuse reduces morbidity and/or mortality?

Inclusion Criteria
Meets criteria for KQ1 and: *Drugs: opiates, cocaine, marijuana, and mixed drugs* *Study designs: randomized controlled trials, controlled clinical trials, prospective, and observational studies* *Publication years: 1994-present, or earlier years if identified in systematic reviews or the 1996 USPSTF report* *Populations: adolescents/teens 12-17, young adults 18-25, adults 26+, or pregnant women* *Intermediate outcomes: abstinence, decreased use, time to relapse, risk behaviors, social/legal.* *Health outcomes: morbidity (infant outcomes, injuries, medical conditions, mental health disorders, quality of life, STD transmission, utilization, violence/unintentional) and mortality.* *Conducted in an U.S. applicable country* *Primary care feasible or referable: see end of appendix for definitions* Special populations (e.g., mentally ill; tracked, but not included)

Exclusion Criteria
Does not evaluate direct evidence that screening for drug misuse reduces morbidity and/or mortality Other drugs besides opiates, cocaine, marijuana, and mixed drugs Non-humans Non-English abstract Setting: Intervention not done in primary care, primary care-feasible, or widely available for primary care referral Population: Selective population not normally seen in primary care (e.g. patients recruited from ER or other specialty setting who are injured or on drugs and do not represent a general patient population) Country: Study not conducted in a country applicable to the U.S. population Outcomes: Does not report designated outcomes Study quality: Does not meet USPSTF criteria for quality Study designs: Editorials, letters, non-systematic reviews, case control studies, case studies, comment/opinion, protocol (no data), pilot studies, abstracts only, etc.

Key Questions 4, 5, & 5a. Does treatment for drug misuse among individuals identified through screening improve morbidity and/or mortality? Does treatment for drug misuse among individuals identified through screening result in decreased drug misuse? Does treatment for drug misuse reduce risk behaviors/improve social/legal outcomes?

Inclusion Criteria
Meets criteria for KQs 4, 5, or 5a and: *Drugs: opiates, cocaine, marijuana, and mixed drugs* *Study designs: systematic reviews and meta-analyses of randomized controlled trials (RCTs) & controlled clinical trials (CCTs), RCTs, CCTs* *Publication years: 1994-present,or earlier years if identified in systematic reviews or the 1996 USPSTF report* *Populations: adolescents/teens 12-17, young adults 18-25, adults 26+, or pregnant women* *Intermediate outcomes: abstinence, decreased use, time to relapse, risk behaviors, social/legal.* *Health outcomes: morbidity (infant outcomes, injuries, medical conditions, mental health disorders, quality of life, STD transmission, utilization, violence/unintentional) and mortality.* *Conducted in an U.S. applicable country* *Primary care feasible or referable: see end of appendix for definitions* Special population (e.g., mentally ill; tracked, but not included)

Appendix B. Inclusion and Exclusion Criteria

Exclusion Criteria
Does not evaluate an intervention targeting drug use, misuse, or abuse Other drugs besides opiates, cocaine, marijuana, and mixed drugs Non-English abstract Non-humans Setting: Intervention not done in primary care, primary care-feasible or widely available for primary care referral Population: Selective population not normally seen in primary care (e.g. patients recruited from ER or other specialty setting who are injured or on drugs and do not represent a general patient population Country: Study not conducted in a country applicable to the US population Outcomes: Does not report designated outcomes Study quality: Does not meet USPSTF criteria for quality Study designs: Studies not identified in systematic reviews, authoritative review, comparative effectiveness studies, editorials, letters, non-systematic reviews, non-comparative studies, case control studies, case studies, comment/opinion, protocol (no data), pilot studies, abstracts only, etc.

Key Question 7. Is decreased use or abstinence following drug misuse reliably associated with reduced morbidity and/or mortality?

Inclusion Criteria
Meets criteria for KQ7 and: *Drugs: opiates, cocaine, marijuana, and mixed drugs* *Study designs:* randomized controlled trials (RCTs), controlled clinical trials, prospective, and observational studies *Publication years: 1994-present, or earlier years if identified in systematic reviews or the 1996 USPSTF report* *Populations: adolescents/teens 12-17, young adults 18-25, adults 26+, or pregnant women* *Intermediate outcomes: abstinence, decreased use, time to relapse, risk behaviors, social/legal.* *Health outcomes: morbidity (infant outcomes, injuries, medical conditions, mental health disorders, quality of life, STD transmission, utilization, violence/unintentional) and mortality.* *Applicable countries* *Primary care feasible or referable* Special population (e.g., mentally ill; tracked, but not included)

Exclusion Criteria
Does not evaluate whether decreased use or abstinence following drug misuse reliably associated with reduced morbidity and/or mortality *Other drugs besides opiates, cocaine, marijuana, and mixed drugs* Non-English abstract Non-humans Setting: Intervention not done in primary care, primary care-feasible, or widely available for primary care referral Population: Selective population not normally seen in primary care (e.g. patients recruited from ER or other specialty setting who are injured or on drugs and do not represent a general patient population) Country: Study not conducted in a country applicable to the US population Outcomes: Does not report designated outcomes (e.g. withdrawal) Study quality: Does not meet USPSTF criteria for quality Study designs: Editorials, letters, non-systematic reviews, non-comparative studies, case control studies, case studies, comment/opinion, protocol (no data), pilot studies, abstracts only, etc.

Appendix B. Inclusion and Exclusion Criteria

OVERALL CRITERIA FOR JUDGING IF AN INTERVENTION IS PRIMARY CARE *FEASIBLE*:

Whom Targeted: Somehow involve individual-level identification of being a patient/in need of intervention

Who Delivered: Usually involve primary care clinicians (physicians in family practice, internal medicine, obstetrics-gynecology, pediatricians, general practitioners), other physicians, nurses, nurse practitioners physician assistants or related clinical staff (dietitians, health educators, others counselors) in some direct or indirect way—or, at least, the intervention would be seen as connected to the health care system by the participant.

How Delivered: To individuals or in small groups (15 or less). Do not involve only or primarily group-level interventions outside the primary care setting to achieve behavioral changes. Generally involve no more than 8 group sessions total and intervention time period is no longer than 12 months.

Where Delivered: Could be delivered anywhere (including via the web, interactive technologies, in the home) if linked to primary care as above.

DEFINITION OF PRIMARY CARE *REFERABLE*:

In order for an intervention to be feasible for primary care *referral*, it would need to be conducted as part of a healthcare setting or else be widely available in the community at a national level (such as a car seat fitting station within a hospital).

Appendix C. U.S. Preventive Services Task Force Quality Rating Criteria*

Diagnostic Accuracy Studies

Criteria:

- Screening test relevant, available for primary care, adequately described
- Study uses a credible reference standard, performed regardless of test results
- Reference standard interpreted independently of screening test
- Handles indeterminate results in a reasonable manner
- Spectrum of patients included in study
- Sample size
- Administration of reliable screening test

Definition of ratings based on above criteria:

Good: Evaluates relevant available screening test; uses a credible reference standard; interprets reference standard independently of screening test; reliability of test assessed; has few or handles indeterminate results in a reasonable manner; includes large number (more than 100) broad-spectrum patients with and without disease.

Fair: Evaluates relevant available screening test; uses reasonable although not best standard; interprets reference standard independent of screening test; moderate sample size (50 to 100 subjects) and a "medium" spectrum of patients.

Poor: Has important limitation such as: uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size of very narrow selected spectrum of patients.

Randomized Controlled Trials (RCTs) and Cohort Studies

Criteria:

- Initial assembly of comparable groups**:** RCTs—adequate randomization, including concealment and whether potential confounders were distributed equally among groups; 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 follow-up or overall high loss to follow-up
- Measurements: equal, reliable, and valid (includes masking of outcome assessment)
- Clear definition of interventions
- Important outcomes considered
- Analysis: adjustment for potential confounders for cohort studies, or intension-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 (follow-up at least 80 percent); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; important outcomes are considered; and appropriate attention to confounders in analysis.

Fair: Studies will be graded "fair" if any or all of the following problems occur, without the important limitations noted in the "poor" category below: Generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred in follow-up; 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.

Poor: Studies will be graded "poor" if any of the following major limitations 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 at all equally among groups (including not masking outcome assessment); and key confounders are given little or no attention.

Case Control Studies

Criteria:

- Accurate ascertainment of cases
- Nonbiased selection of cases/controls with exclusion criteria applied equally to both
- Response rate
- Diagnostic testing procedures applied equally to each group
- Measurement of exposure accurate and applied equally to each group
- Appropriate attention to potential confounding variable

Definition of ratings based on criteria above:

Good: Appropriate ascertainment of cases and nonbiased selection of case and control participants; exclusion criteria applied equally to cases and controls; response rate equal to or greater than 80 percent; diagnostic procedures and measurements accurate and applied equally to cases and controls; and appropriate attention to confounding variables.

Fair: Recent, relevant, without major apparent selection or diagnostic work-up bias but with response rate less than 80 percent or attention to some but not all important confounding variables.

Poor: Major selection or diagnostic work-up biases, response rates less than 50 percent, or inattention to confounding variables.

*Created using information from Harris et al. Current Methods of the USPSTF: A Review of the Process. Am J Prev Med. 2001:20(3S);21-35.

Appendix D. Criteria for Assessing Scientific Quality of Systematic Evidence Reviews*

1. Were the search methods reported? *Were the search methods used to find evidence (original research) on the primary questions stated?* **"Yes" if the review states the databases used, date of most recent searches, and some mention of search terms.**	**Comments:** The purpose of this index is to evaluate the scientific quality (i.e. adherence to scientific principles) of research overviews (review articles) published in the medical literature. It is not intended to measure literary quality, importance, relevance, originality, or other attributes of overviews. The index is for assessing overviews of primary ("original") research on pragmatic questions regarding causation, diagnosis, prognosis, therapy, or prevention. A research overview is a survey of research. The same principles that apply to epidemiological surveys apply to overviews: a question must be clearly specified, a target population identified and accessed, appropriate information obtained from that population in an unbiased fashion, and conclusions derived, sometimes with the help of formal statistical analysis, as is done in "meta-analyses". The fundamental difference between overviews and epidemiological studies is the unit of analysis, not the scientific issues that the questions in this index address. Since most published overviews do not include a methods section, it is difficult to answer some of the questions in the index. Base your answers, as much as possible, on information provided in the overview. If the methods that were used are reported incompletely relative to a specific question, score it as "can't tell", unless there is information in the overview to suggest either the criterion was or was not met.
2. Was the search comprehensive? *Was the search for evidence reasonably comprehensive?* **"Yes" if the review searches at least 2 databases and looks at other sources (such as reference lists, hand searches, queries experts).**	
3. Were the inclusion criteria reported? *Were the criteria used for deciding which studies to include in the overview reported?*	
4. Was selection bias avoided? *Was bias in the selection of studies avoided?* **"Yes" if the review reports how many studies were identified by searches, numbers excluded, and gives appropriate reasons for excluding them (usually because of pre-defined inclusion/exclusion criteria).**	
5. Were the validity criteria reported? *Were the criteria used for assessing the validity of the included studies reported?*	
6. Was validity assessed appropriately? *Was the validity of all the studies referred to in the text assessed using appropriate criteria (either in selecting studies for inclusion or in analyzing the studies that are cited)?* **"Yes" if the review reports validity assessment and did some type of analysis with it (e.g. sensitivity analysis of results according to quality ratings, excluded low-quality studies, etc.)**	

Appendix D. Criteria for Assessing Scientific Quality of Systematic Evidence Reviews*

7. Were the methods used to combine studies reported? *Were the methods used to combine the findings of the relevant studies (to reach a conclusion) reported?* **"Yes" for studies that did qualitative analysis if there is some mention that quantitative analysis was not possible and reasons that it could not be done, or if 'best evidence' or some other grading of evidence scheme used.**	**Comments:**
8. Were the findings combined appropriately? *Were the findings of the relevant studies combined appropriately relative to the primary question the overview addresses?* **"Yes" if the review performs a test for heterogeneity before pooling, does appropriate subgroup testing, appropriate sensitivity analysis, or other such analysis.**	For Question 8, if not attempt has been made to combine findings, and no statement is made regarding the inappropriateness of combining findings, check "No". if a summary (general) estimate is given anywhere in the abstract, the discussion, or the summary section of the paper, and it is not reported how that estimate was derived, mark "No" even if there is a statement regarding the limitations of combining the findings of the studies reviewed. If in doubt, mark "Can't tell".
9. Were the conclusions supported by the reported data? *Were the conclusions made by the author(s) supported by the data and/or analysis reported in the overview?*	For an overview to be scored as "Yes" in Question 9, data (not just citations) must be reported that support the main conclusions regarding the primary question(s) that the overview addresses.
10. What was the overall scientific quality of the overview? *How would you rate the scientific quality of this overview?*	The score for Question 10, the overall scientific quality, should be based on your answers to the first nine questions. The following guidelines can be used to assist with deriving a summary score: If the "Can't tell" option is used one or more times on the preceding questions, a review is likely to have minor flaws at best and it is difficult to rule out major flaws (i.e. a score of 4 or lower). If the "No" option is used on Question 2, 4, 6 or 8, the review is likely to have major flaws (i.e. a score of 3 or less, depending on the number and degree of the flaws).
Each question is scored as Yes, Partially/Can't tell or No	
Extensive Flaws 1 2 **Major Flaws** 3 4 **Minor Flaws** 5 6 **Minimal Flaws** 7	

*Created using information from: 1) Oxman AD, Guyatt GH. Validation of an index of the quality of review articles. *J Clin Epidemiol* 1991; 44(11):1271-1278, and 2) Furlan AD, Clarke J, Esmail R, Sinclair S, Irvin E, Bombardier C. A critical review of reviews on the treatment of chronic low back pain. *Spine* 2001; 26(7):E155-E162.

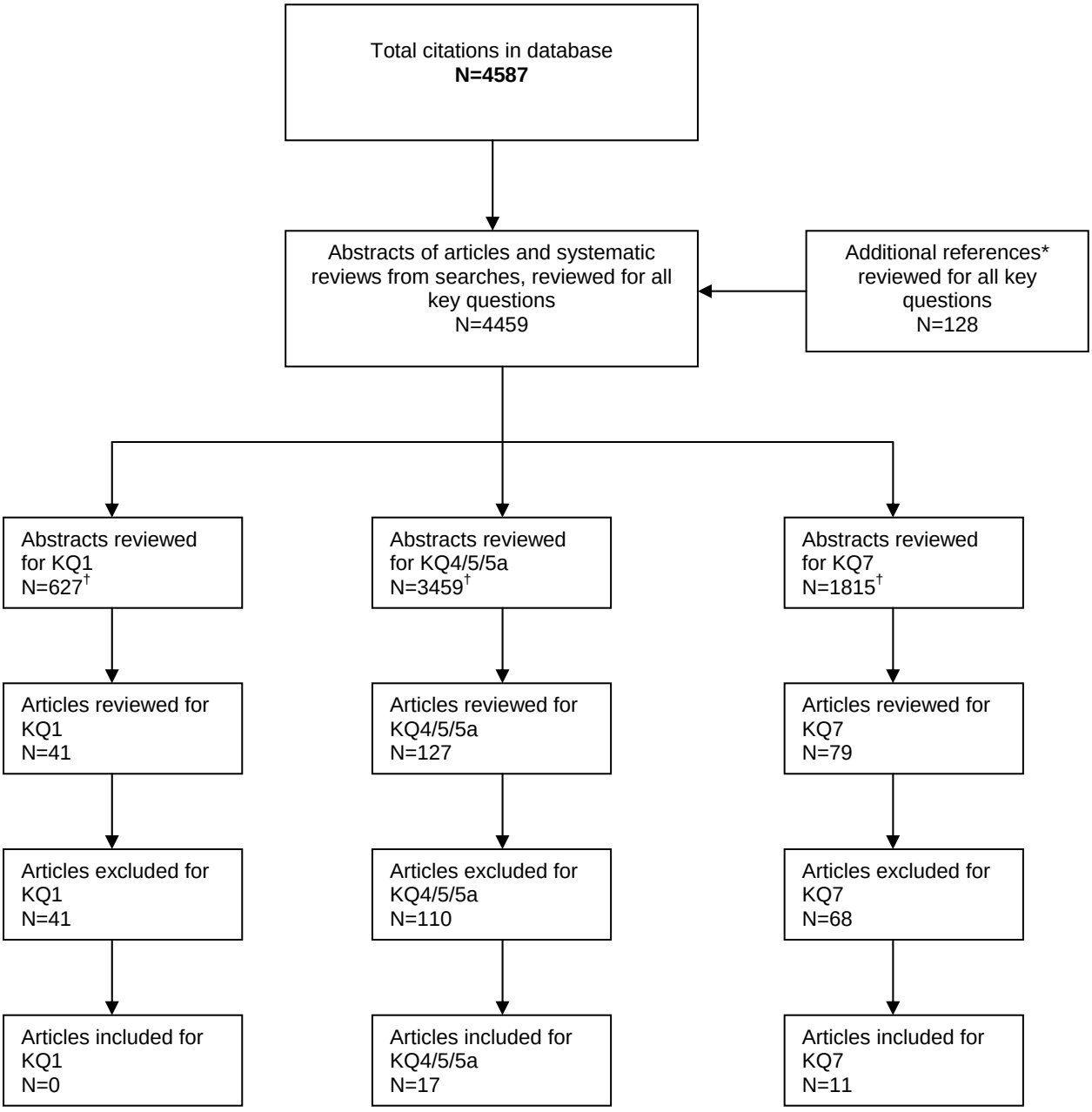
Appendix E. Quality of Prognosis Studies Criteria*

Potential Biases
Study Participation The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results.
Study Attrition Loss to follow-up 9from sample to study population) is not associated with key characteristics (i.e., the study data adequately represent the sample), sufficient to limit potential bias.
Prognostic Factor Measurement The prognostic factor of interest is adequately measures in study participants to sufficiently limit potential bias.
Outcome Measurement The outcome of interest is adequately measured in study participants
Confounding Measurement and Account Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.
Analysis The statistical analysis is appropriate for the design of the stud limiting potential for presentation of invalid results.

Note: Response categories were: Yes; Partly; No; or Unsure

*Created using information from Hayden JA, Cote P, Bombardier C. Evaluation of the quality of prognosis studies in systematic reviews. *Ann Intern Med* 2006; 144(6):427-437.

Appendix F. Search and Selection of the Literature



*Identified from reference lists, suggested by experts, etc.
†Some abstracts were considered for more than one key question.

Appendix G: Excluded Studies

Reference	Reason for Exclusion
Ahmadi J. A controlled trial of buprenorphine treatment for opium dependence: the first experience from Iran. Drug & Alcohol Dependence 66(2):111-4, 2002.	Excluded for quality
Ahmadi J. Methadone versus buprenorphine maintenance for the treatment of heroin-dependent outpatients. 2003.	Comparative effectiveness
Akerele EO BL. Treatment of cocaine/marijuana abuse among schizophrenic individuals: a look at the efficacy of the atypical neuroleptics. 14th Annual Scientific Meeting of 2006.	Comparative effectiveness
Amass L. Thrice-weekly supervised dosing with the combination buprenorphine-naloxone tablet is preferred to daily supervised dosing by opioid-dependent humans. Drug & Alcohol Dependence 1961;(2).	Comparative effectiveness
Amato L, Davoli M, Ferri M, Gowing L, Perucci CA. Effectiveness of interventions on opiate withdrawal treatment: an overview of systematic reviews. Drug & Alcohol Dependence 2004; 73(3):219-226.	Does not report designated outcomes
Amato L, Davoli M, Perucci A, Ferri M, Faggiano F, Mattick P. An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. Journal of Substance Abuse Treatment 2005; 28(4):321-329.	Excluded study design
Amato L, Minozzi S, Davoli M, Vecchi S, Ferri M, Mayet S. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. Cochrane Database of Systematic Reviews 2005;(4).	Comparative effectiveness
American Psychiatric Association. Diagnostic and statistical manual of mental disorders, fourth edition, text revision. 4 ed. Washington DC.: American Psychiatric Association, 2000.	Exclude, kept for background
Anderson F, Paluzzi P, Lee J, Huggins G, Svikis D. Illicit use of clonidine in opiate-abusing pregnant women. Obstetrics & Gynecology 1997; 90(5):790-794.	Comparative effectiveness
Appleby L, Dyson V, Luchins DJ, Cohen LS. The impact of substance use screening on a public psychiatric inpatient population. Psychiatric Services 1997; 48(10):1311-1316.	Does not report designated outcomes
Armstrong MA, Gonzales O, V, Lieberman L, Carpenter DM, Pantoja PM, Escobar GJ. Perinatal substance abuse intervention in obstetric clinics decreases adverse neonatal outcomes. Journal of Perinatology 23(1):3-9, 2003.	Does not evaluate appropriate intervention
Ashley OS, Marsden ME, Brady TM. Effectiveness of substance abuse treatment programming for women: a review. American Journal of Drug & Alcohol Abuse 2003; 29(1):19-53.	Exclude, kept for background
Avants SK, Margolin A, Chang P, Kosten TR, Birch S. Acupuncture for the treatment of cocaine addiction. Investigation of a needle puncture control. J Subst Abuse Treat 1995; 12(3):195-205.	Excluded population
Baker A, Kochan N, Dixon J, Heather N, Wodak A. Controlled evaluation of a brief intervention for HIV prevention among injecting drug users not in treatment. AIDS Care 1994; 6(5):559-570.	Does not evaluate appropriate intervention
Baker A, Lee NK, Claire M, Lewin TJ, Grant T, Pohlman S et al. Brief cognitive behavioural interventions for regular amphetamine users: a step in the right direction. Addiction 2005; 100(3):367-378.	Comparative effectiveness

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Reference	Reason for Exclusion
Baker A, Lewin T, Reichler H, Clancy R, Carr V, Garrett R et al. Evaluation of a motivational interview for substance use within psychiatric in-patient services. Addiction 97(10):1329-37, 2002.	Excluded population
Bale RN, Van Stone WW, Kuldau JM, Engelsing TM, Elashoff RM, Zarcone VP, Jr. 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):179-193.	Comparative effectiveness
Barnett PG, Hui SS. The cost-effectiveness of methadone maintenance. Mt Sinai J Med 2000; 67(5-6):365-374.	Exclude, kept for background
Barnett PG, Rodgers JH, Bloch DA. A meta-analysis comparing buprenorphine to methadone for treatment of opiate dependence. Addiction 2001; 96(5):683-690.	Comparative effectiveness
Bastiaens L, Francis G, Lewis K. The RAFFT as a screening tool for adolescent substance use disorders. Am J Addict 2000; 9(1):10-16.	Does not report designated outcomes
Batki SL, Gruber VA, Bradley JM, Bradley M, Delucchi K. A controlled trial of methadone treatment combined with directly observed isoniazid for tuberculosis prevention in injection drug users. Drug & Alcohol Dependence 66(3):283-93, 2002.	Comparative effectiveness
Bergin C, Cameron CE, Fleitz RS, Patel AV. Measuring prenatal drug exposure. Journal of Pediatric Nursing 16(4):245-55, 2001.	Does not evaluate appropriate intervention
Berglund M. A better widget? Three lessons for improving addiction treatment from a meta-analytical study. Addiction 2005; 100(6):742-750.	Excluded study design
Bergmann PE, Smith MB, Hoffmann NG. Adolescent treatment. Implications for assessment, practice guidelines, and outcome management. Pediatr Clin North Am 1995; 42(2):453-472.	Excluded study design
Beswick T, Best D, Bearn J, Gossop M, Rees S, Strang J. The effectiveness of combined naloxone/lofexidine in opiate detoxification: results from a double-blind randomized and placebo-controlled trial. American Journal on Addictions 12(4):295-305, 2003;-Sep.	Comparative effectiveness
Bibb KW, Stewart DL, Walker JR, Cook VD, Wagener RE. Drug screening in newborns and mothers using meconium samples, paired urine samples, and interviews. Journal of Perinatology 1995; 15(3):199-202.	Comparative effectiveness
Bisaga A, Aharonovich E, Garawi F, Levin FR, Rubin E, Raby WN et al. A randomized placebo-controlled trial of gabapentin for cocaine dependence. 2006.	Comparative effectiveness
Botvin GJ, Baker E, Dusenbury L, Botvin EM, Diaz T. Long-term follow-up results of a randomized drug abuse prevention trial in a white middle-class population. JAMA 1995; 273(14):1106-1112.	Excluded setting
Botvin GJ, Botvin EM. School-based and community based prevention approaches. Substance abuse: A comprehensive textbook. 1995: 910-927.	Excluded study design
Bovasso G. The long-term treatment outcomes of depression and anxiety comorbid with substance abuse. Journal of Behavioral Health Services & Research 2001; 28(1):42-57.	Does not evaluate appropriate intervention

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Reference	Reason for Exclusion
Brady KT, Sonne SC, Malcolm RJ, Randall CL, Dansky BS, Simpson K et al. Carbamazepine in the treatment of cocaine dependence: subtyping by affective disorder. Experimental & Clinical Psychopharmacology 10(3):276-85, 2002.	Excluded for quality
Breslin C, Li S, Sdao-Jarvie K, Tupker E, Ittig-Deland V. Brief treatment for young substance abusers: a pilot study in an addiction treatment setting. Psychology of Addictive Behaviors 16(1):10-6, 2002.	Excluded for quality
Brodie JD, Figueroa E, Dewey SL. Treating cocaine addiction: from preclinical to clinical trial experience with gamma-vinyl GABA. Synapse 2003; 50(3):261-265.	Excluded for quality
Brook JS, Finch SJ, Whiteman M, Brook DW. Drug use and neurobehavioral, respiratory, and cognitive problems: precursors and mediators. J Adolesc Health 2002; 30(6):433-441.	Does not evaluate appropriate intervention
Brown RL, Leonard T, Saunders LA, Papasouliotis O. A two-item screening test for alcohol and other drug problems.[see comment]. Journal of Family Practice 1997; 44(2):151-160.	Exclude, kept for background
Buhler KE. Euphoria, ecstacy, inebriation, abuse, dependence, and addiction: a conceptual analysis. Medicine, Health Care & Philosophy 2005; 8(1):79-87.	Exclude, kept for background
Calsyn DA, Wells EA, Fleming C, Saxon AJ. Changes in Millon Clinical Multiaxial Inventory scores among opiate addicts as a function of retention in methadone maintenance treatment and recent drug use. American Journal of Drug & Alcohol Abuse 2000; 26(2):297-309.	Excluded for quality
Campbell J, Nickel EJ, Penick EC, Wallace D, Gabrielli WF, Rowe C et al. Comparison of desipramine or carbamazepine to placebo for crack cocaine-dependent patients. American Journal on Addictions 12(2):122-36, 2003;-Apr.	Comparative effectiveness
Caplehorn JR, Dalton MS, Cluff MC, Petrenas AM. Retention in methadone maintenance and heroin addicts' risk of death. Addiction 1994; 89(2):203-209.	Does not evaluate appropriate intervention
Caplehorn JR, Dalton MS, Haldar F, Petrenas AM, Nisbet JG. Methadone maintenance and addicts' risk of fatal heroin overdose. Substance Use & Misuse 1996; 31(2):177-196.	Does not evaluate appropriate intervention
Carballo-Dieguez A, Sahs J, Goetz R, el Sadr W, Sorell S, Gorman J. The effect of methadone on immunological parameters among HIV-positive and HIV-negative drug users. Am J Drug Alcohol Abuse 1994; 20(3):317-329.	Excluded study design
Carey KB, Carey MP, Chandra PS. Psychometric evaluation of the alcohol use disorders identification test and short drug abuse screening test with psychiatric patients in India. J Clin Psychiatry 2003; 64(7):767-774.	Excluded study design
Carey KB, Cocco KM, Simons JS. Concurrent validity of clinicians' ratings of substance abuse among psychiatric outpatients. Psychiatric Services 1996; 47(8):842-847.	Comparative effectiveness
Carroll KM, Ball SA, Nich C, Martino S, Frankforter TL, Farentinos C et al. Motivational interviewing to improve treatment engagement and outcome in individuals seeking treatment for substance abuse: A multisite effectiveness study. 2006.	Comparative effectiveness

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Reference	Reason for Exclusion
Carroll KM, Ball SA, Nich C, O'Connor PG, Eagan DA, Frankforter TL et al. Targeting behavioral therapies to enhance naltrexone treatment of opioid dependence: efficacy of contingency management and significant other involvement. Archives of General Psychiatry 58(8):755 -61, 2001.	Comparative effectiveness
Carroll KM, Fenton LR, Ball SA, Nich C, Frankforter TL, Shi J et al. Efficacy of disulfiram and cognitive behavior therapy in cocaine-dependent outpatients: a randomized placebo-controlled trial. Archives of General Psychiatry 61(3):264-72, 2004.	Comparative effectiveness
Carroll KM, Sinha R, Nich C, Babuscio T, Rounsaville BJ. Contingency management to enhance naltrexone treatment of opioid dependence: a randomized clinical trial of reinforcement magnitude. Experimental & Clinical Psychopharmacology 10(1):54-63, 2002.	Comparative effectiveness
Casanova OQ, Lombardero N, Behnke M, Eyler FD, Conlon M, Bertholf RL. Detection of cocaine exposure in the neonate. Analyses of urine, meconium, and amniotic fluid from mothers and infants exposed to cocaine. Archives of Pathology & Laboratory Medicine 1994; 118(10):988-93.	Does not report designated outcomes
Cavacuiti C, Selby P. Managing opioid dependence. Comparing buprenorphine with methadone. Canadian Family Physician 49:876-7, 2003.	Comparative effectiveness
Center for Substance Abuse Treatment. Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction. TIP Series 40;DHHS Publication No. (SMA) 04-3939. 2004. Rockville, MD, Substance Abuse and Mental Health Services Administration. Treatment Improvement Protocol.	Exclude, kept for background
Chaisson RE, Bacchetti P, Osmond D, Brodie B, Sande MA, Moss AR. Cocaine use and HIV infection in intravenous drug users in San Francisco. JAMA 1989; 261(4):561-565.	Excluded study design
Chang G, McNamara TK, Orav EJ, Koby D, Lavigne A, Ludman B et al. Brief intervention for prenatal alcohol use: a randomized trial. Obstet Gynecol 2005; 105(5 Pt 1):991-998.	Does not evaluate appropriate intervention
Chang G, Wilkins-Haug L, Berman S, Goetz MA. Brief intervention for alcohol use in pregnancy: a randomized trial. Addiction 1999; 94(10):1499-1508.	Does not evaluate appropriate intervention
Charuvastra VC, Dalali ID, Cassuci M, Ling W. Outcome study: comparison of short-term vs long-term treatment in a residential community. Int J Addict 1992; 27(1):15-23.	Excluded study design
Chasnoff IJ, McGourty RF, Bailey GW, Hutchins E, Lightfoot SO, Pawson LL et al. The 4P's Plus screen for substance use in pregnancy: clinical application and outcomes. Journal of Perinatology 2005; 25(6):368-374.	Exclude, kept for background
Cherpitel CJ, Borges G. Screening for drug use disorders in the emergency department: performance of the rapid drug problems screen (RDPS). Drug & Alcohol Dependence 2004; 74(2):171-175.	Exclude, kept for background
Chiarotti M, Strano-Rossi S, Offidani C, Fiori A. Evaluation of cocaine use during pregnancy through toxicological analysis of hair. Journal of Analytical Toxicology 1996;(7):555-558.	Does not report designated outcomes
Choopanya K, Des J, Vanichseni S, Mock PA, Kitayaporn D, Sangkhum U et al. HIV risk reduction in a cohort of injecting drug users in Bangkok, Thailand. Journal of Acquired Immune Deficiency Syndromes: JAIDS 2003; 33(1):88-95.	Does not report designated outcomes
Clark KA, Dawson S, Martin SL. The effect of implementing a more comprehensive screening for substance use among pregnant women in North Carolina. Maternal & Child Health Journal 1999; 3(3):161-166.	Comparative effectiveness

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Reference	Reason for Exclusion
Clark N, Lintzeris N, Gijsbers A, Whelan G, Dunlop A, Ritter A et al. LAAM maintenance vs methadone maintenance for heroin dependence. Cochrane Database of Systematic Reviews 2005.	Comparative effectiveness
Coatsworth JD, Santisteban DA, McBride CK, Szapocznik J. Brief Strategic Family Therapy versus community control: engagement, retention, and an exploration of the moderating role of adolescent symptom severity. Family Process 40(3):313-32, 2001.	Excluded for quality
Cohen MH, Cook JA, Grey D, Young M, Hanau LH, Tien P et al. Medically eligible women who do not use HAART: the importance of abuse, drug use, and race. Am J Public Health 2004; 94(7):1147-1151.	Does not evaluate appropriate intervention
Collier CR, Czuchry M, Dansereau DF, Pitre U. The use of node-link mapping in the chemical dependency treatment of adolescents. Journal of Drug Education 31(3):305-17, 2001.	Comparative effectiveness
Comer SD, Sullivan MA, Yu E, Rothenberg JL, Kleber HD, Kampman K et al. Injectable, sustained-release naltrexone for the treatment of opioid dependence: a randomized, placebo-controlled trial. Archives of General Psychiatry 63(2):210-8, 2006.	Comparative effectiveness
Condelli WS, Fairbank JA, Dennis ML, Rachal JV. Cocaine use by clients in methadone programs: significance, scope, and behavioral interventions. J Subst Abuse Treat 1991; 8(4):203-212.	Excluded study design
Cornish JW, Maany I, Fudala PJ, Ehrman RN, Robbins SJ, O'Brien CP. A randomized, double-blind, placebo-controlled study of ritanserin pharmacotherapy for cocaine dependence. Drug & Alcohol Dependence 61(2):183-9, 2001.	Comparative effectiveness
Cornish JW, Maany I, Fudala PJ, Neal S, Poole SA, Volpicelli P et al. Carbamazepine treatment for cocaine dependence. Drug Alcohol Depend 1995; 38(3):221-227.	Excluded for quality
Cornish JW, Metzger D, Woody GE, Wilson D, McLellan AT, Vandergrift B et al. Naltrexone pharmacotherapy for opioid dependent federal probationers. J Subst Abuse Treat 1997; 14(6):529-534.	Excluded population
Covi L, Hess JM, Schroeder JR, Preston KL. A dose response study of cognitive behavioral therapy in cocaine abusers. Journal of Substance Abuse Treatment 23(3):191-7, 2002.	Comparative effectiveness
Craig RJ. Sensitivity of MCMI-III Scales T (drugs) and B (alcohol) in detecting substance abuse. Substance Use & Misuse 1997; 32(10):1385-1393.	Comparative effectiveness
Crits-Christoph P, Siqueland L, Blaine J, Frank A, Luborsky L, Onken LS et al. Psychosocial treatments for cocaine dependence: National Institute on Drug Abuse Collaborative Cocaine Treatment Study. Arch Gen Psychiatry 1999; 56(6):493-502.	Excluded study design
Crits-Christoph P, Siqueland L, McCalmont E, Weiss RD, Gastfriend DR, Frank A et al. Impact of psychosocial treatments on associated problems of cocaine-dependent patients. Journal of Consulting & Clinical Psychology 2001, 69(5):825-30.	Comparative effectiveness
Crosby RD, Pearson VL, Eller C, Winegarden T, Graves NL. Phenytoin in the treatment of cocaine abuse: a double-blind study. Clin Pharmacol Ther 1996; 59(4):458-468.	Excluded for quality
Curran HV, Collins R, Fletcher S, Kee SC, Woods B, Iliffe S. Older adults and withdrawal from benzodiazepine hypnotics in general practice: effects on cognitive function, sleep, mood and quality of life. Psychological Medicine 33(7):1223 -37, 2003.	Comparative effectiveness

Appendix G: Excluded Studies

Reference	Reason for Exclusion
Curran S, Savage C. Patient response to naltrexone: issues of acceptance, treatment effects, and frequency of administration. NIDA Res Monogr 1976;(9):67-69.	Does not report designated outcomes
Curtis NM, Ronan KR, Borduin CM. Multisystemic treatment: a meta-analysis of outcome studies. Journal of Family Psychology 2004; 18(3):411-419.	Comparative effectiveness
D'Alberto A. Auricular acupuncture in the treatment of cocaine/crack abuse: a review of the efficacy, the use of the National Acupuncture Detoxification Association protocol, and the selection of sham points. Journal of Alternative & Complementary Medicine 10(6):985 -1000, 2004.	Excluded for quality
Damos DL, Parker ES. High false alarm rates on a vigilance task may indicate recreational drug use. Journal of Clinical & Experimental Neuropsychology 1994; 16(5):713-722.	Does not report designated outcomes
Dashe JS, Sheffield JS, Olscher DA, Todd SJ, Jackson GL, Wendel GD. Relationship between maternal methadone dosage and neonatal withdrawal. Obstetrics & Gynecology 2002; 100(6):1244-1249.	Does not evaluate appropriate intervention
Daumann J, Jr., Fischermann T, Heekeren K, Thron A, Gouzoulis-Mayfrank E. Neural mechanisms of working memory in ecstasy (MDMA) users who continue or discontinue ecstasy and amphetamine use: evidence from an 18-month longitudinal functional magnetic resonance imaging study. Biol Psychiatry 2004; 56(5):349-355.	Does not report designated outcomes
Davids E, Gastpar M. Buprenorphine in the treatment of opioid dependence. Eur Neuropsychopharmacol 2004; 14(3):209-216.	Excluded study design
Davis TM, Baer JS, Saxon AJ, Kivlahan DR. Brief motivational feedback improves post-incarceration treatment contact among veterans with substance use disorders. Drug & Alcohol Dependence 69(2):197-203, 2003.	Excluded for quality
Dawe S, Powell J, Richards D, Gossop M, Marks I, Strang J et al. Does post-withdrawal cue exposure improve outcome in opiate addiction? A controlled trial. Addiction 1993; 88 (9):1233-1245.	Excluded for quality
de la TR, Domingo-Salvany A, Badia R, Gonzalez G , McFarlane D, San L et al. Clinical evaluation of the Triage analytic device for drugs-of-abuse testing. Clinical Chemistry 1996; 42(9):1433-1438.	Comparative effectiveness
Dean AJ, Bell J, Christie MJ, Mattick RP. Depressive symptoms during buprenorphine vs. methadone maintenance: findings from a randomised, controlled trial in opioid dependence. European Psychiatry: the Journal of the Association of European Psychiatrists 1919;(8):510-513.	Comparative effectiveness
Deas D, Thomas SE. An overview of controlled studies of adolescent substance abuse treatment. American Journal on Addictions 10(2):178-89, 2001.	Excluded study design
Denis C, Fatseas M, Lavie E, Auriacombe M. Pharmacological interventions for benzodiazepine dependence management among benzodiazepine users in outpatient settings. Cochrane Database of Systematic Reviews 2005;(4).	Comparative effectiveness
Denis C, Lavie E, Fatseas M, Auriacombe M. Psychotherapeutic interventions for cannabis abuse and/or dependence in outpatient settings . Cochrane Database of Systematic Reviews 2005;(4).	Comparative effectiveness

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Reference	Reason for Exclusion
Dennis M, Godley SH, Diamond G, Tims FM, Babor T, Donaldson J et al. The Cannabis Youth Treatment (CYT) Study: main findings from two randomized trials. Journal of Substance Abuse Treatment 27(3):197-213, 2004.	Excluded study design
Dhossche D, Rubinstein J. Drug detection in a suburban psychiatric emergency room. Annals of Clinical Psychiatry 1996; 8(2):59-69.	Comparative effectiveness
Dickson PH, Lind A, Studts P, Nipper HC, Makoid M, Therkildsen D. The routine analysis of breast milk for drugs of abuse in a clinical toxicology laboratory. Journal of Forensic Sciences 1994; 39(1):207-214.	Does not report designated outcomes
DiGregorio GJ, Ferko AP, Barbieri EJ, Ruch EK, Chawla H, Keohane D et al. Determination of cocaine usage in pregnant women by a urinary EMIT drug screen and GC-MS analyses. Journal of Analytical Toxicology 1994; 18(5):247-250.	Does not report designated outcomes
Dijkgraaf MG, van der Zanden BP, de Borgie CA, Blanken P, van Ree JM, van den BW. Cost utility analysis of co-prescribed heroin compared with methadone maintenance treatment in heroin addicts in two randomised trials. BMJ 2005; 330(7503):1297.	Excluded study design
Dolan KA, Shearer J, MacDonald M, Mattick RP, Hall W, Wodak AD. A randomised controlled trial of methadone maintenance treatment versus wait list control in an Australian prison system. Drug Alcohol Depend 2003; 72(1):59-65.	Excluded population
Dolan KA, Shearer J, White B, Zhou J, Kaldor J, Wodak AD. Four-year follow-up of imprisoned male heroin users and methadone treatment: mortality, re-incarceration and hepatitis C infection. Addiction 2005; 100(6):820-828.	Excluded setting
Dole VP, NYSWANDER M. A Medical treatment for diacetylmorphine (heroin) addictions. A Clinical trial with methadone hydrochloride. JAMA 1965; 193:646-650.	Exclude, kept for background
Dole VP, Robinson JW, Orraca J, Towns E, Searcy P, Caine E. Methadone treatment of randomly selected criminal addicts. N Engl J Med 1969; 280(25):1372-1375.	Excluded for quality
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):1725-1742.	Kept for use as source document
Eiler K, Schaefer MR, Salstrom D, Lowery R. Double-blind comparison of bromocriptine and placebo in cocaine withdrawal. Am J Drug Alcohol Abuse 1995; 21(1):65-79.	Does not report designated outcomes
El Mohandes A, Herman AA, Nabil El-Khorazaty M, Katta PS, White D, Grylack L. Prenatal care reduces the impact of illicit drug use on perinatal outcomes. J Perinatol 2003; 23(5):354-360.	Does not evaluate appropriate intervention
Esteban J, Gimeno C, Barril J, Aragones A, Climent JM, de la Cruz PM. Survival study of opioid addicts in relation to its adherence to methadone maintenance treatment. Drug & Alcohol Dependence 2003; 70(2):193-200.	Does not evaluate appropriate intervention
Faggiano F, Vigna-Taglianti F, Versino E, Lemma P. Methadone maintenance at different dosages for opiod dependence. Cochrane Database of Systematic Reviews 2005.	Comparative effectiveness
Fals-Stewart W. Behavioral family counseling and naltrexone for male opioid-dependent patients. Journal of consulting and clinical psychology 1971;(3).	Comparative effectiveness

Appendix G: Excluded Studies

Reference	Reason for Exclusion
Farre M, Mas A, Torrens M, Moreno V, Cami J. Retention rate and illicit opioid use during methadone maintenance interventions: a meta-analysis. Drug Alcohol Depend 2002; 65(3):283-290.	Comparative effectiveness
Farren CK, O'Malley S. A pilot double blind placebo controlled trial of sertraline with naltrexone in the treatment of opiate dependence. Am J Addict 2002; 11(3):228-234.	Comparative effectiveness
Feldman JG, Minkoff HL, McCalla S, Salwen M. A cohort study of the impact of perinatal drug use on prematurity in an inner-city population. Am J Public Health 1992; 82(5):726-728.	Excluded study design
Fergusson DM, Horwood LJ, Swain-Campbell N. Cannabis use and psychosocial adjustment in adolescence and young adulthood. Addiction 2002; 97(9):1123-1135.	Exclude, kept for background
Ferri M, Davoli M, Perucci CA. Heroin maintenance for chronic heroin dependents. Update of Cochrane Database Syst Rev. 2003. Cochrane Database of Systematic Reviews 2005.	Comparative effectiveness
Fiellin DA OPC. Methadone maintenance in primary care: a randomized controlled trial. JAMA : the journal of the American Medical Association JAMA, 286(14):1724-31, 2001.	Comparative effectiveness
Fischer G, Ortner R, Rohrmeister K, Jagsch R, Baewert A, Langer M et al. Methadone versus buprenorphine in pregnant addicts: A double-blind, double-dummy comparison study. Addiction, 2006 Feb;101(2):275-81.	Comparative effectiveness
Focchi GR, Leite MC, Andrade AG, Scivoletto S. Use of dopamine agonist pergolide in outpatient treatment of cocaine dependence. Substance Use & Misuse 40(8):1169-77, 2005.	Comparative effectiveness
Fox CH. Cocaine use in pregnancy. J Am Board Fam Pract 1994; 7(3):225-228.	Does not report designated outcomes
Friedmann PD, McCullough D, Saitz R. Screening and intervention for illicit drug abuse: a national survey of primary care physicians and psychiatrists. Archives of Internal Medicine 161(2):248-51, 2001.	Exclude, kept for background
Fuller MG, Fishman E, Taylor CA, Wood RB. Screening patients with traumatic brain injuries for substance abuse. Journal of Neuropsychiatry & Clinical Neurosciences 1994; 6(2):143-146.	Does not report designated outcomes
Gadomski A, Bennett S, Young M, Wissow LS. Guidelines for Adolescent Preventive Services: the GAPS in practice. Archives of Pediatrics & Adolescent Medicine 157(5):426-32, 2003.	Exclude, kept for background
Garcia DC, Romero A, Garcia GC, Ostrea EM, Jr. Gastric fluid analysis for determining gestational cocaine exposure. Pediatrics 98 1996; 98(2):291-293.	Does not report designated outcomes
Gawin FH, Ellinwood EH, Jr. Cocaine and other stimulants. Actions, abuse, and treatment. N Engl J Med 1988; 318(18):1173-1182.	Exclude, kept for background
Geller B, Cooper TB, Sun K, Zimerman B, Frazier J, Williams M et al. Double-blind and placebo-controlled study of lithium for adolescent bipolar disorders with secondary substance dependency. J Am Acad Child Adolesc Psychiatry 1998; 37(2):171-178.	Excluded population

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Reference	Reason for Exclusion
Giacomuzzi S, Kemmler G, Ertl M, Riemer Y. Opioid addicts at admission vs. slow-release oral morphine, methadone, and sublingual buprenorphine maintenance treatment participants, Subst Use Misuse, 41(2):223-44, 2006.	Comparative effectiveness
Giannini AJ, Folts DJ, Feather JN, Sullivan BS. Bromocriptine and amantadine in cocaine detoxification. Psychiatry Res 1989; 29(1):11-16.	Does not evaluate appropriate intervention
Giannini AJ, Loiselle RH, Giannini MC. Space-based abstinence: alleviation of withdrawal symptoms in combinative cocaine-phencyclidine abuse. J Toxicol Clin Toxicol 1987; 25(6):493-500.	Does not report designated outcomes
Gibson DR, Flynn NM, McCarthy JJ. Effectiveness of methadone treatment in reducing HIV risk behavior and HIV seroconversion among injecting drug users. Addiction 2003; 13(14):1807-1818.	Kept for use as source document
Gibson DR, McCusker J, Chesney M. Effectiveness of psychosocial interventions in preventing HIV risk behaviour in injecting drug users. AIDS 1998; 12(8):919-929.	Exclude, kept for background
Giglio JC. A randomized controlled trial of auricular acupuncture for cocaine dependence: treatments vs outcomes.[comment]. Archives of Internal Medicine 161(6):894 -5; author reply 895, 2001.	Does not report designated outcomes
Glanz M, Klawansky S, McAullife W, Chalmers T. Methadone vs. l-alpha-acetylmethadol (LAAM) in the treatment of opiate addiction: a meta-analysis of the randomized, controlled trials. Am J Addict 1997; 6(4):339-349.	Comparative effectiveness
Gorelick DA, Wilkins JN. Bromocriptine treatment for cocaine addiction: Association with plasma prolactin levels. Drug Alcohol Depend., Feb 1;81(2):189-95, 2006.	Comparative effectiveness
Gossop M, Marsden J, Stewart D, Kidd T. Changes in use of crack cocaine after drug misuse treatment: 4-5 year follow-up results from the National Treatment Outcome Research Study (NTORS). Drug & Alcohol Dependence 2002; 66(1):21-28.	Does not evaluate appropriate intervention
Gottfredson DC, Wilson DB. Characteristics of effective school-based substance abuse prevention. Prevention Science 2003; 4(1):27-38.	Excluded setting
Gottheil E, Thornton C, Weinstein S. Effectiveness of high versus low structure individual counseling for substance abuse. American Journal on Addictions.11(4):279-90, 2002.	Comparative effectiveness
Gowing L, Ali R, White J. Buprenorphine for the management of opioid withdrawal. Cochrane Database of Systematic Reviews 2005.	Excluded study design
Gowing L, Ali R, White J. Opioid antagonists and adrenergic agonists for the management of opioid withdrawal. Cochrane Database of Systematic Reviews 2000.	Excluded study design
Gowing L, Farrell M, Ali R, White J. Alpha2 adrenergic agonists for the management of opioid withdrawal. Cochrane Database of Systematic Reviews 2005.	Excluded study design
Gowing L, Farrell M, Bornemann R, Ali R. Substitution treatment of injecting opioid users for prevention of HIV infection. Cochrane Database of Systematic Reviews 2005.	Kept for use as source document

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Reference	Reason for Exclusion
Grabowski J, Rhoades H, Elk R, Schmitz J, Davis C, Creson D et al. Fluoxetine is ineffective for treatment of cocaine dependence or concurrent opiate and cocaine dependence: two placebo-controlled double-blind trials. J Clin Psychopharmacol 1995; 15(3):163-174.	Comparative effectiveness
Grabowski J, Rhoades H, Schmitz J, Stotts A, Daruzska LA, Creson D et al. Dextroamphetamine for cocaine-dependence treatment: a double-blind randomized clinical trial. Journal of Clinical Psychopharmacology 21(5):522-6, 2001.	Comparative effectiveness
Grabowski J, Rhoades H, Silverman P, Schmitz JM, Stotts A, Creson D et al. Risperidone for the treatment of cocaine dependence: randomized, double-blind trial. J Clin Psychopharmacol 2000; 20(3):305-310.	Comparative effectiveness
Greenstein RA, Resnick RB, Resnick E. Methadone and naltrexone in the treatment of heroin dependence. Psychiatr Clin North Am 1984; 7(4):671-679.	Excluded study design
Greenwald MK, Schuh KJ, Hopper JA, Schuster CR, Johanson CE. Effects of buprenorphine sublingual tablet maintenance on opioid drug-seeking behavior by humans. Psychopharmacology 160(4):344-52, 2002.	Comparative effectiveness
Greenwald MK. Early Impact of Methadone Induction for Heroin Dependence: Differential Effects of Two Dose Sequences in a Randomized Controlled Study. Exp Clin Psychopharmacol Feb;14(1):52-67, 2006.	Comparative effectiveness
Greenwell L, Brecht ML. Self-reported health status among treated methamphetamine users. American Journal of Drug & Alcohol Abuse 2003; 29(1):75-104.	Exclude, kept for background
Greenwood GL, Woods WJ, Guydish J, Bein E. Relapse outcomes in a randomized trial of residential and day drug abuse treatment. Journal of Substance Abuse Treatment 1920;(1):15-23, 2001.	Comparative effectiveness
Griffith JD, Rowan-Szal GA, Roark RR, Simpson DD . Contingency management in outpatient methadone treatment: a meta-analysis. Drug Alcohol Depend 2000; 58(1-2):55-66.	Comparative effectiveness
Gureje O, Vazquez-Barquero JL, Janca A. Comparisons of alcohol and other drugs: experience from the WHO Collaborative Cross-Cultural Applicability Research (CAR) Study. Addiction 1996; 91(10):1529-1538.	Exclude, kept for background
Guttinger F, Gschwend P, Schulte B, Rehm J, Uchtenhagen A. Evaluating long-term effects of heroin-assisted treatment: the results of a 6-year follow-up. Eur Addict Res 2003; 9(2):73-79.	Does not evaluate appropriate intervention
Haemmig RB, Tschacher W. Effects of high-dose heroin versus morphine in intravenous drug users: a randomised double-blind crossover study. Journal of Psychoactive Drugs 33(2):105-10, 2001.	Comparative effectiveness
Halikas JA, Crosby RD, Koop LP, Crea F, Nugent SM, Carlson GA. Daily monitored cardiovascular effects of carbamazepine in chronic crack cocaine users. Psychopharmacol Bull 1991; 27(3):345-351.	Does not report designated outcomes
Hall SM, Tunis S, Triffleman E, Banys P, Clark HW, Tusel D et al. Continuity of care and desipramine in primary cocaine abusers. J Nerv Ment Dis 1994; 182(10):570-575.	Excluded for quality

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Reference	Reason for Exclusion
Heading CE. Vivitrex (Alkermes/Cephalon). Current Opinion in Investigational Drugs 7(1):81-8, 2006.	Does not evaluate appropriate intervention
Healey A, Knapp M, Marsden J, Gossop M, Stewart D. Criminal outcomes and costs of treatment services for injecting and non-injecting heroin users: evidence from a national prospective cohort survey. Journal of Health Services & Research Policy 2003; 8(3):134-141.	Does not evaluate appropriate intervention
Henggeler SW, Clingempeel WG, Brondino MJ, Pickrel SG. Four-year follow-up of multisystemic therapy with substance-abusing and substance-dependent juvenile offenders. Journal of the American Academy of Child & Adolescent Psychiatry 2002; 41(7):868-874.	Excluded study design
Herning RI, Better WE, Tate K, Umbricht A, Preston KL, Cadet JL. Methadone treatment induces attenuation of cerebrovascular deficits associated with the prolonged abuse of cocaine and heroin. Neuropsychopharmacology 2003; 28(3):562-568.	Excluded study design
Hopfer CJ, Khuri, E, Crowley TJ, Hooks S. Adolescent heroin use: a review of the descriptive and treatment literature. J Subst Abuse Treat 2002; 23(3):231-237.	Comparative effectiveness
Horrigan TJ, Piazza N. The substance abuse subtle screening inventory minimizes the need for toxicology screening of prenatal patients. Journal of Substance Abuse Treatment 1999; 17(3):243-247.	Does not report designated outcomes
Howard AA, Arnsten JH, Lo Y, Vlahov D, Rich JD, Schuman P et al. A prospective study of adherence and viral load in a large multi-center cohort of HIV-infected women. AIDS 2002; 16(16):2175-2182.	Does not evaluate appropriate intervention
Hubbard RL, Craddock SG, Anderson J. Overview of 5-year followup outcomes in the drug abuse treatment outcome studies (DATOS). J Subst Abuse Treat 2003; 25(3):125-134.	Does not evaluate appropriate intervention
Hulse GK, Milne E, English DR, Holman CD. Assessing the relationship between maternal opiate use and neonatal mortality. Addiction 1998; 93(7):1033-1042.	Excluded for quality
Humphreys K, Wing S, McCarty D, Chappel J, Gallant L, Haberle B et al. Self-help organizations for alcohol and drug problems: toward evidence-based practice and policy. J Subst Abuse Treat 2004; 26(3):151-158.	Excluded study design
Irvin JE, Bowers CA, Dunn ME, Wang MC. Efficacy of relapse prevention: a meta-analytic review. Journal of Consulting & Clinical Psychology 1999; 67(4):563-570.	Comparative effectiveness
Jimenez-Lerma JM, Landabaso M, Iraurgi L, Calle R, Sanz J, Gutierrez-Fraile M. Nimodipine in opiate detoxification: a controlled trial. Addiction 97(7):819-24, 2002.	Comparative effectiveness
Jones HE, Haug N, Silverman K, Stitzer M, Svikis D. The effectiveness of incentives in enhancing treatment attendance and drug abstinence in methadone-maintained pregnant women. Drug & Alcohol Dependence 61(3):297-306, 2001.	Excluded for quality
Jones HE, Johnson RE, Bigelow GE, Silverman K, Mudric T, Strain EC. Safety and efficacy of L-tryptophan and behavioral incentives for treatment of cocaine dependence: a randomized clinical trial. American Journal on Addictions 13(5):421-37, 2004.	Excluded population

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Reference	Reason for Exclusion
Jones HE, Johnson RE, Jasinski DR, O'Grady KE, Chisholm CA, Choo RE et al. Buprenorphine versus methadone in the treatment of pregnant opioid-dependent patients: effects on the neonatal abstinence syndrome. Drug & Alcohol Dependence 2005; 79(1):1-10.	Comparative effectiveness
Jones HE, Wong CJ, Tuten M, Stitzer ML. Reinforcement-based therapy: 12-month evaluation of an outpatient drug-free treatment for heroin abusers. Drug Alcohol Depend, 2005 Aug 1;79(2):119-28.	Comparative effectiveness
Kaminer Y, Burleson JA, Goldberger R. Cognitive-behavioral coping skills and psychoeducation therapies for adolescent substance abuse. Journal of Nervous & Mental Disease 190;(11):737-745.	Comparative effectiveness
Kampman K, Volpicelli JR, Alterman A, Cornish J, Weinrieb R, Epperson L et al. Amantadine in the early treatment of cocaine dependence: a double-blind, placebo-controlled trial. Drug Alcohol Depend 1996; 41(1):25-33.	Comparative effectiveness
Kampman KM PH. A pilot trial of topiramate for cocaine dependence. Drug and alcohol dependence 1975;(3).	Comparative effectiveness
Kampman KM VJM. Effectiveness of propranolol for cocaine dependence treatment may depend on cocaine withdrawal symptom severity. Drug and alcohol dependence 1963; 63(1):69-78.	Comparative effectiveness
Kampman KM, Leiderman D, Holmes T, LoCastro J, Bloch DA, Reid MS et al. Cocaine Rapid Efficacy Screening Trials (CREST): lessons learned. Addiction 2005; 100:102-110.	Excluded study design
Kampman KM, Rukstalis M, Ehrman R, McGinnis DE, Gariti P, Volpicelli JR et al. Open trials as a method of prioritizing medications for inclusion in controlled trials for cocaine dependence. Addict Behav 1999; 24(2):287-291.	Excluded study design
Kampman KM, Volpicelli JR, Alterman AI, Cornish J, O'Brien CP. Amantadine in the treatment of cocaine-dependent patients with severe withdrawal symptoms. Am J Psychiatry 2000; 157(12):2052-2054.	Does not evaluate appropriate intervention
Kaul P, Coupey SM. Clinical evaluation of substance abuse. Pediatrics in Review 23(3):85-94, 2002.	Does not evaluate appropriate intervention
Kim E, Brion LP, Meenan G, Lehrer M, Suresh BR. Perinatal toxicology screening: comparison of various maternal and neonatal samples. Journal of Perinatology 1998; 18(2):116-121.	Comparative effectiveness
Kim YH, Schiff E, Waalen J, Hovell M. Efficacy of acupuncture for treating cocaine addiction: A review paper. J Addict. Dis. 2005;24(4):115-32.	Kept for use as source document
Kirchmayer U, Davoli M, Verster A. Naltrexone maintenance treatment for opioid dependence. Cochrane Database of Systematic Reviews 2005.	Kept for use as source document
Kirchmayer U, Davoli M, Verster AD, Amato L, Ferri M, Perucci CA. A systematic review on the efficacy of naltrexone maintenance treatment in opioid dependence. Addiction 2002; 97(10):1241-1249.	Kept for use as source document

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Reference	Reason for Exclusion
Klein J, Karaskov T, Koren G. Clinical applications of hair testing for drugs of abuse--the Canadian experience. Forensic Science International 2000; 107(1-3):281-288.	Does not report designated outcomes
Knight JR, Sherritt L, Shrier LA, Harris SK, Chang G. Validity of the CRAFFT substance abuse screening test among adolescent clinic patients. Archives of Pediatrics & Adolescent Medicine 2002; 156(6):607-614.	Exclude, kept for background
Knight JR, Sherritt L, Van Hook S, Gates EC, Levy S, Chang G. Motivational interviewing for adolescent substance use: a pilot study. Journal of Adolescent Health 37(2):167-9, 2005.	Excluded for quality
Kongsakon R, Papadopoulos KI, Saguansiritham R. Mirtazapine in amphetamine detoxification: A placebo-controlled pilot study. Int Clin Psychopharmacol. 2005 Sep;20(5):253-6, 2005.	Does not report designated outcomes
Koren G, Klein J. Neonatal hair test for cocaine. Toronto experience. Canadian Family Physician 1997; 43(1215):1217, 1219.	Does not report designated outcomes
Kreek MJ, LaForge KS, Butelman E. Pharmacotherapy of addictions. Nat Rev Drug Discov 2002; 1(9):710-726.	Exclude, kept for background
Kreek MJ. Methadone-related opioid agonist pharmacotherapy for heroin addiction. History, recent molecular and neurochemical research and future in mainstream medicine. Ann N Y Acad Sci 2000; 909:186-216.	Exclude, kept for background
Kristensen O. Buprenorphine and methadone to opiate addicts--a randomized trial. Tidsskrift for den Norske laegeforening 2005 Jan 20;125(2):148-51.	Comparative effectiveness
Krupitsky E, Burakov A, Romanova T, Dunaevsky I, Strassman R, Grinenko A. Ketamine psychotherapy for heroin addiction: Immediate effects and two-year follow-up. J Subst Abuse Treat. 2002; 23(4):273-83.	Comparative effectiveness
Kumpfer KL, Alvarado R, Whiteside HO. Family-based interventions for substance use and misuse prevention. Substance Use & Misuse 2003; 38(11-13):1759-1787.	Does not report designated outcomes
Kwiatkowski CF, Booth RE. Methadone maintenance as HIV risk reduction with street-recruited injecting drug users. Journal of Acquired Immune Deficiency Syndromes: JAIDS 2001; 26(5):483-489.	Does not evaluate appropriate intervention
Ladewig D. Naltrexone--an effective aid in the psychosocial rehabilitation process of former opiate dependent patients Naltrexon--eine wirksame Stutze im psychosozialen Rehabilitationsprozess ehemals Opiatabhangiger. Ther Umsch 1990; 47(3):247-250.	Non-English
Lake J. Psychotropic medications from natural products: a review of promising research and recommendations. Alternative Therapies in Health & Medicine 2000; 6(3):36-45.	Excluded study design
Langendam MW, van Brussel GH, Coutinho RA, van Ameijden EJ. The impact of harm-reduction-based methadone treatment on mortality among heroin users. Am J Public Health 2001; 91(5):774-780.	Does not evaluate appropriate intervention
Latimer WW, Winters KC, D'Zurilla T, Nichols M. Integrated family and cognitive-behavioral therapy for adolescent substance abusers: a stage I efficacy study. Drug & Alcohol Dependence 71(3):303-17, 2003.	Comparative effectiveness

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Reference	Reason for Exclusion
Leiderman DB, Shoptaw S, Montgomery A, Bloch DA, Elkashef A, LoCastro J et al. Cocaine Rapid Efficacy Screening Trial (CREST): a paradigm for the controlled evaluation of candidate medications for cocaine dependence. Addiction 100 Suppl 1:1-11, 2005.	Comparative effectiveness
Lemoine P, Kermadi I, Garcia-Acosta S, Garay RP, Dib M. Double-blind, comparative study of cyamemazine vs. bromazepam in the benzodiazepine withdrawal syndrome. Prog Neuropsychopharmacol Biol Psychiatry. 2006 Jan;30(1):131-7.	Comparative effectiveness
Lerner A, Sigal M, Bacalu A, Shiff R, Burganski I, Gelkopf M. A naltrexone double blind placebo controlled study in Israel. Isr J Psychiatry Relat Sci 1992; 29(1):36-43.	Excluded for quality
Leshner AI. Science-based views of drug addiction and its treatment. JAMA 282(14):1314-6, 1999.	Exclude, kept for background
Levin FR, McDowell D, Evans SM, Nunes E, Akerele E, Donovan S et al. Pharmacotherapy for marijuana dependence: a double-blind, placebo-controlled pilot study of divalproex sodium. American Journal on Addictions 13(1):21-32, 2004;-Feb.	Comparative effectiveness
Liddle HA, Dakof GA, Parker K, Diamond GS, Barrett K, Tejeda M. Multidimensional family therapy for adolescent drug abuse: results of a randomized clinical trial. American Journal of Drug & Alcohol Abuse 27(4):651 -88, 2001.	Comparative effectiveness
Lima MS, Reisser Lima AAP, Soares BGO, Farrell M. Antidepressants for cocaine dependence]. Cochrane Database of Systematic Reviews 2003.	Kept for use as source document
Lima Reisser A, Lima MS, Soares BGO, Farrell M. Carbamazepine for cocaine dependence. Cochrane Database of Systematic Reviews 2002.	Kept for use as source document
Linde K, Vickers A, Hondras M, ter Riet G, Thormahlen J, Berman B et al. Systematic reviews of complementary therapies - an annotated bibliography. Part 1: acupuncture. BMC Complement Altern Med 2001; 1:3.	Non-English
Ling W, Charuvastra C, Collins JF, Batki S, Brown LS, Jr., Kintaudi P et al. Buprenorphine maintenance treatment of opiate dependence: a multicenter, randomized clinical trial. Addiction 1998; 93(4):475-486.	Excluded for quality
Litt MD, Kadden RM, Stephens RS. Coping and Self-Efficacy in Marijuana Treatment: Results From the Marijuana Treatment Project. J Consult Clin Psychol. 2005 Dec;73(6):1015-25.	Exclude, kept for background
Lollis CM, Strothers HS, Chitwood DD, McGhee M. Sex, drugs, and HIV: does methadone maintenance reduce drug use and risky sexual behavior? J Behav Med 2000; 23(6):545-557.	Does not evaluate appropriate intervention
Longshore D, Grills C, Annon K. Effects of a culturally congruent intervention on cognitive factors related to drug-use recovery . Subst Use Misuse 1999; 34(9):1223-1241.	Does not report designated outcomes
Longshore D, Hsieh S, Danila B, Anglin MD. Methadone maintenance and needle/syringe sharing. Int J Addict 1993; 28(10):983-996.	Excluded study design
Magura S, Staines GL, Blankertz L, Madison EM. The effectiveness of vocational services for substance users in treatment. Subst Use Misuse 2004; 39(13-14):2165-2213.	Excluded study design

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Reference	Reason for Exclusion
Malcolm R, Herron J, Sutherland SE, Brady KT. Adverse outcomes in a controlled trial of pergolide for cocaine dependence. Journal of Addictive Diseases 1920;(1):81-92, 2001.	Comparative effectiveness
Malcolm R, Kajdasz DK, Herron J, Anton RF, Brady KT. A double-blind, placebo-controlled outpatient trial of pergolide for cocaine dependence. Drug Alcohol Depend 2000; 60(2):161-168.	Comparative effectiveness
Malcolm R, LaRowe S, Cochran K, Moak D, Herron J, Brady K et al. A controlled trial of amlodipine for cocaine dependence: a negative report. Journal of Substance Abuse Treatment 28(2):197-204, 2005.	Comparative effectiveness
Margolin A, Avants SK, Holford TR. Interpreting conflicting findings from clinical trials of auricular acupuncture for cocaine addiction: does treatment context influence outcome? Journal of Alternative & Complementary Medicine 8(2):111-21, 2002.	Comparative effectiveness
Margolin A, Kleber HD, Avants SK, Konefal J, Gawin F, Stark E et al. Acupuncture for the treatment of cocaine addiction: a randomized controlled trial. JAMA 2002; 287(1):55-63.	Comparative effectiveness
Margolin A, Kosten TR, Avants SK, Wilkins J, Ling W, Beckson M et al. A multicenter trial of bupropion for cocaine dependence in methadone-maintained patients. Drug Alcohol Depend 1995; 40(2):125-131.	Excluded population
Margolin A. Acupuncture for substance abuse. Current Psychiatry Reports 5(5):333-9, 2003.	Comparative effectiveness
Marques AC, Formigoni ML. Comparison of individual and group cognitive-behavioral therapy for alcohol and/or drug-dependent patients. Addiction 96(6):835-46, 2001.	Comparative effectiveness
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):515-532.	Kept for use as source document
Marsden J, Gossop M, Stewart D, Best D, Farrell M, Lehmann P et al. The Maudsley Addiction Profile (MAP): a brief instrument for assessing treatment outcome. Addiction 1998; 93(12):1857-1867.	Does not report designated outcomes
Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. Cochrane Database of Systematic Reviews 2005.	Kept for use as source document
Mattick RP, Kimber J, Breen C, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database of Systematic Reviews 2005.	Kept for use as source document
Mayet S, Farrell M, Ferri M, Amato L, Davoli M. Psychosocial treatment for opiate abuse and dependence. Cochrane Database of Systematic Reviews 2005.	Kept for use as source document

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Reference	Reason for Exclusion
McCarthy G, Myers B, Siegfried N. Treatment for Methaqualone dependence in adults. Cochrane Database of Systematic Reviews 2005.	Excluded setting
McCarthy JJ, Leamon MH, Parr MS, Anania B. High-dose methadone maintenance in pregnancy: maternal and neonatal outcomes. American Journal of Obstetrics & Gynecology 2005; 193(3 Pt 1):606-610.	Does not evaluate appropriate intervention
Mcclanahan TM. A comparative evaluation of cognitive-behavioral therapy and insight-oriented psychotherapy in the treatment of comorbid substance abuse, anxiety, and depression in substance abusing females. 2001. Dissertation.	Comparative effectiveness
McCoy CB, Metsch LR, Comerford M, Zhao W, Coltes AJ, Messiah SE. Trends of HIV risk behaviors in a cohort of injecting drug users and their sex partners in Miami, Florida, 1988-1998. AIDS & Behavior 2005; 9(2):187-199.	Does not evaluate appropriate intervention
McKay JR LKSDPH. The Effectiveness of Telephone-Based Continuing Care for Alcohol and Cocaine Dependence. Archives of General Psychiatry 1962;(2).	Comparative effectiveness
McKay JR, Lynch KG, Pettinati HM, Shepard DS. An examination of potential sex and race effects in a study of continuing care for alcohol- and cocaine- dependent patients. Alcohol Clin Exp Res. 2003; 27(8):1321-3.	Comparative effectiveness
McKay JR, Merikle E, Mulvaney FD, Weiss RV, Koppenhaver JM. Factors accounting for cocaine use two years following initiation of continuing care. Addiction 96(2):213-25, 2001.	Comparative effectiveness
McLellan AT, Lewis DC, O'Brien CP, Kleber HD. Drug dependence, a chronic medical illness: implications for treatment, insurance, and outcomes evaluation. JAMA 2000; 284(13):1689-1695.	Exclude, kept for background
Meandzija B, O'Connor PG, Fitzgerald B, Rounsaville BJ, Kosten TR. HIV infection and cocaine use in methadone maintained and untreated intravenous drug users. Drug & Alcohol Dependence 1994; 36(2):109-113.	Excluded study design
Meeker JE, Mount AM, Ross W. Detection of drug abuse by health professionals. Occupational Health & Safety 2002; 71(8):46-50.	Does not evaluate appropriate intervention
Meier PS, Barrowclough C, Donmall MC. The role of the therapeutic alliance in the treatment of substance misuse: a critical review of the literature. Addiction 2005; 100(3):304-316.	Does not evaluate appropriate intervention
Mello NK, Mendelson JH, Kuehnle JC, Sellers MS. Operant analysis of human heroin self-administration and the effects of naltrexone. J Pharmacol Exp Ther 1981; 216(1):45-54.	Does not evaluate appropriate intervention
Messina N, Farabee D, Rawson R. Treatment responsivity of cocaine-dependent patients with antisocial personality disorder to cognitive-behavioral and contingency management interventions. Journal of Consulting & Clinical Psychology 2003; 71(2):320-329.	Excluded study design

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Reference	Reason for Exclusion
Metrebian N. Prescribing drug of choice to opiate dependent drug users: a comparison of clients receiving heroin with those receiving injectable methadone at a West London drug clinic. Drug and alcohol review 1920;(3).	Comparative effectiveness
Metzger DS, Woody GE, McLellan AT, O'Brien CP, Druley P, Navaline H et al. Human immunodeficiency virus seroconversion among intravenous drug users in- and out-of-treatment: an 18-month prospective follow-up. J Acquir Immune Defic Syndr 1993; 6(9):1049-1056.	Excluded study design
Midanik LT, Zahnd EG, Klein D. Alcohol and drug CAGE screeners for pregnant, low-income women: the California Perinatal Needs Assessment. Alcoholism: Clinical & Experimental Research 1998; 22(1):121-125.	Does not report designated outcomes
Miller WR, Yahne CE, Tonigan JS. Motivational interviewing in drug abuse services: A randomized trial. J Consult Clin Psychol. 2003 Aug;71(4):754-63.	Comparative effectiveness
Milton S, Crino R, Hunt C, Prosser E. The effect of compliance-improving interventions on the cognitive-behavioural treatment of pathological gambling. J Gambl Stud 2002; 18(2):207-229.	Does not evaluate appropriate intervention
Modestin J, Nussbaumer C, Angst K, Scheidegger P , Hell D. Use of potentially abusive psychotropic substances in psychiatric inpatients. European Archives of Psychiatry & Clinical Neuroscience 1997; 247(3):146-153.	Does not report designated outcomes
Moner SE. Acupuncture and addiction treatment. J Addict Dis 1996; 15(3):79-100.	Excluded for quality
Montoya ID PKR. Open-label pilot study of bupropion plus bromocriptine for treatment of cocaine dependence. American Journal of Drug and Alcohol Abuse 1928;(1).	Comparative effectiveness
Montoya ID, Gorelick DA, Preston KL, Schroeder JR, Umbricht A, Cheskin LJ et al. Randomized trial of buprenorphine for treatment of concurrent opiate and cocaine dependence. Clin Pharmacol Ther 2004; 75(1):34-48.	Comparative effectiveness
Montoya ID, Levin FR, Fudala PJ, Gorelick DA. Double-blind comparison of carbamazepine and placebo for treatment of cocaine dependence. Drug Alcohol Depend 1995; 38(3):213-219.	Comparative effectiveness
Morgenstern J, Blanchard KA, Morgan TJ, Labouvie E, Hayaki J. Testing the effectiveness of cognitive-behavioral treatment for substance abuse in a community setting: within treatment and posttreatment findings. Journal of Consulting & Clinical Psychology 69(6):1007-17, 2001.	Comparative effectiveness
Morgenstern J, Bux DAJ, Labouvie E, Morgan T, Blanchard KA, Muench F. Examining mechanisms of action in 12-Step community outpatient treatment. Drug Alcohol Depend. 2003;72(3):237-47.	Comparative effectiveness
Musselman DL, Kell MJ. Prevalence and improvement in psychopathology in opioid dependent patients participating in methadone maintenance. J Addict Dis 1995; 14(3):67-82.	Does not evaluate appropriate intervention
National Institute on Drug Abuse. Prescription Medication. 10-5-2005.	Exclude, kept for background

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Reference	Reason for Exclusion
National Research Council, Institute of Medicine. New Treatments for Addiction: Behavioral, Ethical, Legal and Social Questions. Washington, DC: National Academies Press, 2004.	Exclude, kept for background
Nich C, McCance-Katz EF, Petrakis IL, Cubells JF , Rounsaville BJ, Carroll KM. Sex differences in cocaine-dependent individuals' response to disulfiram treatment. Addict Behav 2004; 29(6):1123-1128.	Excluded study design
Nunes EV, McGrath PJ, Quitkin FM, Ocepek-Welikson K, Stewart JW, Koenig T et al. Imipramine treatment of cocaine abuse: possible boundaries of efficacy. Drug Alcohol Depend 1995; 39(3):185-195.	Comparative effectiveness
O'Connor AD, Rusyniak DE, Bruno A. Cerebrovascular and cardiovascular complications of alcohol and sympathomimetic drug abuse. Med Clin North Am 2005; 89(6):1343-1358.	Exclude, kept for background
Office of National Drug Control Policy. Healing America's Drug Users: Getting Treatment Resources Where They Are Needed. 2005.	Exclude, kept for background
O'Leary Tevyaw T, Monti PM. Motivational enhancement and other brief interventions for adolescent substance abuse: Foundations, applications and evaluations. Addiction. 2004;99 Suppl 2:63-75.	Exclude, kept for background
Parran T, Jr., Weber E, Tasse J, Anderson B, Adelman C. Mandatory toxicology testing and chemical dependence consultation follow-up in a level-one trauma center. Journal of Trauma-Injury Infection & Critical Care 1995; 38(2):278-280.	Comparative effectiveness
Peck JA, Reback CJ, Yang X, Rotheram-Fuller E, Shoptaw S. 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-i108.	Does not report designated outcomes
Peirce JM, Petry NM, Stitzer ML, Blaine J, Kellogg S, Satterfield F et al. Effects of lower-cost incentives on stimulant abstinence in methadone maintenance treatment: a National Drug Abuse Treatment Clinical Trials Network study. Archives of General Psychiatry 63(2):201-8, 2006.	Comparative effectiveness
Petitjean S, Stohler R, Deglon JJ, Livoti S, Waldvogel D, Uehlinger C et al. Double-blind randomized trial of buprenorphine and methadone in opiate dependence. Drug & Alcohol Dependence 62(1):97-104, 2001.	Comparative effectiveness
Petrie J, Bunn F, Byrne G. Parenting programmes for preventing tobacco, alcohol or drugs abuse in children under 18. Cochrane Database of Systematic Reviews 2005.	Comparative effectiveness
Petry NM, Petrakis I, Trevisan L, Wiredu G, Boutros NN, Martin B et al. Contingency management interventions: from research to practice. American Journal of Psychiatry 158(5):694-702, 2001.	Comparative effectiveness
Poling J, Oliveto A, Petry N, Sofuoglu M, Gonsai K, Gonzalez G et al. Six-month trial of bupropion with contingency management for cocaine dependence in a methadone-maintained population. Archives of General Psychiatry 63(2):219-28, 2006.	Comparative effectiveness
Pope HG, Jr., Gruber AJ, Hudson JI, Cohane G, Huestis MA, Yurgelun-Todd D. Early-onset cannabis use and cognitive deficits: what is the nature of the association? Drug & Alcohol Dependence 2003; 69(3):303-310.	Does not evaluate appropriate intervention

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Reference	Reason for Exclusion
Power R, Hartnoll R, Chalmers C. Help-seeking among illicit drug users: some differences between a treatment and nontreatment sample. Int J Addict 1992; 27(8):887-904.	Excluded study design
Prendergast ML, Podus D, Chang E. Program factors and treatment outcomes in drug dependence treatment: an examination using meta-analysis. Substance Use & Misuse 2000; 35(12-14):1931-1965.	Does not evaluate appropriate intervention
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.	Excluded study design
Preston KL, Umbricht A, Wong CJ, Epstein DH. Shaping cocaine abstinence by successive approximation. Journal of Consulting & Clinical Psychology 69(4):643-54, 2001.	Comparative effectiveness
Rabinowitz J. Outcomes of Naltrexone Maintenance Following Ultra Rapid Opiate Detoxification Versus Intensive Inpatient Detoxification. American Journal on Addictions 1911;(1).	Comparative effectiveness
Racine AD, Joyce TJ, Anderson R. The association between prenatal care and birth weight among women exposed to cocaine in New York City: a correction. JAMA 1994; 271(15):1161-1162.	Excluded study design
Raisch DW, Fye CL, Boardman KD, Sather MR. Opioid dependence treatment, including buprenorphine/naloxone. Annals of Pharmacotherapy 36(2):312-21, 2002.	Exclude, kept for background
Rawson RA, Huber A, McCann M, Shoptaw S, Farabee D, Reiber C et al. A comparison of contingency management and cognitive-behavioral approaches during methadone maintenance treatment for cocaine dependence. Archives of General Psychiatry 59(9):817-24, 2002.	Comparative effectiveness
Rawson RA, Marinelli-Casey P, Anglin MD, Dickow A, Frazier Y, Gallagher C et al. A multi-site comparison of psychosocial approaches for the treatment of methamphetamine dependence. Addiction 2004; 99(6):708-717.	Comparative effectiveness
Rawson RA, Tennant FS, Jr. Five-year follow-up of opiate addicts with naltrexone and behavior therapy. NIDA Res Monogr 1984; 49:289-295.	Excluded for quality
Rayburn WF, Bogenschutz MP. Pharmacotherapy for pregnant women with addictions. American Journal of Obstetrics & Gynecology 191;(6):1885-1897.	Excluded for quality
Rayburn WF, Bogenschutz MP. Pharmacotherapy for pregnant women with addictions. American Journal of Obstetrics & Gynecology 2004;(6):1885-1897.	Excluded study design
Reid MS, Angrist B, Baker S, Woo C, Schwartz M, Montgomery A et al. A placebo-controlled screening trial of celecoxib for the treatment of cocaine dependence. Addiction 100 Suppl 1:32-42, 2005.	Comparative effectiveness

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Reference	Reason for Exclusion
Remien RH, Goetz R, Rabkin JG, Williams JB, Bradbury M, Ehrhardt AA et al. Remission of substance use disorders: gay men in the first decade of AIDS. J Stud Alcohol 1995; 56 (2):226-232.	Does not evaluate appropriate intervention
Reynaud-Maurupt C, Carrieri MP, Gastaud JA, Pradier C, Obadia Y, Moatti JP. Impact of drug maintenance treatment on injection practices among French HIV-infected IDUs. The MANIF 2000 Study Group. AIDS Care 2000; 12(4):461-470.	Does not evaluate appropriate intervention
Riggs PD, Hall SK, Mikulich-Gilbertson SK, Lohman M, Kayser A. A randomized controlled trial of pemoline for attention-deficit/hyperactivity disorder in substance-abusing adolescents. J Am Acad Child Adolesc Psychiatry 2004; 43(4):420-429.	Excluded population
Ritter AJ, Lintzeris N, Clark N, Kutin JJ, Bammer G, Panjari M. A randomized trial comparing levo-alpha acetylmethadol with methadone maintenance for patients in primary care settings in Australia. Addiction 98(11):1605-13, 2003.	Comparative effectiveness
Robertson JR, Ronald PJ, Raab GM, Ross AJ, Parpia T. Deaths, HIV infection, abstinence, and other outcomes in a cohort of injecting drug users followed up for 10 years. BMJ 1994; 309(6951):369-372.	Does not evaluate appropriate intervention
Rogne GS, Myrvang B, Opjordsmoen S. Criminality in drug addicts: a follow-up study over 25 years. Eur Addict Res 2004; 10(2):49-55.	Does not evaluate appropriate intervention
Roozen HG, Boulogne JJ, van Tulder MW, van den BW, De Jong CA, Kerkhof AJ. A systematic review of the effectiveness of the community reinforcement approach in alcohol, cocaine and opioid addiction. Drug & Alcohol Dependence 2004; 74(1):1-13.	Excluded for quality
Rosenbaum M, Washburn A, Knight K, Kelley M, Irwin J. Treatment as harm reduction, defunding as harm maximization: the case of methadone maintenance. J Psychoactive Drugs 1996; 28(3):241-249.	Does not evaluate appropriate intervention
Saleh SS, Vaughn T, Hall J, Levey S, Fuortes L, Uden-Holmen T. Effectiveness of case management in substance abuse treatment. Care Management Journals 3(4):172-7, 2002.	Excluded population
Saunders B, Wilkinson C, Phillips M. The impact of a brief motivational intervention with opiate users attending a methadone programme. Addiction 1995; 90(3):415-424.	Excluded for quality
Schildhaus S, Gerstein D, Brittingham A, Cerbone F, Dugoni B. Services research outcomes study: overview of drug treatment population and outcomes. Substance Use & Misuse 2000; 35(12-14):1849-1877.	Does not evaluate appropriate intervention
Schmitz JM, Averill P, Stotts AL, Moeller FG, Rhoades HM, Grabowski J. Fluoxetine treatment of cocaine-dependent patients with major depressive disorder. Drug & Alcohol Dependence 63(3):207-14, 2001.	Comparative effectiveness

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Reference	Reason for Exclusion
Schottenfeld RS, Pakes JR, Kosten TR. Prognostic factors in Buprenorphine- versus methadone-maintained patients. Journal of Nervous & Mental Disease 1998; 186(1):35-43.	Does not report designated outcomes
Schumacher JE, Milby JB, Raczynski JM, Caldwell E, Engle M, Carr J et al. Validity of self-reported crack cocaine use among homeless persons in treatment. Journal of Substance Abuse Treatment 1995; 12(5):335-339.	Does not report designated outcomes
Scott CK, Dennis ML, Foss MA. Utilizing Recovery Management Checkups to shorten the cycle of relapse, treatment reentry, and recovery. Drug & Alcohol Dependence 78(3):325-38, 2005.	Does not report designated outcomes
Sees KL, Delucchi KL, Masson C, Rosen A, Clark HW, Robillard H et al. Methadone maintenance vs 180-day psychosocially enriched detoxification for treatment of opioid dependence: a randomized controlled trial. JAMA 2000; 283(10):1303-1310.	Excluded for quality
Sege R, Stringham P, Short S, Griffith J. Ten years after: examination of adolescent screening questions that predict future violence-related injury. Journal of Adolescent Health 1999; 24(6):395-402.	Does not report designated outcomes
Seifert J, Metzner C, Paetzold W, Borsutzky M, Passie T, Rollnik J et al. Detoxification of opiate addicts with multiple drug abuse: a comparison of buprenorphine vs. methadone. Pharmacopsychiatry 35(5):159-64, 2002.	Comparative effectiveness
Serpelloni G, Carrieri MP, Rezza G, Morganti S, Gomma M, Binkin N. Methadone treatment as a determinant of HIV risk reduction among injecting drug users: a nested case-control study. AIDS Care 1994; 6(2):215-220.	Excluded study design
Shoptaw S, Watson DW, Reiber C, Rawson RA, Montgomery MA, Majewska MD et al. Randomized controlled pilot trial of cabergoline, hydergine and levodopa/carbidopa: Los Angeles Cocaine Rapid Efficacy Screening Trial (CREST). Addiction 100 Suppl 1:78-90, 2005.	Comparative effectiveness
Shufman EN, Porat S, Witztum E, Gandacu D, Bar-Hamburger R, Ginath Y. The efficacy of naltrexone in preventing reabuse of heroin after detoxification. Biol Psychiatry 1994; 35(12):935-945.	Excluded for quality
Silva dL, Oliveira Soares BG, Pereira Reisser AA, Farrell M. Pharmacological treatment of cocaine dependence: a systematic review. Addiction 2002; 97(8):931-949.	Kept for use as source document
Silverman K, Svikis D, Robles E, Stitzer ML, Bigelow GE. A reinforcement-based therapeutic workplace for the treatment of drug abuse: six-month abstinence outcomes. Experimental & Clinical Psychopharmacology 9(1):14-23, 2001.	Excluded for quality
Silverman K, Wong CJ, Higgins ST, Brooner RK, Montoya ID, Contoreggi C et al. Increasing opiate abstinence through voucher-based reinforcement therapy. Drug Alcohol Depend 1996; 41(2):157-165.	Excluded study design
Simoens S, Matheson C, Bond C, Inkster K, Ludbrook A. The effectiveness of community maintenance with methadone or buprenorphine for treating opiate dependence. Br J Gen Pract 2005; 55(511):139-146.	Comparative effectiveness

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Reference	Reason for Exclusion
Simpson TL, Westerberg VS, Little LM, Trujillo M . Screening for childhood physical and sexual abuse among outpatient substance abusers. Journal of Substance Abuse Treatment 11(4):347-58, 1994.	Does not evaluate appropriate intervention
Sipkoff M. Insurers give substance abuse new identity: it's a disease. Managed Care 14(4):18-20, 23-4, 26, 2005.	Exclude, kept for background
Smith GC, Clarke DM, Handrinos D. Recognising drug and alcohol problems in patients referred to consultation-liaison psychiatry . Medical Journal of Australia 1995; 163(6):307, 310-302.	Does not report designated outcomes
Soares BGO, Lima MS, Lima Reisser A, Farrell M. Dopamine agonists for cocaine dependence. Cochrane Database of Systematic Reviews 2005.	Kept for use as source document
Sofuoglu M, Singha A, Kosten TR, McCance-Katz FE , Petrakis I, Oliveto A. Effects of naltrexone and isradipine, alone or in combination, on cocaine responses in humans. Pharmacol Biochem Behav. 2003 Jul;75(4):801-8.	Does not evaluate appropriate intervention
Sorensen JL, Copeland AL. Drug abuse treatment as an HIV prevention strategy: a review. Drug & Alcohol Dependence 2000; 59(1):17-31.	Excluded study design
Soyka M, Hock B, Kagerer S, Lehnert R, Limmer C, Kuefner H. Less impairment on one portion of a driving-relevant psychomotor battery in buprenorphine-maintained than in methadone-maintained patients: results of a randomized clinical trial. Journal of Clinical Psychopharmacology 25(5):490-3, 2005.	Comparative effectiveness
Srisurapanont M, Jarusuraisin N, Kittirattanapaiboon P. Treatment for amphetamine dependence and abuse. Cochrane Database of Systematic Reviews 2005.	Kept for use as source document
Stanton MD, Shadish WR. Outcome, attrition, and family-couples treatment for drug abuse: a meta-analysis and review of the controlled, comparative studies. Psychol Bull 1997; 122(2):170-191.	Comparative effectiveness
Stein MD, Anderson B, Charuvastra A, Maksad J, Friedmann PD. A brief intervention for hazardous drinkers in a needle exchange program. J Subst Abuse Treat 2002; 22(1):23-31.	Does not report designated outcomes
Stein MD, Charuvastra A, Maksad J, Anderson BJ. A randomized trial of a brief alcohol intervention for needle exchangers (BRAINE). Addiction 2002; 97(6):691-700.	Does not report designated outcomes
Stella L, D'Ambra C, Mazzeo F, Capuano A, Del Franco F, Avolio A et al. Naltrexone plus benzodiazepine aids abstinence in opioid-dependent patients. Life Sciences 77(21):2717 -22, 2005.	Comparative effectiveness
Stephens RS, Babor TF, Kadden R, Miller M, Marijuana Treatment Project Research Group. The Marijuana Treatment Project: rationale, design and participant characteristics. Addiction 97 Suppl 1:109-24, 2002.	Does not report designated outcomes
Stephens RS, Roffman RA, Curtin L. Comparison of extended versus brief treatments for marijuana use. J Consult Clin Psychol 2000; 68(5):898-908.	Excluded for quality

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Reference	Reason for Exclusion
Sterk CE, Theall KP, Elifson KW, Kidder D. HIV risk reduction among African-American women who inject drugs: a randomized controlled trial. AIDS & Behavior 2003; 7(1):73-86.	Does not evaluate appropriate intervention
Sterk CE, Theall KP, Elifson KW. Effectiveness of a risk reduction intervention among African American women who use crack cocaine. AIDS Education & Prevention 2003; 15(1):15-32.	Does not evaluate appropriate intervention
Stine SM, Krystal JH, Kosten TR, Charney DS. Mazindol treatment for cocaine dependence. Drug Alcohol Depend 1995; 39(3):245-252.	Comparative effectiveness
Stoffel VC, Moyers PA. An evidence-based and occupational perspective of interventions for persons with substance-use disorders. Am J Occup Ther 2004; 58(5):570-586.	Excluded study design
Stoller KB, Bigelow GE, Walsh SL, Strain EC. Effects of buprenorphine/naloxone in opioid-dependent humans . Psychopharmacology 154(3):230-42, 2001.	Comparative effectiveness
Strain EC, Stitzer ML, Liebson IA, Bigelow GE. Methadone dose and treatment outcome. Drug Alcohol Depend 1993; 33(2):105-117.	Exclude, kept for background
Substance Abuse and Mental Health Services Administration. Overview of Findings from the 2004 National Survey on Drug Use and Health. Office of Applied Studies, editor. DUH Series H-27, DHHS Publication No. SMA 05-0461. 2005.	Exclude, kept for background
Substance Abuse and Mental Health Services Administration. Results from the 2004 National Survey on Drug Use and Health: National Findings. NSDUH series H-28, DHHS Publication No. SMA 05-4062. 2005. Rockville, MD, SAMHSA, Office of Applied Studies.	Exclude, kept for background
Substance Abuse and Mental Health Services, Office of Applied Studies. National Survey of Substance Abuse Treatment Services (N-SSATS): 2003. Data on Substance Abuse Treatment Facilities. ASIS Series: S-24; DHHS Publication No. (SMA) 04-3966. 2003. Rockville, MD, Office of Applied Studies.	Exclude, kept for background
Sullivan LE, Metzger DS, Fudala PJ, Fiellin DA. Decreasing international HIV transmission: the role of expanding access to opioid agonist therapies for injection drug users. Addiction 2005; 100(2):150-158.	Exclude, kept for background
Svikis D, Henningfield J, Gazaway P, Huggins G, Sosnow K, Hranicka J et al. Tobacco use for identifying pregnant women at risk of substance abuse. Journal of Reproductive Medicine 1997; 42(5):299-302.	Does not report designated outcomes
Swedish Council on Technology Assessment in Health Care (SBU). Treatment of alcohol and drug abuse: an evidence-based review. Int J Technol Assess Health Care 2002; 18(1):145-154.	Excluded for quality
Tait RJ, Hulse GK, Robertson SI, Sprivulis PC. Emergency department-based intervention with adolescent substance users: 12-month outcomes. Drug & Alcohol Dependence 2005; 79(3):359-363.	Exclude, kept for background
Tait RJ, Hulse GK. A systematic review of the effectiveness of brief interventions with substance using adolescents by type of drug. Drug & Alcohol Review 2003; 22(3):337-346.	Excluded for quality

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Reference	Reason for Exclusion
Tapert SF, Aarons GA, Sedlar GR, Brown SA. Adolescent substance use and sexual risk-taking behavior. J Adolesc Health 2001; 28(3):181-189.	Does not evaluate appropriate intervention
Tennant FS, Jr., Tarver AL. Double-blind comparison of desipramine and placebo in withdrawal from cocaine dependence. NIDA Res Monogr 1984; 55:159-163.	Does not evaluate appropriate intervention
Tian X, Krishnan S. Efficacy of auricular acupressure as an adjuvant therapy in substance abuse treatment: a pilot study. Alternative Therapies in Health & Medicine 12(1):66-9, 2006.	Excluded for quality
Torrens M, Fonseca F, Mateu G, Farre M. Efficacy of antidepressants in substance use disorders with and without comorbid depression. A systematic review and meta-analysis. Drug & Alcohol Dependence 2005; 78(1):1-22.	Kept for use as source document
Tran TN, Detels R, Long HT, Lan HP. Drug use among female sex workers in Hanoi, Vietnam. Addiction 2005; 100(5):619-625.	Excluded study design
Treatment options for opiate addiction. J Ky Med Assoc 2004; 102(5):221-224.	Excluded study design
Turner BJ, Markson L, Hauck W, Cocroft J, Fanning T. Prenatal care of HIV-infected women: analysis of a large New York State cohort. Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology 1995; 9(4):371-378.	Does not evaluate appropriate intervention
U.S.Department of Health and Human Servicies, National Institute of Health, National Institute on Drug Abuse. Drug Addiction Research and the Health of Women. Wetherington C, Roman A, editors. 1998.	Exclude, kept for background
U.S.Preventive Services Task Force . Screening for Drug Abuse. Guide to Clinical Preventive Services, Second Edition. Lippincott Williams & Wilkins, 1996: 583-594.	Exclude, kept for background
Ursitti F, Klein J, Koren G. Confirmation of cocaine use during pregnancy: a critical review. Therapeutic Drug Monitoring 23(4):347-53, 2001.	Does not evaluate appropriate intervention
Van Amerongen D. Trying to reach the pregnant substance-abuser: learning from failure. Hmo Practice 1996; 10(2):80-82.	Does not report designated outcomes
van den BW. Medical prescription of heroin to treatment resistant heroin addicts: two randomised controlled trials. BMJ (Clinical research ed) 327;(7410).	Comparative effectiveness
Vanichseni S, Wongsuwan B, Choopanya K, Wongpanich K. A controlled trial of methadone maintenance in a population of intravenous drug users in Bangkok: implications for prevention of HIV. Int J Addict 1991; 26(12):1313-1320.	Non-English
Vorma H, Naukkarinen H, Sarna S, Kuoppasalmi K. Symptom severity and quality of life after benzodiazepine withdrawal treatment in participants with complicated dependence. Addict Behav 2004; 29(6):1059-1065.	Does not report designated outcomes

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Reference	Reason for Exclusion
Waldron HB, Kaminer Y. On the learning curve: the emerging evidence supporting cognitive-behavioral therapies for adolescent substance abuse. Addiction 99 Suppl 2:93-105, 2004.	Comparative effectiveness
Waldron HB, Slesnick N, Brody JL, Turner CW, Peterson TR. Treatment outcomes for adolescent substance abuse at 4- and 7-month assessments. Journal of Consulting & Clinical Psychology 69(5):802-13, 2001.	Comparative effectiveness
Washington State Department of Health. Substance Abuse During Pregnancy: Guidelines for Screening. Taylor P, Zaichkin J, Bailey D, editors. 2002.	Exclude, kept for background
Waxmonsky JG, Wilens TE. Pharmacotherapy of adolescent substance use disorders: a review of the literature. Journal of Child & Adolescent Psychopharmacology 15(5):810-25, 2005.	Excluded study design
Weaver GD, Turner NH, O'Dell KJ. Depressive symptoms, stress, and coping among women recovering from addiction. J Subst Abuse Treat 2000; 18(2):161-167.	Excluded study design
Weisner C, Mertens J, Parthasarathy S, Moore C, Lu Y. Integrating primary medical care with addiction treatment: a randomized controlled trial. JAMA 286(14):1715 -23, 2001.	Comparative effectiveness
Weiss RD, Griffin ML, Gallop RJ, Najavits LM, Frank A, Crits-Christoph P et al. The effect of 12-step self-help group attendance and participation on drug use outcomes among cocaine-dependent patients. Drug & Alcohol Dependence 77(2):177-84, 2005.	Excluded for quality
Weiss RD, Najavits LM, Greenfield SF, Soto JA, Shaw SR, Wyner D. Validity of substance use self-reports in dually diagnosed outpatients. American Journal of Psychiatry 1998; 155(1):127-128.	Comparative effectiveness
Weizman T, Gelkopf M, Melamed Y, Adelson M, Bleich A. Cannabis abuse is not a risk factor for treatment outcome in methadone maintenance treatment: a 1-year prospective study in an Israeli clinic. Australian & New Zealand Journal of Psychiatry 38(1-2):42-6, 2004.	Does not evaluate appropriate intervention
Wells EA, Calsyn DA, Clark LL, Saxon AJ, Jackson TR. Retention in methadone maintenance is associated with reductions in different HIV risk behaviors for women and men. American Journal of Drug & Alcohol Abuse 1996; 22(4):509-521.	Does not evaluate appropriate intervention
Werner MJ, Joffe A, Graham AV. Screening, early identification, and office-based intervention with children and youth living in substance-abusing families. Pediatrics 1999; 103(5):1099-1112.	Does not report designated outcomes
West SL, O'Neal KK, Graham CW. A meta-analysis comparing the effectiveness of buprenorphine and methadone. J Subst Abuse 2000; 12(4):405-414.	Comparative effectiveness
Westermeyer J, Canino G. Culture and Substance Related Disorders. DSM-IV Sourcebook. American Psychiatric Association, 1997.	Exclude, kept for background

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Reference	Reason for Exclusion
Wickizer T, Maynard C, Atherly A, Frederick M, Koepsell T, Krupski A et al. Completion rates of clients discharged from drug and alcohol treatment programs in Washington State. Am J Public Health 1994; 84(2):215-221.	Does not report designated outcomes
Wiebel WW, Jimenez A, Johnson W, Ouellet L, Jovanovic B, Lampinen T et al. Risk behavior and HIV seroincidence among out-of-treatment injection drug users: a four-year prospective study. Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology 1996; 12(3):282-289.	Does not evaluate appropriate intervention
Williams RJ, Chang SY. A comprehensive and comparative review of adolescent substance abuse treatment outcome. Clinical Psychology: Science and Practice 2000; 7(2):138-166.	Comparative effectiveness
Wingert WE, Feldman MS, Kim MH, Noble L, Hand I, Yoon JJ. A comparison of meconium, maternal urine and neonatal urine for detection of maternal drug use during pregnancy. Journal of Forensic Sciences 1994; 39(1):150-158.	Comparative effectiveness
Winhusen T, Somoza E, Harrer JM, Moore E, Ussery T, Kropp F et al. Metyrapone and cocaine: a double-blind, placebo-controlled drug interaction study. Pharmacology, Biochemistry & Behavior 80(4):631-8, 2005.	Does not report designated outcomes
Winhusen TM, Somoza EC, Harrer JM, Mezinskis JP , Montgomery MA, Goldsmith RJ et al. A placebo-controlled screening trial of tiagabine, sertraline and donepezil as cocaine dependence treatments. Addiction 100 Suppl 1:68-77, 2005.	Comparative effectiveness
Wolff K, Farrell M, Marsden J, Monteiro MG, Ali R, Welch S et al. A review of biological indicators of illicit drug use, practical considerations and clinical usefulness. Addiction 1999; 94(9):1279-1298.	Does not report designated outcomes
Woo C, Reid MS, Leiderman D, Montgomery A, Majewska D, Baker S, Schwartz M, O'Leary S, Duffy M, Conner E, Robinsnon J, Rotrosen J. A clinical trial of celebrex versus placebo for the treatment of cocaine dependence. Drug and alcohol dependence Vol 63 Suppl 1, pp. 172, 2001.	Comparative effectiveness
Wood E, Spittal P, Li K, Kerr T, Miller CL, Hogg RS et al. Inability to access addiction treatment and risk of HIV infection among injection drug users. Journal of Acquired Immune Deficiency Syndromes: JAIDS 2004; 36(2):750-754.	Does not evaluate appropriate intervention
Woody GE, McLellan AT, Bovasso G, Kurtz J, O'Brien CP. Methadone maintenance and opioid positive urine: a test of 80 mg vs 120 mg and MET vs DC. Drug and alcohol dependence Vol 63 Suppl 1, pp 173, 2001.	Comparative effectiveness
Woody GE, Gallop R, Luborsky L, Blaine J, Frank A, Salloum IM et al. HIV risk reduction in the National Institute on Drug Abuse Cocaine Collaborative Treatment Study. Journal of Acquired Immune Deficiency Syndromes: JAIDS 2003; 33(1):82-87.	Does not report designated outcomes
Yao HY, Wang ZZ, Jiang DL, Sun JF, Niu ZX. Evaluation of the effect of interventions for the female drug abusers. Biomedical & Environmental Sciences 15(4):341-6, 2002.	Does not evaluate appropriate intervention
Ying L, Man Jia Z, Fan Rong L. Acupuncture for opioid dependence. Cochrane Database of Systematic Reviews 2005.	Comparative effectiveness

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Reference	Reason for Exclusion
Zimmermann P, Muhlig S, Sonntag D, Buhringer G, Wittchen HU. Review on psychotherapeutic interventions for cannabis disorders. Sucht 2004; 50(5):334-342.	Kept for use as source document
Zuckerman B, Frank DA, Hingson R, Amaro H, Levenson SM, Kayne H et al. Effects of maternal marijuana and cocaine use on fetal growth. N Engl J Med 1989; 320(12):762-768.	Excluded study design