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Screening for Illicit Drug Use, Including Nonmedical Use of Prescription Drugs: An Updated Systematic Review for the U.S. Preventive Services Task Force

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Structured Abstract

Objective: We conducted this systematic review to support the U.S. Preventive Services Task Force in updating its 2008 recommendation on screening adolescents and adults, including pregnant women, for illicit drug use. Our review addressed 5 key questions (KQ): 1a. Does primary care screening for drug use in adolescents and adults, including pregnant women, reduce drug use or improve other risky behaviors? 1b. Does primary care screening for drug use in adolescents and adults, including pregnant women, reduce morbidity or mortality or improve other health, social, or legal outcomes? 2. What is the accuracy of drug use screening instruments? 3. What are the harms of primary care screening for drug use in adolescents and adults, including pregnant women? 4a. Do counseling interventions to reduce drug use, with or without referral, reduce drug use or improve other risky behaviors in screen-detected persons? 4b. Do counseling interventions to reduce drug use, with or without referral, reduce morbidity or mortality or improve other health, social, or legal outcomes in screen-detected persons? 5. What are the harms of interventions to reduce drug use in screen-detected persons?

Data Sources: We performed a search of MEDLINE, PubMed Publisher-Supplied, PsycINFO, and the Cochrane Central Register of Controlled Trials for studies published through June 7, 2018. Studies included in three related USPSTF reviews were re-evaluated for potential inclusion. We supplemented searches by examining reference lists from related articles and expert recommendations and searched federal and international trial registries for ongoing trials.

Study Selection: Two researchers reviewed 17,919 titles and abstracts and 271 full-text articles against prespecified inclusion criteria. For all KQs, we included studies among adolescents and adults aged 12 years and older, including pregnant women. Studies targeting illicit psychoactive drug use or nonmedical pharmaceutical drug use were included; those targeting nonpsychoactive drugs (e.g., laxatives, anabolic steroids) were excluded. For KQs 1 and 3, we included studies that compared individuals who received screening with those who received no screening or who received usual care, including randomized trials or nonrandomized controlled trials. For KQ 2, we included studies that reported the accuracy (sensitivity and specificity) of standardized screening instruments compared with structured clinical interviews or biologic verification and that took place in a setting that was applicable to primary care. For KQ 4 and 5 about counseling interventions, only randomized and nonrandomized trials among screen-detected persons were included. Trials among persons who sought drug treatment or were referred or mandated to receive drug treatment were excluded. Interventions could include any brief counseling approach designed to reduce drug use, with or without referral. Studies of medication-assisted therapy (i.e., the use of methadone, buprenorphine, or naltrexone plus counseling) to treat opioid use disorders were excluded given that use of this therapy limited to adults with a diagnosed opioid use disorder (typically severe and non-screen detected). We conducted dual, independent critical appraisal of all provisionally included studies and abstracted all important study details and results from all studies rated fair or good quality. Data were abstracted by one reviewer and confirmed by another.

Data Analysis: We synthesized data separately for each KQ and subpopulation (i.e., adolescents, young adults and adults, and pregnant and postpartum women). The data for KQ 2 did not allow for quantitative pooling due to the limited number of contributing studies for each screening instrument and condition, so we synthesized the data qualitatively through tables and narrative

synthesis. For drug use outcomes, we ran random effects meta-analyses using the DerSimonian and Laird method to calculate the pooled differences in mean changes in drug use days; data was too sparse to pool for binary data on drug abstinence. We examined statistical heterogeneity among the pooled studies using standard χ^2 tests and estimated the proportion of total variability in point estimates using the I^2 statistic. We graded the strength of the overall body of evidence based on the consistency and precision of the results, reporting bias, and study quality.

Results: We found no evidence that addressed the benefits and harms of screening for drug use. Twenty-eight studies (n=65,720) addressed the accuracy of 30 drug use screening instruments; each specific screening instrument has not been studied more than once or twice. Studies among adolescents mainly focused on detecting cannabis use. They found that sensitivity for detecting any cannabis use or unhealthy cannabis use of frequency-based and risk assessment screen tools (all validated against structured clinical interview alone) ranged from 0.68 to 0.98 (95% CI range, 0.64 to 0.99) and specificity ranging from 0.82 to 1.00 (95% CI range, 0.80 to 1.00). Among adults, frequency-based and risk assessment drug screening tools (all but two validated against structured clinical interview alone) showed sensitivity for detecting unhealthy use of any drug ranging from 0.71 to 0.94 (95% CI range, 0.62 to 0.97) and specificity ranging from 0.87 to 0.97 (95% CI range, 0.83 to 0.98). For identifying drug use disorders among adults, sensitivity ranged from 0.85 to 1.00 (95% CI range, 0.67 to 1.00) and specificity ranged from 0.67 to 0.93 (95% CI, 0.58 to 0.95) when using the same cutoffs. Sensitivity for detecting any prenatal drug use using frequency-based and risk assessment (all validated against hair or urine analyses) was lower than the estimates for any drug use in non-pregnant adults (only rarely based on validation against biologic samples) and ranged from 0.37 to 0.76 (95% CI range, 0.24 to 0.86). Specificity was comparable and ranged from 0.68 to 0.83 (95% CI range, 0.55 to 0.91). We included 27 trials that addressed the effectiveness of a counseling intervention on changes in drug use or improved health, social, or legal outcomes among a screen-detected population. Across all 27 trials (n analyzed=8705), in general, there was no consistent effect of the interventions on rates of self-reported or biologically confirmed drug use at 3- to 12-month followup. Likewise, across 13 trials reporting the effects of the interventions on health, social, or legal outcomes (n-analyzed=4304), none of the trials found a statistically significant difference between intervention and control groups on any of these measures at 3- to 12-month followup. Of four trials providing information regarding potential harms, none found any evidence of harm.

Limitations: This review was not intended to be a comprehensive review of the evidence for treating drug use or drug use disorders and therefore, only trials of interventions among screen-detected populations that were applicable to primary care were included.

Conclusions: Several screening instruments with acceptable sensitivity and specificity have been developed to screen for drug use and drug use disorders in primary care, although in general, the accuracy of each tool has not been evaluated in more than one study and there is no evidence on the benefits or harms of screening versus no screening for drug use. Brief interventions for reducing the use of illicit drugs or the nonmedical use of prescription drugs in screen-detected primary care patients are unlikely to be effective for decreasing drug use or drug use consequences. Given the burden of drug use, more research is needed on approaches to identify and effectively intervene with patients exhibiting risky patterns of drug use in primary care.

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Chapter 1. Introduction

Scope and Purpose

In 2008, the U.S. Preventive Services Task Force (USPSTF) concluded that there was insufficient evidence to recommend for or against screening adolescents and adults, including pregnant women, for illicit drug use.[1] This recommendation was based on a staged evidence review of the literature published between 1994 and April 2006[2] and a supplemental assessment of screening instruments.[3] The staged review included research related to screening or treatment (including behavioral interventions) for marijuana, cocaine, opioids, or combined drug use and included evidence for adolescents and adults, including pregnant women. Subsequently, in 2014, the USPSTF issued another insufficient evidence recommendation specifically for children and adolescents, focused on interventions to *prevent* and *reduce* illicit drug or nonmedical pharmaceutical use among children and adolescents who had not already been diagnosed with a substance use disorder.[4] The 2014 review focused on children and adolescents did not include a screening framework.[5]

The objective of this review is to systematically review the evidence on the benefits and harms of screening for drug use among adolescents and adults, including pregnant women, as well as the benefits and harms of subsequent interventions for drug use among a screen-detected population. This review also synthesizes the evidence on the diagnostic accuracy of screening instruments to detect unhealthy drug use.

Condition Definition

Substance use typically refers to substances that affect mental processes (e.g., cognition, affect) when they are ingested, inhaled, injected, or taken through other administration routes. These substances have psychoactive properties and can include licit (legal) and illicit (illegal) substances, such as alcohol, tobacco, marijuana, and prescription drugs such as opioids and morphine derivatives, depressants, and stimulants. In this review, we focus on illicit drug use and the nonmedical use of prescription and over-the-counter drugs. Nonmedical use (also known as "extramedical use") refers to use of a prescription or over-the-counter drug in ways other than prescribed (i.e., more frequently or for a longer duration) or by people other than the prescribed individual. Use of marijuana/cannabis, regardless of its legal status for medical or recreational use, is included in this review given its psychoactive properties and the evidence (and lack of evidence) regarding the health effects of its use.[6]

Individuals generally use these substances to "get high" or for other unapproved indications. There are no widely agreed-upon standards for "unhealthy" use of drugs given that *any* amount of some drugs can cause negative health consequences. As examples, a single use of cocaine can lead to a myocardial infarction, any drug injection can lead to HIV infection, and drug-impaired driving can lead to serious injury or death. Therefore, in this report, we include screening for and treating the full spectrum of drug use that can result in health consequences, hereafter called "unhealthy drug use." This includes any use (of any amount, frequency or duration regardless of health consequences), heavy use, use that has already resulted in consequences but not yet as a

diagnosable disorder (often referred to as problem use, misuse, or hazardous use), or use that meets criteria for a drug use disorder (i.e., DSM-IV abuse or dependence or DSM-5 use disorder) (**Appendix A**). A complete list of illicit, prescription, and over-the-counter drugs including their common and "street" names, the Drug Enforcement Administration controlled substance schedule, the common route of administration, and possible health effects is provided in **Appendix B.**

Burden and Prevalence of Drug Use

Drug use is among the most common causes of preventable death in the United States[7, 8] and a leading cause of years lived in disability.[8] Although the proportion of deaths attributable to unintentional injuries (e.g., drug poisonings, motor vehicle crashes) has remained relatively stable at around 5 percent, intentional and nonintentional drug poisonings (including "overdoses") have increased each year to become the leading cause of injury death, with over 11,000 more deaths in 2011 than in 2005.[9] The age-adjusted rate of death from drug poisonings (including all intents) increased from 10.1 per 100,000 in 2005 to 12.3 per 100,000 in 2011.[9] The National Vital Statistics System reported over 70,000 drug overdose deaths in 2017.[10] The National Drug Intelligence Center reported in 2011 that the cost of illicit drug use exceeded $193 billion, including direct and indirect costs in the three main areas of crime, health, and productivity.[11]

The National Survey on Drug Use and Health (NSDUH), administered by the Substance Abuse and Mental Health Services Administration (SAMHSA), is the primary source of epidemiologic data on the use of illicit and misuse of prescription drugs, alcohol, and tobacco by the U.S. civilian, noninstitutionalized population aged 12 or older.[12] In 2017, an estimated 30.5 million Americans aged 12 or older (11.2% of the population aged 12 or older) were current illicit drug users, meaning they had used an illicit drug (marijuana/hashish, cocaine [including crack], heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used nonmedically) during the month prior to the survey interview (**Table 1**).[12] The estimate for illicit drug use in Americans is largely driven by marijuana use (9.6%; 26.0 million current users) and nonmedical use of prescription psychotherapeutic drugs (2.2%; 6.0 million current users), in particular, pain relievers (1.2%; 3.2 million current users). Marijuana was used by 85.3 percent of current illicit drug users, while an estimated 19.5 percent of illicit drug users used psychotherapeutic drugs nonmedically, including opioids (11.6%), pain relievers (10.6%), tranquilizers (5.7%), stimulants including methamphetamine (2.5%), and sedatives (1.2%). Other illicit drugs were used by a smaller percentage of current illicit drug users aged 12 years and older: cocaine (7.1%), hallucinogens (4.7%), and inhalants (1.8%).[12]

To put the rates of drug use in context with the use of other substances, in 2017 the rate of previous-month binge alcohol use (5 or more drinks on the same occasion on at least 1 day in the past 30 days) in persons ages 12 years or older was 24.5 percent and current tobacco use was 22.4 percent.[12] Illicit drug use was approximately 10 times higher in persons who smoked cigarettes and drank alcohol during the previous month (34.4%) than in those who neither smoked cigarettes nor drank alcohol during the previous month (3.5%).[12]

In 2017, an estimated 7.2 percent of the population aged 12 or older (19.7 million people) was classified with substance dependence or abuse in the previous year based on responses to NSDUH questions. Of these, 2.3 million (0.9%) people were classified with dependence on or abuse of alcohol and illicit drugs, 5.2 million (1.9%) had dependence or abuse of illicit drugs but not alcohol, and 12.2 million (4.5%) had dependence or abuse of alcohol but not illicit drugs.[12]

The prevalence of drug use is not equally distributed across the U.S. population. Subpopulations that experience a higher prevalence of drug use include young adults, males, certain racial and ethnic minority groups, and individuals living with mental health conditions.[12]

Age. Young adults, aged 18 to 25 years, have the highest rate of current illicit drug use (24.2%), followed by adolescents aged 12 to 17 years old (7.9%) (**Table 1**).[12]

Sex. In general, current illicit drug use among individuals aged 12 years or older was higher for males (13.7%) than females (8.8%). Males were more likely than females to use marijuana (11.9 vs. 7.3%), cocaine (1.1 vs. 0.5%), and hallucinogens (0.7 vs. 0.4%).[12]

Racial/ethnic groups. Rates of current illicit drug use among those aged 12 years or older in 2017 varied by race and ethnicity, with the highest rates among those reporting two or more races (17.1%) and American Indians or Alaska Natives (17.6%), followed by blacks (13.1%), whites (11.6%), Native Hawaiians or Pacific Islanders (10.4%), Hispanics or Latinos (9.8%), and Asians (4.5%).[12]

Persons with mental health conditions. An estimated 3.4 percent of adults had any type of mental illness and met the criteria for dependence or abuse for alcohol or illicit drugs in the previous 12 months, while 1.3 percent had a serious mental illness and met criteria for a substance use disorder. Among adolescents aged 12 to 17 years in 2017, 0.8 percent had a substance use disorder and experienced a major depressive episode in the previous year.[12]

Pregnant women. Pregnant women are approximately half as likely as nonpregnant women of the same age to use drugs. Based on 2017 data, 8.5 percent of pregnant women aged 15 to 44 were current illicit drug users, while 14.0 percent of nonpregnant women in this age group were drug users.[12] Rates of use among pregnant women also differ by age groups. The rate of current illicit drug use was 11.0 percent among pregnant women aged 18 to 25 and 7.2 percent among pregnant women aged 26 to 44. These rates are likely conservative estimates since they only reflect previous-month use, not use during the entire pregnancy. They are also limited to women who knew they were pregnant at the time of the survey. At least one study has shown that women tend to have higher rates of illicit drug use (not including prescription drug misuse) during the first trimester than the second or third; thus, pregnant women who do not yet know they are pregnant may have rates of drug use closer to the nonpregnant female population.[13] Likewise, there is a rich literature base documenting under-reporting of drug use among pregnant and postpartum women, likely due to social stigma as well as fear of socio-legal consequences such as losing custody of one's infant.[14-17]

Other Risk Factors for Drug Use

Risk factors for drug use in U.S. adults include a history of childhood adversity (i.e., physical abuse, witnessed fights at home, neglect by parent or guardian, sexual assault), family history of addiction (i.e., drug or alcohol problems in first-degree relatives), a pre-existing personality or mood disorder, previous nicotine dependence, and alcohol dependence.[18] Additional risk factors related to drug use during pregnancy include lack of prenatal care and cigarette smoking.[19, 20] Among adolescents, risk factors are aggressive behavior in childhood, lack of parental supervision, poor social skills, drug experimentation, availability of or access to drugs at school, and community poverty.[21] Factors associated with increased risk for misuse of prescribed drugs vary by type of prescription drug, but include a history of other substance use or misuse, history of mental illness, acute and chronic pain, physical health problems (i.e., fatigue or headaches), heightened physiological reactions to drugs (i.e., having a greater subjective euphoric reaction), and greater prescription access (e.g., excessive exposure to prescription opioids or benzodiazepines, having a larger prescribed dosage of opioids).[22] It is generally argued that many of these factors play a role in the onset or continuation of drug use although it is unclear whether many of these risks are causes, consequences, or correlates of drug use.

Screening for Drug Use

Screening for drug use in primary care can help to manage the quality and safety of health care as well as to identify unhealthy drug use that requires intervention. Knowledge of a patient's use of prescription and non-prescription drugs, including nonmedical use of prescription drugs and illicit drug use, is often part of a comprehensive medication history. Drug use information has implications for the diagnosis and management of medical and psychiatric conditions, screening for other health risk behaviors, selection of medications, and for monitoring medication interactions, effectiveness and side effects. Since primary care practitioners have a limited amount of time to address multiple health concerns, the ideal instrument to screen for drug use would be brief, validated for a primary care population, and able to identify the full spectrum of drug use. Drug screening tools are generally very brief and are intended to identify any use ("yes/no"). Some screening tools may also provide additional risk-based assessment that estimates current risk related to use. However, screening tools are not intended as tools for diagnosing substance use disorders or as assessments to determine characteristics that may influence treatment decisions and contribute to the success of treatment including the patient's substance use behavior, readiness to change, related problems, and other areas of psychological and social functioning.[23] Screening for drug use is more difficult than screening for unhealthy alcohol use since screening tools need to target a range of drugs, including prescription drugs, not simply one substance. Further, the amount of each drug that constitutes a health risk is not well defined and differs across each substance.[24] Laboratory testing, including hair or urine samples, can also be used to identify current use of some drugs, but is generally not considered useful for population-based screening given the limitations of typically only detecting recent use, requiring testing for a wide variety of drugs, the costs of the tests, and providing no information about the severity of use.[24] Additionally, specific concerns related to routine laboratory drug testing among pregnant and postpartum women exist given reporting mandates and legal requirements that vary from state to state.[25]

Interventions to Reduce Drug Use

Treatment to reduce drug use may include psychosocial interventions and/or medications. Screening for substance use, brief intervention, and referral to treatment (the SBIRT model) has been promoted to reduce the health burden related to substance use.[26] Brief interventions are typically administered by primary care clinicians and are used as an early intervention approach to reduce current drug use and risks related to drug use. These interventions target individuals with any use, heavy use, or use that has already resulted in consequences but not yet as a diagnosable disorder (often referred to as problem use, misuse, or hazardous use),.[27] Brief interventions are generally conducted in person in a primary care setting, and range from 5 minutes of brief advice to 15 to 30 minutes of brief counseling, typically over the course of one to four sessions.[26] The two most common counseling interventions used in SBIRT programs are brief versions of motivational interviewing (MI) and cognitive behavioral therapy (CBT), which may be used in adults, pregnant women, and adolescent populations.[26, 28] These types of treatments are often collectively called psychosocial treatments. MI is a person-centered counseling style designed to strengthen personal motivation for and commitment to a specific goal by eliciting and exploring the person's own reasons for change.[29] CBT interventions help individuals identify and correct unhealthy behaviors by applying a range of skills (e.g., coping strategies, exploration of positive and negative consequences of continued drug use) that can be used to stop unhealthy substance use.[30] Other counseling strategies include counseling on mindfulness-based approaches (including meditation) and general counseling such as fact-based education regarding drug use and health risks along with suggestions for minimizing harm (with or without components of MI or CBT). All of these counseling approaches can be delivered in an individual or group format and can include family and friends for social support. For adults with drug use disorders, referral to more extensive treatment that includes more intensive psychosocial interventions and medical treatment may be indicated. Three U.S. Food and Drug Administration (FDA)-approved medications are available for treating opioid use disorders: methadone, buprenorphine and naltrexone.[31, 32] Additionally, naloxone is approved to treat a known or suspected opioid overdose.

Current Clinical Practice in the United States

Available data on current clinical practice regarding screening for drug use is more than a decade old. National survey data from 2000 indicate that less than one-third of primary care physicians screen for substance use, and less than 20 percent describe themselves as "very prepared" to identify alcohol abuse (19.9%) or illicit drug use (16.9%).[33] In this survey, clinicians did not screen, missed, or misdiagnosed patients' substance use for reasons including lack of training, skepticism about treatment effectiveness, time constraints, perceived patient resistance, and discomfort discussing substance use.[33] A 2001 study of 604 American College of Gynecology (ACOG) members found that 87 percent of respondents reported asking their pregnant patients about drug use at their first prenatal visit, while 98 percent reported screening for tobacco use.[34] Among pregnant women reporting drug use, 97 percent of their clinicians discussed adverse effects of drug use and 95 percent advised abstinence.[34] Almost half of clinicians reported referring their patients for treatment, and one-third reported administering periodic drug screens.[34]

Recommendations of Others

Recommendations and statements from other organizations about screening and treatment for drug use reflect differences by subpopulations among existing guidelines (**Table 2**). The American Academy of Family Physicians (AAFP) (2014) and the Department of Veterans Affairs (VA) (2015) agree with the 2008 USPSTF recommendation that there is insufficient evidence to assess the balance of benefits and harms of screening for drug use among adults. The American Academy of Pediatrics (AAP) recommends that pediatricians increase their capacity in substance use (including alcohol use) detection, assessment and intervention and become familiar with adolescent SBIRT practices and their potential to be incorporated into universal screening and comprehensive care of adolescents in the medical home. ACOG (2014) released three Committee Opinions that advocated for providers to be educated about established techniques for screening and intervention and that all women should be routinely asked about their use of drugs, including the nonmedical use of prescription drugs, both prior to and early in pregnancy.

Previous USPSTF Recommendation

In 2008, the USPSTF concluded that the current evidence was insufficient to assess the balance of benefits and harms of screening adolescents, adults, and pregnant women for illicit drug use (I statement).[1]

Chapter 2. Methods

Scope and Purpose

This review is an update of the 2008 review[2] that supported the USPSTF recommendation for screening for drug misuse among adolescents and adults, including pregnant women.[1] The USPSTF will use this report to update its 2008 recommendation. Our update includes all studies from the previous review that met our updated inclusion criteria, as well as studies published since the previous review.

Key Questions and Analytic Framework

With input from the USPSTF, we developed an Analytic Framework (**Figure 1**) and five Key Questions (KQs) to guide the search and selection of studies, data abstraction, and data synthesis.

1. a. Does primary care screening for drug use* in adolescents and adults, including pregnant women, reduce drug use or improve other risky behaviors?
   b. Does primary care screening for drug use* in adolescents and adults, including pregnant women, reduce morbidity or mortality or improve other health, social, or legal outcomes?
2. What is the accuracy of drug use screening instruments?
3. What are the harms of primary care screening for drug use in adolescents and adults, including pregnant women?
4. a. Do counseling interventions to reduce drug use, with or without referral, reduce drug use or improve other risky behaviors in screen-detected persons?**
   b. Do counseling interventions to reduce drug use, with or without referral, reduce morbidity or mortality or improve other health, social, or legal outcomes in screen-detected persons?**
5. What are the harms of interventions to reduce drug use in screen-detected persons?**

*Includes illicit drug use and nonmedical pharmaceutical drug use.
**A separate report refers to these "counseling interventions" as "interventions" under Key Questions 4 and 5 and as "psychosocial interventions" in the body of the report.[35]

Data Sources and Searches

We conducted dual, independent reviews to re-evaluate 48 studies included in three related USPSTF reviews, using the inclusion/exclusion criteria as a guide.[2, 3, 5] We then searched the following databases for relevant English-language literature published between January 1, 2006 (for KQs 1, 3, 4, and 5), January 1, 1998 (KQ2), and June 7, 2018: MEDLINE, PubMed (for publisher-supplied records only), PsycINFO, and the Cochrane Central Register of Controlled Trials. A research librarian developed and executed the search, which was peer-reviewed by a second research librarian (**Appendix C Literature Search Strategies**). We also examined the reference lists of other previously published reviews and primary studies. We supplemented our searches with suggestions from experts and articles identified through news and table-of-contents alerts. We also searched ClinicalTrials.gov (https://ClinicalTrials.gov/) and the WHO International Clinical Trials Registry Platform (www.who.int/ictrp) for ongoing trials. We

imported the literature from these sources directly into EndNote® X7 (Thomson Reuters, New York, NY).

Study Selection

We developed criteria for including or excluding studies based on the original review[2] and expert consultation (**Appendix C Table 1**). For all KQs, we included studies among adolescents and adults aged 12 years and older, including pregnant women. We included studies that enrolled patients attending primary care clinical settings, emergency departments, or behavioral health assessment clinics as well as persons recruited from schools or the general community (a few of which specifically recruited persons based on their current drug use). Studies targeting illicit psychoactive drug use or nonmedical pharmaceutical drug use were included; those targeting nonpsychoactive drugs (e.g., laxatives, anabolic steroids) were excluded. For KQs 1 and 3, we included studies that compared individuals who received screening with those who received no screening or who received usual care, including randomized trials or nonrandomized controlled trials. For KQ 2, we included studies of screening accuracy reporting sensitivity and specificity (or data to calculate) compared with a structured or semi-structured clinical interviews or biological samples to detect any drug use, unhealthy drug use, or drug use disorders and excluded case-control studies. We included studies of brief standardized screening instruments or a set of questions that screened directly for drug use or drug use risk or those that indirectly screened for drug use with questions regarding alcohol use or other risky behaviors. We did not include studies that examined the accuracy of laboratory testing as a screening tool. Included screening instruments could be conducted in person or via telephone, mail, or electronically. For all screening questions (KQs 1-3), screening had to be population based and take place in a setting that was applicable to primary care; screening taking place in settings such as behavioral or mental health clinics or substance abuse treatment facilities were excluded. Development studies that recruited participants for the sole purpose of creating a screening tool were excluded. If a study recruited a separate validation sample, only the validation sample was used.

For questions related to intervention effectiveness and harms (KQ 4 and KQ 5), only studies in which at least 50 percent of the enrolled sample was recruited via population-based screening (i.e., individual outreach to members of a defined population [or random or consecutive sample] who have been identified as potentially eligible) were eligible. Studies who screened all potential participants by asking 1-2 questions regarding current drug use to determine eligibility were also included. Interventions could include any counseling approach designed to reduce drug use, with or without referral, including brief interventions delivered in-person or through virtual delivery. Studies of medication-assisted therapy (i.e., the use of methadone, buprenorphine, or naltrexone plus counseling) to treat opioid use disorders were excluded given that these treatments are limited to adults with a diagnosed opioid use disorder (typically severe and non-screen detected). Additionally, trials of interventions aimed at preventing drug use initiation or those using contingency management or vocational rehabilitation were excluded. We also excluded comparative effectiveness trials that compared two active interventions with no true control group.

This review addressed drug use outcomes (either as self-reported or through biologic verification) and other related behavioral outcomes, and health, social, and legal outcomes such

as morbidity, mortality, obstetrical, perinatal, and neonatal outcomes, quality of life, and drug-related problems, such as legal problems and social and family relations. We only included these outcomes if reported at least 3 months after baseline measurement (except for studies among pregnant women for which any followup was accepted). Harms included any serious harm at any time point after the screening or intervention began, including reports of stigma, labeling or discrimination, privacy issues, or demoralization due to failed quit attempts. For all KQs, studies limited to persons seeking or referred for treatment for illicit drug use or nonmedical pharmaceutical use, persons with psychotic disorders, persons receiving chronic opioid therapy, and other groups not generalizable to primary care (e.g., persons court-mandated to receive substance use treatment, persons who are incarcerated) were not included. We required that studies take place in developed countries as defined as "very high" on the 2014 Human Development Index of the United Nations[36] to ensure that the evidence was applicable to a U.S. setting.

Using the inclusion and exclusion criteria as a guide, two reviewers independently screened all records based on their titles and abstracts. Subsequently, at least two reviewers assessed the full text of potentially relevant studies, including all the previously included studies, using a standard form that outlined the eligibility criteria. Disagreements were resolved through discussion and consensus. Title and abstract and full-text review was conducted in DistillerSR (Evidence Partners, Ottawa, Canada). We kept detailed records of all included and excluded studies, including the reason for their exclusion.

Quality Assessment and Data Abstraction

Two reviewers independently used USPSTF criteria to assess the methodological quality of all eligible studies in DistillerSR. Disagreements were resolved by consensus and, if needed, consultation with a third independent reviewer. We assigned each study a quality rating of "good," "fair," or "poor" according to the USPSTF's study design-specific criteria (**Appendix C Table 2**).[37] Good-quality studies were those that met nearly all specified quality criteria. For studies of accuracy, we rated studies as good quality if they recruited patients consecutively or randomly, administered the index tool blinded to, or at least prior to, the reference standard, used a reference standard that could accurately classify the target condition, interpreted the reference standard independently from the screening tool, and administered the screening tool and reference standard on the same day to all participants. For studies of psychosocial interventions, we rated trials as good quality if comparable groups were assembled initially and maintained throughout the study, reliable and valid measurement instruments were used and applied equally to the groups, procedures for maintaining fidelity to the intervention were in place, followup was adequate (i.e., ≥85%), data were complete, and there was no evidence of selective reporting. Fair-quality studies did not meet these criteria but did not have serious threats to their internal validity related to the design, execution, or reporting of the study. Studies rated as poor quality had several important limitations and were excluded from this review.

We abstracted descriptive and outcome data from each included study into detailed abstraction forms using DistillerSR. One reviewer completed primary data abstraction, and a secondary reviewer checked all data for accuracy and completeness. Data collection for all KQs included general characteristics of the study (e.g., author, year, study design) and characteristics of the

sample (e.g., age and clinical characteristics of the population and setting, country). For studies of accuracy, data collection also included characteristics of the screening tool, reference standard, and target conditions as well as accuracy results. We abstracted the optimal cutoff for each screening tool, either as defined by the author or selected by the reviewer as the best balance of sensitivity and specificity reported. For intervention studies, data collection also included description of the intervention (e.g., type, provider, frequency, duration), outcome measurement details (e.g., followup, instruments), and results. We contacted authors when data reporting was incomplete, or data points required clarification. In cases where data was only presented in graphical format, we used WebPlotDigitizer© Version 3.10 to extract data and provide estimates of the within-group means and variance at followup.

Data Synthesis and Analysis

We synthesized data separately for each KQ and subpopulation (i.e., adolescents, young adults and adults, and pregnant and postpartum women). The data for KQ 2 did not allow for quantitative pooling due to the limited number of contributing studies and the variability in screening instruments and target conditions, so we synthesized the data qualitatively through tables and narrative synthesis and created forest plots (without pooling) to illustrate each trial's results. We grouped the data by the type of screening instrument, the specific target condition, and substance or substances the screening instrument addressed (e.g., drugs *and* alcohol, drugs only, or specific drugs such as cannabis, prescription drugs, or cocaine). Types of screening instruments were grouped as 1) frequency-based screening instruments (addressing any use and/or frequency of use), 2) risk assessment instruments (addressing the potential consequences of drug use, typically those that are indicators of a use disorder and often in combination with drug use frequency), and 3) indirect screening instruments (did not screen for drug use directly but assessed other correlates of drug use, such as alcohol use, tobacco use, partner substance use, and other social factors).

If a study reported results for more than one substance that would fit into one group, we selected the more inclusive option (e.g., if a study reported results for "all drugs" and "illicit drugs," we report the result for "all drugs" only). Given the variability in target conditions presented across the trials, we collapsed the conditions into four groups: any use, unhealthy use (variably defined in the studies), use disorder (DSM-IV abuse or dependence, DSM-5 use disorder), or dependence (DSM-IV dependence or DSM-5 moderate-severe use disorder). (**Appendix A** describes relation between DSM-IV and DMS-5 criteria.) The target condition of "unhealthy use" included conditions such as the full spectrum of unhealthy use (e.g., problem use or a use disorder), meeting any DSM criterion for a use disorder, heavy use (e.g., using a substance twice or more per day) or negative consequences or problems related to drug use.

For studies on the accuracy of screening instruments (KQ 2), we calculated confidence intervals (CIs)[38, 39] in Stata 13.1 (StataCorp LLC, College Station, TX) using data from 2x2 tables that included true positives, false positives, false negatives, and true negatives. If these data were not reported directly, we created 2x2 tables based on the total sample size, number of persons with the diagnosis according to the reference standard, sensitivity, and specificity. We report a range of sensitivity and specificity across eligible studies to provide an overall description of findings.

For studies measuring the effectiveness of counseling interventions (KQ 4), we computed a random-effects models on drug use days, the most commonly reported outcome across studies. We standardized drug use days to be the number of days of drug use in the past 7 days dividing means and standard deviations by 4.3 for recall in the last 30 days and 12.9 for recall in the last 90 days. The tables of results present the original data for the precise recall period for each study. We computed two separate models at 3 and 6-12 months of followup to assess short- and long-term effects and incorporated cannabis use days into the models when drug use days was not a reported outcome. We used the Profile Likelihood (PL) model for pooling.

Grading the Strength of the Body of Evidence

We graded the strength of the overall body of evidence for each KQ. We adapted the Evidence-based Practice Center approach,[40] which is based on a system developed by the Grading of Recommendations Assessment, Development and Evaluation Working Group.[41] Our method explicitly addresses four of the five Evidence-based Practice Center-required domains: consistency (similarity of effect direction and size), precision (degree of certainty around an estimate), reporting bias (potential for bias related to publication, selective outcome reporting, or selective analysis reporting), and study quality (i.e., study limitations). We did not address the fifth required domain—directness—as it is implied in the structure of the KQs (i.e., pertains to whether the evidence links the interventions directly to a health outcome).

Consistency was rated as reasonably consistent, inconsistent, or not applicable (e.g., single study). Precision was rated as reasonably precise, imprecise, or not applicable (e.g., no evidence). Reporting bias was rated as suspected, none suspected, or not applicable (e.g., when there is insufficient evidence for an outcome). Study quality reflects the quality ratings of the individual studies and indicates the degree to which the included studies for a given outcome have a high likelihood of adequate protection against bias. The body-of-evidence limitations field highlights important restrictions in answering the overall KQ (e.g., lack of replication of interventions, nonreporting of outcomes important to patients).

We graded the overall strength of evidence as high, moderate, or low. “High” indicates high confidence that the evidence reflects the true effect and that further research is very unlikely to change our confidence in the estimate of effects. “Moderate” indicates moderate confidence that the evidence reflects the true effect and that further research may change our confidence in the estimate of effect and may change the estimate. “Low” indicates low confidence that the evidence reflects the true effect and that further research is likely to change our confidence in the estimate of effect and is likely to change the estimate. A grade of “insufficient” indicates that evidence is either unavailable or does not permit estimate of an effect. We developed our overall strength of evidence grade based on consensus discussion involving at least two reviewers.

Expert Review and Public Comment

A draft of the Analytic Framework, KQs, and inclusion and exclusion criteria were posted on the USPSTF Web site for public comment from August 4, 2016, through August 31, 2016. In response, the USPSTF revised the exclusion of studies limited to persons with concomitant mental health disorders to indicate that only studies limited to persons with psychotic disorders

(e.g., schizophrenia) were excluded. Studies limited to persons with other mental health conditions, such as depression, anxiety, attention deficit hyperactivity disorder, and post-traumatic stress disorder are included. Other minor modifications and clarifications were made as appropriate, including updating some of the conditions (e.g., bath salts) and settings (e.g., school health clinics) that would be included in the review. Public comments on the Draft Research Plan for Screening and Behavioral Counseling Interventions for Unhealthy Alcohol Use in Adolescents and Adults, Including Pregnant Women were also reviewed given the similar scope of the two reviews. Based on those comments, the USPSTF modified the criteria to clarify that interventions that target persons with dependent drug use are out of scope for these reviews. Therefore, pharmacotherapy interventions (including medication-assisted therapy) were excluded from the review. A final research plan was posted on the USPSTF Web site on October 20, 2016. Two subsequent scope changes were made during the review to include a broader evidence base: 1) including results reported at 3-month or longer followup (as opposed to 6-months or longer) and 2) including studies that screened for and/or provided drug use interventions in emergency departments.

USPSTF Involvement

We worked with three USPSTF members at key points throughout this review, particularly when determining the scope and methods and developing the Analytic Framework and KQs. The USPSTF members approved the final Analytic Framework, KQs, and inclusion and exclusion criteria after revisions reflecting the public comment period. AHRQ funded this review under a contract to support the work of the USPSTF. An AHRQ Medical Officer provided project oversight, reviewed the draft report, and assisted in the external review of the report.

Chapter 3. Results

We reviewed a total of 17,921 abstracts and 273 articles for all KQs (**Appendix D**). The lists of included studies (55 trials in 74 publications) and excluded studies (with reasons for exclusion) are available in **Appendix E** and **Appendix F**, respectively. A list of abbreviations relating to the screening tools and reference standards is provided in **Appendix G.**

Key Questions 1–3: Overall Summary of Results for Screening for Drug Use

No trials examined the benefits (KQ 1) or harms (KQ 3) of screening for drug use. We identified 28 studies[15, 42-68] (reported in 37 publications[15, 42-77]) that addressed the accuracy of drug use screening instruments (KQ 2). Only one study among adolescents[46] and one study among adults[49] were included in the previous report[3] to support the USPSTF recommendation. There was considerable heterogeneity in the populations (**Table 3**), screening tools (**Table 4**), substances addressed, reference standards, and target conditions included in each study. In general, each specific screening instrument has not been studied more than once or twice. Eleven studies recruited adolescents,[42, 46, 52, 54, 56, 57, 59, 60, 64, 66, 67] 12 studies recruited adults,[43-45, 48-51, 55, 61, 62, 65, 68] and five studies recruited pregnant or postpartum women[15, 47, 53, 58, 63] (**Table 3**). None of the studies focused specifically on young adults (i.e., 18- 25-year-olds) or older adults (i.e., ≥65 years); however, one study recruited participants from a Veterans Affairs hospital and the mean age was 62.6 years[44] and another recruited adults 50 years or older and reported subgroup results for older adults.[65] The majority of studies were conducted in the United States[15, 42-52, 54, 56, 58, 61-66] (21 of 28) and recruited patients from primary care (17 of 28).[42-48, 50-54, 56, 62-64, 67] The number of screened participants ranged from 100 to 42,923; 20 studies screened fewer than 1000 participants.

Most of the studies used a structured diagnostic interview to determine the substance use condition, although various versions were used (e.g., ADI, CIDI, DISC-IV, MINI) and sometimes the interview was used in combination with other screening instruments (e.g., ASSIST), the TLFB, or biologic confirmation. For pregnant or postpartum women, three of the five studies[15, 47, 58] relied solely on hair or urine analysis to determine substance use during pregnancy. The majority of the studies were fair quality (17 of 28); among these, risk of bias resulted from a variety of reasons, including: not reporting enough information regarding the order and timing of the reference standard and screening tool; not clearly reporting whether the researchers had knowledge of the index tool results during the administration and interpretation of the reference standard; not presenting a range of cutoff values and selecting only the optimal or an *a priori* threshold; and/or unclear reporting of whether participant recruitment was random or consecutive.

Thirty screening tools were evaluated in the included studies. The screening tools varied in the number of questions (range 1–31 questions) and subsequent administration time, administration method (interviewer-administered in person or via phone or self-administered electronically or via paper-pencil), and the substances addressed. Most of the screening tools addressed the use of *any* drug (with or without addressing alcohol and tobacco use). Among these, the majority

included an assessment of nonmedical use of prescription drugs either through a specific question or prior to administering the screening participants were told that drug use included nonmedical use of prescription medications. Four screening tools asked only about cannabis use; three only asked about alcohol use; and one only asked about cigarette use and other social factors. A list of all the included screening tools and their full names is provided in **Table 4**.

We organized the results within population subgroups by the type of screening instrument: 1) frequency-based screening instruments (addressing any use and/or frequency of use), 2) risk assessment instruments (addressing the potential consequences of drug use, typically those that are indicators of a use disorder and often in combination with drug use frequency), and 3) indirect screening instruments (did not screen for drug use directly but assessed other correlates of drug use, such as alcohol use, tobacco use, partner substance use, and other social factors).

For adolescents, most of the studies focused on detecting cannabis use conditions. All studies validated responses solely against structured clinical interviews. Sensitivity of the frequency-based (**Figure 2**) and risk assessment tools (**Figure 3 and Figure 4**) for detecting any cannabis use or unhealthy cannabis use ranged from 0.68 to 0.98 (95% CI range, 0.64 to 0.99) and specificity ranged from 0.82 to 1.00 (95% CI range, 0.80 to 1.00). Sensitivity and specificity for identifying a cannabis use disorder for frequency-based and risk assessment tools ranged from 0.80 to 0.98 (95% CI range, 0.41 to 1.00) and 0.81 to 0.95 (95% CI range, 0.79 to 0.98), respectively; the low prevalence of cannabis use disorder and small sample size in one study resulted in less overall precision in the estimates of sensitivity when compared to other cannabis use conditions.

Among adults, frequency-based tools (**Figure 5 and Figure 6**) and risk assessment screening tools (**Figure 7 and Figure 8**) showed sensitivity for detecting unhealthy use of any drug (not including alcohol) ranging from 0.71 to 0.94 (95% CI range, 0.62 to 0.97) and specificity ranging from 0.87 to 0.97 (95% CI range, 0.83 to 0.98). For identifying drug use disorders among adults, sensitivity for frequency-based and risk assessment tools ranged from 0.85 to 1.00 (95% CI range, 0.67 to 1.00) and specificity ranged from 0.67 to 0.93 (95% CI, 0.58 to 0.95) when using the same tool cutoffs. In studies that examined unhealthy use of specific drugs, the ranges of sensitivity were lower and less precise for detecting unhealthy use or use disorders for prescription opioids and prescription sedatives (sensitivity ranged from 0.38 to 0.89 [95% CI range, 0.29 to 0.94] as compared with other classes of drugs, although confidence intervals generally overlapped. Specificity was comparable and ranged from 0.79 to 0.99 [95% CI range, 0.71 to 0.99])

Sensitivity and specificity for detecting any prenatal drug use (based on validation against hair or urine analysis) was generally lower than the estimates found for any drug use in non-pregnant adults (only rarely based on validation against biologic sample analyses) and ranged from 0.37 to 0.76 (95% CI range, 0.24 to 0.86) and 0.68 to 0.83 (95% CI range, 0.55 to 0.91). The 4P's Plus, which indirectly screens for drug use, had a sensitivity of 0.87 (95% CI, 0.71 to 0.95) and specificity of 0.76 (95% CI, 0.70 to 0.82) for detecting any prenatal *alcohol or drug* use when compared with a diagnostic interview.

Across all studies, there was no clear pattern of better accuracy when looking at interviewer-administration versus self-administration of the screening tools. In studies that included biologic

confirmation of drug use in addition to a structured clinical interview, sensitivity was lower when compared with the structured clinical interview alone. Indirect screeners (i.e., those that did not ask directly about drug use) generally had similar specificity, but lower sensitivity in detecting unhealthy drug use or use disorders among adolescents (range, 0.20 to 0.54 [95% CI range, 0.17 to 0.60]) and adults (0.59 to 0.72 [95% CI range, 0.48 to 0.82]) as compared with the frequency-based and risk assessment tools. Among pregnant women, indirect screeners had comparable accuracy with the direct screeners.

Key Question 1a. Does primary care screening for drug use in adolescents and adults, including pregnant women, reduce drug use or improve other risky behaviors?

Key Question 1b. Does primary care screening for drug use in adolescents and adults, including pregnant women, reduce morbidity or mortality or improve other health, social, or legal outcomes?

We identified no trials that addressed the effects of screening for drug use on drug use outcomes, risky behaviors (such as alcohol or tobacco use or risky sexual behaviors) or health, social, or legal outcomes.

Key Question 2. What is the accuracy of drug use screening instruments?

Adolescents

Study and Population Characteristics

Eleven studies (n=13,330), four rated as good quality and seven as fair quality, evaluated the accuracy of screening instruments among adolescents (**Table 3**).[42, 46, 52, 54, 56, 57, 59, 60, 64] Seven of the studies recruited participants from primary care[42, 46, 52, 54, 56, 60, 64] or the emergency department[66] in the United States; the remaining four studies recruited youth from schools or the broader community within European countries.[57, 59, 60, 67] Sample sizes ranged from 136 to 5787. Most participants in the U.S.-based studies were nonwhite. Race and ethnicity were not reported for the studies conducted in Europe. In all but one of the nine studies, in which 71.5 percent of participants were male,[59] sex was evenly distributed. Three of the four studies conducted in Europe restricted inclusion to adolescents who had used cannabis in the previous year[57] or month[59] or were current cannabis users.[55]

Two studies reported the prevalence of unhealthy use of alcohol or any drugs at 18.5 percent[56] and 26.8 percent,[46] whereas two other studies reported unhealthy use of cannabis at 15.3 percent[54] and 19.7 percent.[64] Any use of drugs was only reported for cannabis in two studies; in these studies, prevalence of previous-year cannabis use among adolescents was 18.4 percent[52] and 36.6 percent.[64] All eleven studies reported the prevalence of a use disorder (alcohol, any drug, or cannabis) or dependence. The prevalence of cannabis use disorders (the most commonly reported condition) ranged from 5.9 percent to 35.7 percent among adolescents.

We included tool accuracy measures for four target conditions across the nine studies, including *unhealthy* drug use (variably defined as any drug use, heavy use, problem use, and/or drug use disorders) 4 studies[46, 52, 54, 56, 64]); *any* drug use (cannabis specifically, 2 studies[52, 64]); *drug use disorders* (8 studies[42, 46, 52, 54, 56, 64]), and dependence alone (6 studies[46, 54, 56, 57, 59, 60]). Two studies[57, 59] reported only the accuracy of screening instruments to detect dependence. All eleven studies used a structured diagnostic interview to diagnose a drug use disorder or dependence based on DSM-IV or DSM-5 standard criteria. None of the studies among adolescents included biological confirmation of self-reported use.

Fourteen different screening tools were evaluated. Five instruments—the CRAFFT, CAST, AUDIT, POSIT, and the single-item cannabis frequency question—were evaluated in more than one study among adolescents (**Table 4**). While the target conditions for this review were required to focus on drug use, many of the screening tools queried participants about their use of all substances, including alcohol and tobacco. Six tools asked about general substance use including drugs and alcohol with or without tobacco (ASSIST, BSTAD, CRAFFT, PESQ-PS, POSIT, POSIT-revised); five instruments asked about cannabis use only (ASSIST-LITE for cannabis, CAST, CPQ-A-S, single-item cannabis-frequency question, SDS); and three instruments that assessed alcohol only were used as indirect instruments for detecting drug use (AUDIT, AUDIT-C, NIAAA Youth Screen). Two screeners addressed only the frequency of use; most assessed risks associated with use in addition to frequency. The number of questions included in each screening tool ranged from 1 to 18, with 10 questions or less for all but four screening tools (CPQ-A-S, PESQ-PS, POSIT, and POSIT revised). Six studies had an interviewer administer the screening tool (s) in person,[46, 52, 54, 56, 66, 67] three studies had participants self-administer the screening tool (s) electronically,[52, 59, 64] three studies had the participants self-administer the tool on paper,[57, 60, 64] and one study had an interviewer administer the screening tool over the phone.[55] One study split its sample and had half the participants self-administer the screening tool electronically, while the other half were administered the tool in person by an interviewer.[42]

Detailed Results: Tool Accuracy

Results related to the sensitivity and specificity and corresponding 95% confidence intervals for all screening tools and target conditions among adolescents are presented in **Table 5.**

Frequency-based screening tools. Two studies evaluated a single-item cannabis-frequency question,[52, 66] and one study[42] examined the BSTAD to detect any cannabis use or a cannabis use disorder (**Figure 2**). The single item about cannabis-use frequency in the previous 12 months was found to have a sensitivity of 0.72 and 0.79 (95% CI range, 0.52 to 0.91) and specificity of 1.00 and 0.99 (95% CI range, 0.94 to 1.00) in detecting any cannabis use for self-administered and interviewer-administered versions, respectively. To detect cannabis use disorder, sensitivity ranged from 0.86 to 0.96 (95% CI range, 0.41 to 0.98) and specificity ranged from 0.86 to 0.93 (95% CI range, 0.82 to 0.96). Similarly, the BSTAD at a cutoff of 2 or more had a sensitivity of 0.80 (95% CI, 0.69 to 0.89) and specificity of 0.93 (95% CI, 0.91 to 0.95) for detecting a cannabis use disorder.

Risk assessment screening tools. Ten studies evaluated nine different risk-assessment screening tools among adolescents (**Figure 3 and Figure 4**).[46, 52, 54, 56, 57, 59, 60, 64] All of the studies

evaluated the screening tool accuracy in detecting cannabis use or alcohol *or* drug use. The sensitivity and specificity for detecting any cannabis use of the CRAFFT (0.68 [95% CI, 0.64 to 0.72] and 0.92 [95% CI, 0.90 to 0.94] and PESQ-PS (0.72 [95% CI, 0.68 to 0.75] and 0.93 [95% CI, 0.91 to 0.94] were similar to estimates for the single-item cannabis frequency question. For detecting unhealthy cannabis use, sensitivity ranged from 0.84 to 0.98 [95% CI range, 0.79 to 0.99] and specificity ranged from 0.82 to 0.91 [95% CI range, 0.80 to 0.94] among three different instruments (ASSIST, CRAFFT, and PESQ-PS) (**Figure 3**). Sensitivity and specificity was similar for the CRAFFT in detecting unhealthy use of drugs or alcohol. More studies evaluated the ability of these tools, using the same cut-points, to detect a cannabis use disorder or dependence. Across nine different screening instruments, the ASSIST, ASSIST-Lite, and PESQ-PS had the best sensitivity in detecting a cannabis use disorder (≥0.90) whereas the CRAFFT, POSIT, and POSIT revised had the highest specificity (≥0.90).

Indirect screening tools. Two studies[64, 66] evaluated the accuracy of three different alcohol screening instruments—the AUDIT, AUDIT-C, and NIAAA Youth Screen—to identify cannabis use and unhealthy cannabis use. Sensitivity was much lower for these instruments than in the frequency-based and risk assessment screeners, ranging from 0.20 to 0.70 (95% CI range, 0.17 to 0.80); specificity was comparable, ranging from 0.82 to 0.99 (95% CI, 0.78 to 0.99).

Differences by subpopulations. Three studies examined differences in the accuracy of the CRAFFT[46, 56, 67] and one study in the accuracy of the POSIT between males and females.[67] For the detection of alcohol or drug dependence, use disorder, and unhealthy use, the CRAFFT and POSIT both generally performed better for males than females with an increased or equivalent sensitivity. However, the confidence intervals for both groups overlapped, indicating there could be no difference between the groups.

One study[67, 77] examined differences by age (12-14, 15-16, and 17-18 years) in the accuracy of the CRAFFT and POSIT to detect substance use disorder. Accuracy for both the CRAFFT and POSIT were similar across adolescent age groups.

Adults

Study and Population Characteristics

We included 12 studies (n=49,961), six of them good quality and the others fair quality, that evaluated the accuracy of 15 different screening tools to detect drug use or drug use problems in non-pregnant adults (**Table 3**).[43, 45, 48-51, 55, 61, 62, 65, 68] There were considerable differences among the studies in terms of the populations, screening tools, and target conditions. All but two of the studies took place in the United States; the remaining studies[55, 68] recruited previous-year cannabis users in France. Among the studies in the United States, most recruited participants directly within primary care; however, one study recruited participants from an emergency department,[65] one study used data from a representative sample of U.S. adults (n=42,923),[61] and another recruited adults (n=139) who were seeking evaluation for attention-deficit/hyperactivity disorder (ADHD) at a specialty clinic.[49] One study[44] recruited participants from primary care clinics within a U.S. Department of Veterans Affairs health care system; the majority of participants in this study were male (95.3%), with a mean age of 63 years. Another study[62] focused specifically on caregivers of children <6 years and included mostly females (94%). For

the remaining studies, the proportion of female participants ranged from 30.9 to 67.9 percent. Excluding the large U.S.-based national sample (n=42,923), sample sizes ranged from 139 to 2057. Within the eight studies that reported the race and ethnicity of participants, the percent of nonwhite participants ranged from 4.3 percent to 82.9 percent; the majority of nonwhite participants was black. Most participants in the studies had a high school education or higher.

Three studies[43-45] reported the prevalence of unhealthy drug use ranging from 14.2 percent to 37.9 percent; three studies[43, 50, 65] reported the prevalence of unhealthy drug use for specific drugs ranging from 2 percent (for unhealthy use of prescription sedatives) to 38.4 percent (for unhealthy prescription opioid use). Any previous-year drug use, as reported in three studies,[43, 45, 61] ranged from 5.7 percent (in the large, nationally representative sample[61]) to 40.4 percent (in primarily black primary care patients[45]). In six studies,[43-45, 49, 61, 62] any drug use disorder ranged from 1.8 to 16.7 percent (dependence ranged from 0.6 percent[61] for dependence of any drug to 12.6[55] percent for cannabis specifically in three studies). Two studies [55, 68] including adolescents and adults aged 15-64 years who had used cannabis in the previous year had a much higher prevalence of cannabis use disorder at 28.9 percent and 34.1 percent. One study,[65] including adults 50 years or older recruited from an emergency department and using prescription drugs, reported a prevalence of prescription drug use disorder of 58.9 percent (16.1 percent with moderate-severe use disorder).

We included tool accuracy measures for four target conditions across the 12 studies—*any* drug use (4 studies),[45, 51, 61, 70] *unhealthy* drug use (variably defined as any drug use, heavy use, problem use, and/or drug use disorders) 5 studies),[43-45, 50, 65, 70] drug use disorders (all 12 studies), and dependence alone (6 studies).[45, 51, 55, 61, 65, 68] To determine the target conditions of drug use disorder or dependence, all 12 studies used a structured diagnostic interview such as the CIDI or MINI-Plus. Reference standards for the target conditions of unhealthy use or any use often included oral fluid tests or the Timeline Followback method (to identify current use) as well as the structured interview. Three studies also used other questionnaires, usually combined with the structured interview, as reference standards—the Short Inventory of Problems-Alcohol and Drugs, the ASSIST, and the Inventory of Drug Use Consequences.

Consistent with the included evidence for adolescents, screening tools addressed only the frequency of drug use (single-item drug frequency, SUBS, TAPS-1), frequency of drug use along with further risk assessment (ASSIST, ASSIST-Drug, CAST, DAST-2, DAST-10, DAST-28, PDUQp, PSQ, SoDU, TAPS, TICS), or indirect questions (single-item HED frequency) (**Table 4**). Most of the drug-specific screeners addressed *any* drug use with or without questions related to alcohol or tobacco use, but four screeners only asked about cannabis use (single-item cannabis frequency, CAST, ASSIST-Lite Cannabis, CPQ-A-S), one screener asked only about prescription drug use (PDUQp), and five screeners queried participants on their use of specific types of drugs (ASSIST-2, BSTAD, ASSIST, SUBS, TAPS). Five studies had an interviewer administer the screening tool (s) in person,[44, 45, 48, 49, 61] four studies had participants self-administer the screening tool (s) electronically,[43, 51, 62, 65] and two studies had an interviewer administer the screening tool over the phone.[55, 68] One study[50] evaluated both interviewer- and self-administered versions of the same screening tool.

Detailed Results: Tool Accuracy

Results related to the sensitivity and specificity and corresponding 95% confidence intervals for all screening tools and target conditions among adults are presented in **Table 6.**

Frequency-based screening tools. Three studies[43, 45, 50, 70, 74] examined the accuracy of a single-item drug-frequency question, one study[43] examined the SUBS, and one study examined the TAPS-1.[50, 74] (**Figure 5 and Figure 6**). Two studies[43, 45, 70] reported tool accuracy for any drug use and unhealthy drug use with sensitivity ranging from 0.71 to 0.94 (95% CI range, 0.61 to 0.97) and specificity ranging from 0.86 to 0.96 (95% CI range, 0.82 to 0.98). These two studies examined the accuracy of the single-item frequency question when using a structured clinical interview only and the interview plus biologic confirmation as the reference standard to identify any drug use and unhealthy use of any drugs. Both studies found that sensitivity was lower and specificity higher when compared with the reference standard including biologic confirmation of use versus the diagnostic interview alone, although confidence intervals overlapped. For any drug use disorder and any drug dependence, sensitivity ranged from 0.85 to 1.0 (95% CI range, 0.75 to 1.0) and specificity ranged from 0.74 to 0.89 (95% CI range, 0.68 to 0.92).

Two studies[43, 50, 74] also reported the accuracy of the SUBS and the TAPS-1 in identifying unhealthy use and use disorder of prescription drugs and illicit drugs. To identify unhealthy use of prescription drugs, sensitivity ranged from 0.56 to 0.85 (95% CI range, 0.41 to 0.99) and specificity ranged from 0.91 to 0.92 (95% CI range, 0.89 to 0.94). Tools that aimed to identify prescription drug use disorder had similar performance, with sensitivity ranging from 0.59 to 0.89 (95 % CI range, 0.39 to 0.94) and specificity ranging from 0.89 to 0.91 (95% CI range, 0.86 to 0.92). The sensitivity for the SUBS and TAPS-1 in identifying unhealthy use and use disorder of illicit drugs was higher than prescription drugs, but the specificity was similar.

Risk assessment screening tools. Nine studies[44, 45, 49-51, 55, 62, 65, 68, 75] evaluated 11 screening tools that included risk assessment: ASSIST, ASSIST-Drug, CAST, DAST-2, DAST-10, DAST-28, PDUQp, PSQ, SoDU, TAPS, and TICS (**Figure 7**). For any drug use and unhealthy use of any drugs, sensitivity ranged from 0.80 to 0.92 (95% CI range, 0.70 to 0.96) and specificity ranged from 0.92 to 0.97 (95% CI range, 0.87 to 0.98). For any drug use disorder and dependence, sensitivity ranged from 0.92 to 1.0 (95% CI range, 0.67 to 1.0) and specificity ranged from 0.67 to 0.93 (95% CI range, 0.58 to 0.96). One notable exception was the PSQ that includes two questions to assess drug and alcohol use for both the respondent *and* their partner, which had a sensitivity of 0.29 (95% CI, 0.08 to 0.64) (specificity of 0.95 [95% CI, 0.91 to 0.97]) to identify any drug use disorder.[62]

The accuracy for detecting use, unhealthy use, or use disorders of specific drugs (cannabis, cocaine, cocaine or methamphetamine, heroin, prescription opioid, prescription sedative) was reported for four screening tools—the ASSIST, CAST, PDUQp, and TAPS (**Figure 8**). Sensitivity to detect any use or unhealthy use ranged from 0.44 to 0.95 (95% CI range, 0.35 to 0.99) and specificity ranged from 0.79 to 1.0 (95% CI range, 0.71 to 1.0). Sensitivity and specificity was generally higher for detecting unhealthy use of cannabis than in detecting unhealthy use of cocaine, heroin, or prescription medications, although 95% confidence intervals overlapped for all estimates. Sensitivity was the lowest for the detection of unhealthy prescription opioids (0.44 to 0.71) and prescription sedatives (0.63 to 0.66); specificity was

comparable with other substances (0.79 to 0.99). For use disorder and dependence, sensitivity ranged from 0.38 to 0.90 (95% CI range, 0.29 to 0.94) and specificity ranged from 0.75 to 1.00 (95% CI range, 0.70 to 1.00). Again, the lower sensitivity values were from the PDUQp and TAPS screening tools for prescription opioid and prescription sedative-use disorders.

Indirect screening tools. Two studies[45, 61, 73] evaluated a single-item question assessing heavy episodic drinking to identify unhealthy drug use or use disorders. For detecting any drug use and unhealthy drug use, sensitivity ranged from 0.59 to 0.63 (95% CI range, 0.48 to 0.72) and specificity ranged from 0.72 to 0.80 (95% CI range, 0.65 to 0.87. For detecting any drug use disorder and dependence, sensitivity ranged from 0.68 to 0.72 (95% CI range, 0.50 to 0.82) and specificity ranged from 0.65 to 0.77 (95% CI range, 0.58 to 0.78). Sensitivity was highest for cannabis use (sensitivity ranging from 0.73 to 0.78 [95% CI range, 0.70 to 0.84] and specificity ranging from 0.77 to 0.78 [95% CI range, 0.76 to 0.79]) and cocaine use (sensitivity ranging from 0.76 to 0.78 [95% CI range, 0.62 to 0.85] and specificity ranging from 0.84 to 0.86 [95% CI range, 0.84 to 0.86]), but lowest for prescription drugs (sensitivity ranging from 0.57 to 0.60 [95% CI range, 0.50 to .70], specificity ranging from 0.76 to 0.77 [95% CI range, 0.76 to 0.78).

Differences by subpopulations. One study examined prespecified differences by sex, education, age, and ethnicity in the accuracy of self-administered versions of the SUBS and a single-item drug-frequency question to detect unhealthy drug use.[43, 70] For both the SUBS and the single-item drug-frequency question, sensitivity was lower for females versus males, Hispanic versus non-Hispanic, those with less than a high school education versus those with a high school education or higher, and those age 21 to 50 years versus those age 51 to 65 years. However, the only statistically significant difference for SUBS was for sensitivity and specificity for males versus females.[43] For the single-item drug-frequency question, sensitivity was statistically significantly lower among those with less than a high school education (0.63) versus those with a high school education or higher (0.79) ($p<0.01$); there was not a statistically significant difference in specificity between the two groups.[70]

One study[65] examined differences in the accuracy of the PDUQp to detect unhealthy use and use disorders of prescription opioids for adults aged 50-64 and those aged 65 years or older. Sensitivity was much lower, and specificity was higher for adults 65 years or older versus those aged 50-64 years, with most of the confidence intervals not overlapping. However, the authors noted that adjusting the cutoff to 5 or 7 for adults 65 years or older could improve tool performance for screening purposes.

Pregnant and Postpartum Women

Study and Population Characteristics

We identified five studies (n=2429), one of them good quality[58] and four of them fair quality,[15, 47, 53, 63] that evaluated the accuracy of drug screening instruments to detect any drug use or drug use disorders during pregnancy (**Table 3**). Three studies recruited women during pregnancy[47, 53, 63] whereas the other two[15, 58] recruited women directly following delivery. These latter two studies[15, 58] were conducted by the same author group and had partially overlapping samples. Grekin et al.[15] evaluated the accuracy of the DAST-10 in identifying last-trimester drug use among the full sample, whereas Ondersma et al.[58] included these same women as their

developmental sample for a new instrument (the WIDUS) and a separate sample of 100 women to cross-validate the accuracy of both the DAST-10 and WIDUS. We only included data from the cross-validation sample (n=100). Across the five studies, four took place in the United States and one was conducted in Hong Kong. Three of the studies targeted women with low SES, with either a Medicaid or Medicaid-managed plan for all women in the study[47] or public assistance for the majority of women.[15, 58] In the U.S.-based samples, the majority of women were black.

The prevalence of any prenatal drug use was highly variable across the four studies that reported it, ranging from 1.2 percent (in the sample of women from Hong Kong[53]) to 41 percent using drugs in the last trimester of pregnancy (among a sample of low-income, majority black women).[58] One study reported that 7 percent of pregnant women met diagnostic criteria for drug abuse, drug dependence, or both, primarily for cannabis use.[63]

The five studies evaluated the accuracy of five different instruments including the 4P's Plus,[47] a modified version of the first two questions of the ASSIST (hereafter called ASSIST-2),[58] DAST-10,[15, 53, 58] PRO,[63] and WIDUS[58] **(Table 4).** Only three of the instruments (the ASSIST-2, DAST-10, and PRO) directly screen for drug use and drug-related problems prior to pregnancy and/or during pregnancy. The 4P's plus focuses on use of cigarettes and alcohol prior to knowing pregnancy status as well as whether their parents or partner ever had problems with alcohol *or* drugs and the WIDUS was designed as an indirect screener and asks about social issues (marital status), stress, depression, and cigarette use. Three studies[15, 53, 58] relied on hair and/or urine analyses to confirm drug use (detection windows of 24–48 hours for urine analysis and 90 days for hair analysis) whereas the other two used structured clinical interviews.[47, 63]

Detailed Results: Tool Accuracy

Results related to the sensitivity and specificity and corresponding 95% confidence intervals for all screening tools and target conditions among adults are presented in **Table 7.** In general, the sensitivity and specificity for detecting prenatal drug use or use disorders was much lower than what was seen in non-pregnant adults. The tools with the highest sensitivity—the PRO (0.89) and 4P's Plus (0.87)—were the only tools that were not evaluated against a reference standard that included biologic confirmation, but rather were based on clinical interviews.

Frequency-based screening tools. One study evaluated the use of a modified two-question ASSIST to detect any prenatal drug use. Sensitivity was 0.41 (95% CI, 0.28 to 0.57) and specificity was 0.83 (95% CI, 0.72 to 0.91) when drug use was confirmed with hair and urine analyses.[58]

Risk assessment screening tools. Three studies evaluated the accuracy of the DAST-10 at a cutoff of 1 or more to detect any prenatal drug use,[15, 53, 58] one study evaluated the PRO in identifying drug abuse or dependence (in pregnant women),[63] and one[58] took results from both the ASSIST-2 and WIDUS to detect any prenatal drug use. Sensitivity for detecting any prenatal drug use ranged from 0.37 to 0.76 (95% CI range, 0.24 to 0.86) and specificity ranged from 0.68 to 0.83 (95% CI range, 0.55 to 0.91). The PRO resulted in a sensitivity of 0.89 (95% CI, 0.77 to 0.95) and specificity of 0.74 (95% CI, 0.71 to 0.77) for identifying drug abuse or dependence based on a clinical interview as the reference standard.

Indirect screening tools. A confirmation of any cigarette or alcohol use on the 4P's plus had a sensitivity and specificity of 0.87 (95% CI, 0.71 to 0.95) and 0.76 (95% CI, 0.70 to 0.82), respectively, to identify any alcohol or drug use in the month prior to knowledge of pregnancy or after as reported in a structured clinical interview.[47] The WIDUS, designed as an indirect screener, had a sensitivity of 0.68 (95% CI, 0.53 to 0.80) and specificity of 0.69 (95% CI, 0.57 to 0.80) for correctly identifying any prenatal drug use.

Key Question 3. What are the harms of primary care screening for drug use in adolescents and adults, including pregnant women?

We identified no trials that addressed the harms of screening for drug use.

Key Questions 4–5: Overall Summary of Results for Interventions to Reduce Drug Use

We included 27 trials (reported in 37 publications) that addressed the effectiveness of a counseling intervention on changes in drug use or improved health, social, or legal outcomes among a screen-detected population (**Table 8**).[78-110] All but two trials were conducted in the United States; one trial took place in Chile[102] and another took place in Germany.[111] Three trials specifically targeted adolescents,[78, 96, 107] five trials targeted young adults,[80, 93, 94, 101, 105] 14 targeted adults,[81-83, 87-89, 102-104, 108, 109, 112] and five targeted pregnant[106, 110] and postpartum[98-100] women. We rated four of the trials among adults[82, 95, 103, 104] as good quality and the remaining 23 trials as fair quality. Only one trial among adults[81] was included in the previous USPSTF review.

Fifteen trials addressed any type of drug use (and in some cases also addressed alcohol use),[82, 83, 87-89, 95, 96, 98-100, 102-104, 110, 112] nine trials focused specifically on marijuana use (with or without targeting alcohol use),[78, 80, 93, 94, 101, 105-107, 109] one targeted opioid or alcohol use,[108] one targeted cocaine and heroin use only,[81] and one focused on misuse of prescription drugs.[111] Within all of the trials, all participants were systematically screened for substance use prior to entry (using frequency-based or risk assessment instruments or 1-2 questions about current drug use) to determine their study eligibility and baseline substance use. The thresholds of drug use for inclusion varied across the trials ranging from any previous-year use to weekly use in the previous 3 months (**Table 9**). In four studies, drug use screening and intervention took place in an emergency or urgent care setting;[80, 82, 83, 109] the one trial in Chile screened adults presenting in primary care, emergency rooms, or police stations.[102] The trial that took place in Germany screened adults being admitted to internal, surgical, or gynecological wards of a hospital.[111] The remaining 22 trials screened participants presenting for a primary care office visit or those responding to direct mailing or generic advertising. The interventions were very similar across the trials, generally consisting of one brief in-person or computer-based personalized feedback session with up to two booster telephone calls (**Table 10**). Most of the interventions were based on principles of motivational interviewing and were administered by trained mental or behavioral health specialists or were self-directed. One intervention focused on a system-level intervention of collaborative care to facilitate behavioral or medication-assisted therapy for those at risk of an opioid or alcohol use disorder.[108] Only two of the interventions included interaction with the participants' primary care team,[87, 88] although several of the other interventions took place in the participants' primary care clinics.

Across all 27 trials (n analyzed=8705), there was no consistent effect of the interventions on rates of self-reported or biologically confirmed **drug use** at 3- to 12-month followup (KQ 4a). Within each study, the frequency and quantity of drug use generally decreased, and rates of abstinence increased in both intervention and control groups, with no statistically significant between-group differences detected. Among young adults and adults, a meta-analysis of 10 out of the 19 studies that reported days of drug use resulted in a nonsignificant difference in the mean change in drug use in the past 7 days between intervention and control groups at both 3 months (mean difference [MD], -0.07 [95% CI, -0.25 to 0.11]; k=9; n=3183; I^2=16.1%) (**Figure 9)** and 6 to 12 months (MD, 0.01 [95% CI, -0.25 to 0.22]; k=10; n=3632; I^2=48.6%) (**Figure 10**). Likewise, across 14 trials reporting the effects of the interventions on **health, social, or legal outcomes** (KQ 4b) (n=4590), none of the trials found a statistically significant difference between intervention and control groups on any of these measures at 3- to 12-month followup. Four of the 27 trials (n=1161)—two targeting marijuana use among college students and two targeting any drug use among postpartum women—reported no **harms** or unintended effects from participation in the trials among intervention or control group participants.

Key Question 4a. Do counseling interventions to reduce drug use, with or without referral, reduce drug use or improve other risky behaviors in screen-detected persons?

Key Question 4b. Do counseling interventions to reduce drug use, with or without referral, reduce morbidity or mortality or improve other health, social, or legal outcomes in screen-detected persons?

Key Question 5. What are the harms of interventions to reduce drug use in screen-detected persons?

Adolescents

Study, Population, and Intervention Characteristics

We included three fair-quality trials (n=741) that addressed interventions to reduce drug use among screen-detected "at-risk" adolescents, all with a mean age of 16 years (**Table 8**).[78, 96, 107] Participants in all three trials were recruited in U.S.-based primary care settings, and were mostly black (61%[107] and 84%[96]) or Hispanic (66%[78]) and female (57 to 71%). Limited data on participants' education or socioeconomic status were reported, with the exception of one trial, which reported that 5.8 percent of adolescents had dropped out of school.[107] One trial targeted both alcohol and drug use,[96] one targeted both cannabis and alcohol,[78] while the remaining one specifically targeted cannabis use.[107] In the former two trials, adolescents were eligible if they were considered at risk for a substance use disorder (CRAFFT score of 2 or 3) or alcohol use disorder, whereas the latter only enrolled adolescents who reported any previous-year cannabis use. Baseline cannabis use in all trials indicated that on average, adolescents were using cannabis 1 to 3 days per month (**Table 9**). All three trials included one personalized counseling session either in person with trained mental or behavioral health specialist or via a computerized session using principles of motivational interviewing and personalized and normative feedback (**Table**

10 and **Table 11**). Retention rates were high all trials, with more than 80 percent of participants completing 6-month followup.

Detailed Results: Drug Use and Other Risky Behaviors (KQ 4a)

All three trials reported the effects of the interventions on self-reported frequency of drug and alcohol use at 3- to 12-month followup (**Table 12**).[96, 107] In general, there was no difference between change in drug use at 3, 6 and 12 months among adolescents taking part in one individual counseling session versus those taking part in usual care or attention control conditions. One trial reported small effects of the intervention on the frequency of cannabis use over 6 months among males, but not among females or the full sample.[96] A secondary, exploratory analysis of 46 participants reporting heavy cannabis use at baseline (10 or more days of use in the past month), found a greater probability of heavy cannabis use at 6 months in the control group (38.1%) versus those in the intervention (16.6%).[97] Despite one trial's intervention targeting cannabis use only, the only statistically significant benefit was limited to the frequency of non-cannabis drug use at 6 months among adolescents randomized to the computer-based, but not therapist-led, brief intervention.[107] This same trial also observed no statistically significant changes in the frequency of driving under the influence of cannabis within or between any of the groups over time.[107] The remaining trial found no differences in self-reported frequency or quantity of cannabis use at 3-, 6-, or 12-months followup.[78] No differences in the frequency of alcohol use were reported within these trials. Effects of the interventions on other behavioral measures such as risky sexual behaviors were not reported by these two trials.

Detailed Results: Health, Social, and Legal Outcomes (KQ 4b)

Two of the three trials among adolescents reported effects on health, social, or legal outcomes, specifically cannabis-related consequences (n=622) (**Table 13**).[107] In one trial, the mean number of cannabis-related consequences (e.g., had a fight, argument, bad feelings with a friend; missed out on other things because you spent too much money on cannabis; kept smoking when you promised yourself not to) significantly decreased among adolescents in the therapist-led brief intervention over time (baseline, 14.2; 3 months, 12.5; 6 months, 11.3; 12 months, 11.1) and among adolescents in the computer-based brief intervention from baseline (14.3) to 3 months (11.5) and 6 months (10.5), while no significant change was seen in the control group (baseline, 14.0; 3 months, 13.6; 6 months, 11.0; 12 months, 11.5). Differences in these changes were not statistically difference between groups at 6 or 12 months; only the change in the number of cannabis-related consequences at 3 months for the computer-based intervention participants was significantly improved compared with the control group (mean difference in change, -0.24 [standard error, 0.12], $p<0.05$). In the other trial, the number of cannabis-related consequences decreased among intervention participants while they increased among control group participants and a statistically significant effect was found at 12 months ($p=0.04$); this difference was not apparent, however, at 3- or 6-months followup.[78]

Detailed Results: Harms (KQ 5)

None of the three trials among adolescents reported on harms related to the intervention.

Adults

Study, Population, and Intervention Characteristics

Nineteen (n=8110) (sample size range 65 to 1175) evaluated the effectiveness of interventions to reduce drug use among young adults or adults (**Table 8**).[80-83, 87-89, 93-95, 101-105, 108, 109, 111, 112] All but two trials[89, 102] took place in the United States. Five trials recruited primarily white young adults with a mean age of ranging from 18 to 20.5 years whereas the remaining 14 trials targeted adults 18 and older. The latter trials among adults generally represented both younger adults and middle-aged adults (mean age ranged from 28.4 to 55.1 years), mostly male (74%), non-white (14% to 86%), and lower socioeconomic adults. When reported, a history of or current homelessness was common (30 to 61%) as were rates of medical comorbidities (e.g., 56% with at least one mental health illness, 46% with a mood disorder, 85% with a comorbidity such as hypertension, HIV, or depression). In most trials, participants were recruited and universally screened for drug use upon presenting to primary care clinics, including walk-in and reproductive health clinics (e.g., student health, urgent care, women's, and homeless clinics),[81, 89, 95, 101, 112] safety-net primary care clinics,[103] Federally Qualified Health Centers,[87, 88, 108] and urban primary care clinics.[104] Five trials recruited, screened, and intervened within an emergency department[80, 82, 83, 102, 109] and one[111] recruited patients being admitted to an internal, surgical, or gynecologic ward of a hospital. The remaining trials directly recruited incoming college students via mail[93, 94] or through generic advertising.[105]

The methods of screen detection, drugs targeted, and eligibility criteria varied across the trials (**Table 9**). All five trials among young adults focused on reducing cannabis use whereas most of the trials among general adults targeted adults at moderate risk of drug use or a drug use disorder for *any* drug type. Four focused on specific drugs including one trial that targeted use of cocaine and/or heroin[81], one that targeted alcohol and opioid use,[108] one that targeted alcohol and cannabis use,[109] and one that targeted prescription drug misuse.[111] Few studies[87-89, 95, 102, 105, 112] excluded adults who screened at high risk for a drug use disorder (e.g., ASSIST score ≥27, meeting criteria for drug dependence); in those that did, only one[89] had a formal referral process in place for substance use treatment. As a result, rates of current drug use at baseline were high in most trials; however, within notable variability *within* trials. For instance, the prevalence of cannabis use in the past 30 days ranged from 44 to 76 percent, the prevalence of cocaine use ranged from 9 to 93, and the prevalence of opioid use (illicit and prescribed) ranged from 4 to 45 percent (in trials reporting these measures). In studies that reported it, participants were averaging drug use on about half of the days of the month. Only four trials reported the proportion of participants with a drug use disorder or drug dependence at baseline; in all four trials approximately one-third to one-half of the sample had cannabis dependence,[105] a cannabis use disorder,[95] heroin or prescription opioid abuse or dependence,[108] or prescription drug dependence.[111]

Despite the range in drug use and risk for a drug use disorder within and between trials, the included interventions (22 interventions in 19 trials) were generally similar in content and intensity (**Table 10** and **Table 11**). All but one intervention[108] was a brief intervention provided during one to two sessions ranging in length from 3 minutes to 60 minutes per session. In most of the interventions, counseling was provided in-person by trained peers, social workers, health educators, or mental or behavioral health specialists. Only four trials included interaction with a

primary care provider.[87, 88, 95, 108] Four trials tested a computer-based, self-directed brief intervention.[82, 93, 101, 112] About one-third of the interventions also provided booster telephone counseling sessions occurring approximately 2 weeks following the in-person counseling session, although completion of these telephone calls was generally low. The content of the sessions was generally the same, comprising personalized normative feedback and using features of motivational interviewing to establish rapport and discuss the links between drug use and health concerns, heighten discrepancies between negative drug use outcomes and valued goals, enhance self-efficacy about behavior change, and provide options for change. Only two trials[81, 83] specifically offered referrals for further drug use treatment following brief intervention; several others provided general information on drug treatment options in their communities. The one remaining trial consisted of a system-level collaborative care intervention designed to facilitate treatment for a probable opioid or alcohol use disorder.[108] Patients in the intervention group met with a care coordinator to assess motivation and encourage patients to meet with a therapist for evaluation and treatment planning and all patients were tracked and re-contacted to evaluate treatment progress. Treatment within the clinic included a 6-session brief psychotherapy treatment and/or medication-assisted therapy (MAT) with either sublingual buprenorphine/naloxone for opioid use disorders or long-acting injectable naltrexone for alcohol use disorders. All therapists and clinicians were offered training (and waivered in the case of MAT) to provide treatment. The comparators in these trials included usual primary care or minimal interventions such as generic information for drug use treatment options in their local community.

Detailed Results: Drug Use and Other Risky Behaviors (KQ 4a)

There was no consistent evidence of a benefit of brief interventions on self-reported drug use compared with controls at 3-, 6-, or 12-months followup within the trials among screen-detected adults (n analyzed=7090) (**Table 14**). The measured outcomes were variable, including days of drug use (for cannabis specifically, the "primary" or most frequently used drug, or any drug), number of joints smoked, drug use abstinence/discontinuation (for specific drugs or any drugs), and drug use severity as measured by the Addiction Severity Index or ASSIST. Only one study[108] reported the proportion of participants meeting the criteria for drug abuse or dependence and few studies confirmed self-reported drug use with biologic confirmation.

The most commonly reported outcome was the number of days using drugs in the past 30 or 90 days (**Table 14**). In general, self-reported drug use days decreased in both the intervention and control groups over time, with no statistically significant differences between groups. The absolute change in drug use days in intervention and controls groups ranged considerably. Across studies, changes in drug use days ranged from an increase of 1.2 days/90 days (0.1/7 days) to a decrease of 8 days/30 days (-1.9/7 days) among intervention participants. Among control participants, the range was an increase of 2.1 days/90 days (0.2/7 days) to a decrease of 8.4 days/30 days (-2.0/7 days). In a pooled analysis of nine trials that reported mean changes in drug use days at 3 months followup, the mean difference in change in past 7-day use of drugs between intervention and control groups was not statistically significant (mean difference [MD], -0.07 [95% CI, -0.25 to 0.11]; k=9; n=3183; I^2=16.1%) (**Figure 9**). Likewise, no association was found between brief interventions and drug use days in the last 7-days in trials reporting longer term followup at 6- to 12-months (MD, 0.01 [95% CI, -0.25 to 0.22]; k=10; n=3632; I^2=48.6%) (**Figure 10**).

Of the eight trials that reported a binary outcome of use vs. no use or drug use abstinence, four fair-quality trials found a statistically significant reduction in the proportion of participants using drugs at followup although the effects were generally small and inconsistent across drug types and different followup time points within studies (**Table 14**).[80, 81, 88, 105] For instance, in the two trials among young adults that reported the odds of cannabis use at followup, one found an effect of the intervention at 12 but not 3 months[80] and the other found an effect at 3, but not 6 months.[105] In the small pilot replication study of Project QUIT, 5 of 21 patients in the intervention group (25%) versus 15 out of 26 patients in the control group (56%) self-reported using their "highest scoring drug" (aka, primary drug) at 3 months following a brief intervention and up to 2 phone calls over 6 weeks (OR, 0.10 [95% CI, 0.10 to 0.99], p<0.05).[88] Outcomes at longer term followup were not measured in this study. Finally, one trial among 778 adults with moderate-to-severe cocaine and heroin use reported a borderline statistically significant benefit of one motivational interviewing session on biologically confirmed use of cocaine and/or opiates at 6 months (intervention group: 17.4% vs. control group: 12.8%; adjusted OR, 1.51 [95% CI, 0.98 to 2.26], p=0.052).[81] However, the same study found no statistically significant effect for levels of cocaine and heroin use as measured by hair samples at 6 months (p=0.058 for cocaine and p=0.186 for heroin). There were no differences between groups in the rates of abstinence or use in the remaining four trials.

The effects of the interventions on other behavioral outcomes such as alcohol use or risky sexual behaviors were consistent with the drug use outcomes, finding no benefit.

Detailed Results: Health, Social, and Legal Outcomes (KQ 4b)

Eleven of the 19 trials among adults (n analyzed=3833) reported the effects of the interventions on health, social, or legal outcomes with none finding a statistically significant effect after 3 to 12-months of followup (**Table 15**). Among young adults, all five studies[80, 93, 94, 101, 105] reported the effects of the interventions on cannabis-related consequences as measured by the Rutgers Marijuana Problem Index or Marijuana Problem Scale, although modifications were evident and the number of items and scales differed across all five trials. Example items included: "driving after cannabis use," "not able to do your homework or study for a test," "missed out on other things because you spent too much money on marijuana," and "had intense anxiety or panic attacks." Where reported, scores decreased[94, 101] or slightly increased[80, 93] within both intervention and control groups from baseline to 3-12 months, and no statistically significant differences were seen between groups. Among adults, no differences were seen in changes in quality of life,[87, 104, 108] drug use consequences,[103, 104, 108, 109] mental health symptoms,[104] or healthcare utilization,[95, 103, 104, 108] including entering substance use treatment. In the ASPIRE trial,[91, 104] despite the brief interventions including formal referral to treatment when indicated, no differences were found between intervention and control groups in the receipt of additional treatment within the 6 months following study entry. Among persons taking part in the brief intervention (one 10- to 15-minute structured interview), 18 percent received any additional treatment versus 17 percent of those in the control group (adjusted odds ratio, 1.11 [95% CI, 0.57, 2.15], p=0.76). In contrast, persons taking part in the 2-session motivational interviewing arm had *lower* odds of receiving treatment (10%) versus those in the control group (17%) (adjusted OR, 0.36 [95% CI, 0.17, 0.78], p=0.02).[91]

Detailed Results: Harms (KQ 5)

Only two of the 19 trials among adults reported on harms related to the intervention (n=518). In those two trials, no adverse events were reported by college students taking part in a one-hour in-person[94] or web-based[93] personalized feedback session addressing marijuana use.

Pregnant and Postpartum Women

Study, Population, and Intervention Characteristics

We identified five fair-quality trials among postpartum[98-100] and pregnant women (**Table 8**).[106, 110] In the trials by Ondersma et al.,[98-100] primarily low-income African American women (n=107 to 502) were recruited during their inpatient hospitalization for childbirth. In the first two trials,[98, 99] women reporting any illicit drug use *in the month before becoming pregnant* were eligible to participate (**Table 9**). Just over a quarter (25.7%) of the women screened positive and agreed to participate. Marijuana was the most prevalent drug used, with 62.6 percent[99] and 86.5 percent[98] reporting daily or near daily marijuana use in the 3 months prior to pregnancy. In the 2018 trial,[100] women were indirectly screened for drug use risk using the WIDUS; rates of drug use at baseline (pre-pregnancy or during pregnancy) were not reported in this study. In all three trials, baseline assessments were self-administered anonymously on a computer tablet, then randomization and the intervention or the attention control were administered immediately after on the same computer tablet. All three interventions were a single 20-minute session following motivational interviewing principles; control participants spent the same amount of time on the computer tablet watching and providing feedback on video clips unrelated to drug use (**Table 10** and **Table 11**).

In both trials among pregnant women, women in the first two trimesters of pregnancy were recruited from reproductive health clinics (n=183[110] and n=50[106]). Women were eligible to participate if they reported using alcohol or illicit drugs in the previous month or scored positively for risk of alcohol or drug use (**Table 9**). In one trial,[110] opiate users were given a referral to a local methadone maintenance facility. At baseline, 44 and 70 percent of women reported marijuana use during pregnancy. One intervention was a 60-minute computerized motivational interviewing session[106] whereas the other intervention was the most intense of the interventions included in this review (**Table 10** and **Table 11**) and consisted of six 30-minute individual counseling sessions combining motivational enhancement therapy and cognitive behavioral therapy, delivered by research nurses during routine prenatal and immediate postnatal care visits.[110]

Detailed Results: Drug Use and Other Risky Behaviors (KQ 4a)

Results on drug use outcomes were mixed and inconsistent in the trials among postpartum women (**Table 16**). In the first Ondersma trial (n=107), there was a statistically significant effect of the intervention on any drug use and non-cannabis use frequency in the 4 months following birth; but, no effect was found on total abstinence.[99] In contrast, in the 2014 trial, at 3 months following delivery, 26.4 percent versus 9.9 percent of intervention versus control participants were abstinent from drugs as assessed by self-report and biological verification (OR, 3.28 [95% CI, 1.3 to 8.39], p-value=0.010). This difference, however, did not remain statistically significant

at 6 months followup (OR, 1.47 [95% CI, 0.53–4.12], p-value=0.456). Likewise, women in the intervention group reported fewer days of drug use in the previous 3 months (median 31.6 days) than women in the control group (median, 77.2 days) at 6 months (p=0.207), but this difference was not statistically significant.[98] In the 2018 trial, there was no effect of the intervention at 3 or 6 months on drug use days or self-reported or biologically-confirmed drug use.[100]

Findings were also mixed in the two trials among pregnant women (n=213). One small trial (n=50) reported that 23 percent versus 42 percent of intervention versus control women were using any alcohol or cannabis use at 4 months followup (OR=0.16 [95% CI, 0.04 to 0.74], p=0.02).[106] In the trial by Yonkers (n=104), substance use decreased among women in both the intervention and control groups between baseline (prenatally) and delivery, but increased again after 3 months postdelivery, and no statistically significant differences were found between groups at any time point, based on both self-report and urine samples.[110] No studies evaluated effects of interventions on risky behaviors related to sexual activity or alcohol or tobacco use.

Detailed Results: Health, Social, and Legal Outcomes (KQ 4b)

Only one trial reported results related to health outcomes. Within one trial among pregnant women (n=163), 10.1 percent versus 20.2 percent of intervention and control women gave birth preterm (i.e., <37 weeks gestation) (p=0.08) and 14.5 percent versus 20.2 percent of intervention and control participants delivered a low-birthweight infant (i.e., <2500 grams) (p=0.41).[110]

Detailed Results: Harms (KQ 5)

In both studies among postpartum women, no women experienced any harms or unintended effects based on their participation in an electronic screening and brief intervention (n=643).[98, 100]

Chapter 4. Discussion

Summary of Evidence

A summary of our findings, including our overall assessment of the strength of evidence for each Key Question, is presented in **Table 17**.

Benefits and Harms of Screening

We identified no studies that addressed the benefits or harms of screening (vs. no screening) for drug use in primary care. Several screening instruments have been developed to identify drug use and risks associated with drug use for primary care settings; however, these instruments have not been evaluated in more than one or two studies. Given this lack of replication and the heterogeneity in the studies, we believe the strength of this body of evidence is low **(Table 17**). Some frequency-based screening instruments only include questions related to the use of and/or frequency of drugs (and may ask about alcohol and tobacco use) while others also include an assessment of the patient's risk level (i.e., specific indicators of a disorder, including experiencing drug-related consequences) for individuals with positive screening results. In general, both types of instruments (frequency-based and fuller risk assessments instruments) have sensitivity greater than or equal to 0.80 and specificity greater than or equal to 0.85 for identifying unhealthy drug use and drug use disorders when validated against structured diagnostic interviews. While one frequency-based screening tool (TAPS-1) had adequate performance to detect unhealthy use and use disorder of prescription drugs, sensitivity and specificity estimates for other screening tools were generally lower and less precise for the detection of prescription medication problem use and disorders than other drugs, which may result from confusion about what constitutes nonmedical use. The low prevalence of prescription drug misuse and other drug types (cocaine, heroin) also leads to poor precision in some estimates.

Other studies evaluated instruments to identify unhealthy drug use through indirect questions, such as assessing the frequency of heavy drinking episodes or other indicators of an alcohol use disorder and not asking participants about their drug use specifically. These instruments generally did not perform as well in detecting unhealthy drug use or drug use disorders. Such instruments, however, may be important where under-reporting of drug use is of concern such as in studies among pregnant women.

Sensitivity and specificity estimates were also lower for identifying any drug use or unhealthy drug use when confirmed by a biologic reference standard versus a diagnostic interview in the two studies that included both reference standards. There was no clear pattern for better performance for interview-administered versus self-administered (either paper-pencil or electronic) instruments. Additionally, all screening instruments were validated under confidential conditions; it is not known how their performance would differ if patients knew that their health care providers would be informed of the results.

The prevalence of drug use greatly affects the positive predictive values (PPV) of screening tools and therefore can be used to inform clinical actions (**Table 18**). Looking across a range of

sensitivities and specificities based on our review, the PPV is quite low (≤50% for adults) given the low prevalence of any drug use and extremely low prevalence for specific classes of drugs. Put another way, approximately one-half or greater of participants who screen positive for drug use or unhealthy drug use may not actually have use that indicates the need for brief psychosocial interventions or referral to treatment. In this case, further assessment to define patients' risk level may help determine the appropriateness of brief interventions or treatment as well as the need for arranging referral for further support.

Benefits and Harms of Interventions

The previous review to support the USPSTF recommendation included only one trial[81] that addressed treatment for drug use among an "asymptomatic" screen-detected population. Given the USPSTF determination of insufficient evidence in 2008 and a call to action for more research among primary care screen-detected populations,[113, 114] results from several well-conducted trials that were subsequently published were included in this review. Despite the increase in the number of relevant trials, there are still few studies that have evaluated the effectiveness of interventions among systematically screened populations for reducing drug use. We identified 27 eligible trials, with heterogeneity in the target populations and drugs targeted. Across all 27 trials, in general, there was no effect of brief, personalized interventions on rates of self-reported or biologically confirmed drug use or drug-related consequences. Three fair-quality trials among adolescents (n=741)—all targeting cannabis use and/or alcohol and other drug use—found no effect on self-reported drug use at 3-, 6- or 12-month followup. Likewise, there was no consistent evidence of a benefit of brief interventions on self-reported drug use compared with controls at 3-, 6-, or 12-months followup within the trials among screen-detected adults (n analyzed=7090). In general, self-reported drug use days decreased in both the intervention and control groups over time, with no statistically significant differences between groups. Finally, five fair-quality trials among pregnant and postpartum women (n=943) found mixed and inconsistent effects of brief interventions on women's self-reported drug use at 3-6 months followup. Fourteen of these 27 trials reported the effects of the interventions on health, legal, or social consequences related to drug use, and none found differences between groups.

There was some evidence, although not definitive, that interventions limited to participants with more severe drug problems[81] or subgroup analyses among those at higher risk (e.g., greater use of stimulant and opiate abuse[103]) may result in reduced drug use (although not related consequences), whereas no clear benefits were seen in those with lower baseline drug severity, including predominantly marijuana users. Although none of the trials took place in settings or during time periods that allowed legal recreational marijuana use, the legalization climate nationally may have served to normalize marijuana use and reduce motivation to change. Because there are no identified guidelines for a point at which marijuana-related consequences can be minimized and potential positives maximized,[6] it is clear that there will continue to be numerous challenges for clinical practice[115] and public health assessment and policy[6, 116, 117] related to marijuana use.

Regardless of the effectiveness of brief interventions in addressing drug use following screening, asking about drug use in primary care, particularly among patients with a higher propensity for drug use (e.g., history of abuse, family history of addiction, known alcohol use disorder, mood disorder), may still be clinically justified to ensure the quality and safety of health care. Knowing

patients' drug use status and the specific types of drugs being used can inform possible drug-medication interactions, potential issues with medication adherence, safe prescribing of certain other classes of medications (e.g., narcotics, amphetamines), and overall health-related quality of life.

Comparison with 2008 USPSTF Review

This update review differs in scope from the 2008 USPSTF review on this subject,[2] which resulted in a different body of evidence. First, the 2008 review used a staged approach that focused on evidence for *critical* KQs that addressed the overarching question on direct evidence of benefit from screening and the health benefits of drug treatment (the current KQ 1 and KQ 3). Given that the evidence was considered insufficient on these critical KQs, further systematic review to include the other key questions in the analytic framework (i.e., harms and tool accuracy) were deemed unwarranted. Subsequently, a separate supplemental review was conducted that specifically related to KQ 2 on the accuracy of screening tools.[3] In this current review, we addressed all five KQs regardless of the sufficiency or results related to each question. We omitted the original KQ related to the relationship between decreased drug use or abstinence and morbidity and mortality. We planned to address this question contextually (rather than through systematic search and selection methods) to frame the results of the review; however, given the lack of effectiveness on drug use outcomes seen in the included trials, we do not provide a robust summary here. The previous review found fair evidence that stopping or reducing drug "misuse" is related to reduced mortality and morbidity, although none of that evidence was derived from individuals screened for drug misuse in primary care settings. Second, while the 2008 review intended to only include treatment trials among screen-detected samples, 16 of the 17 included treatment trials were conducted among treatment-seeking, instead of primary-care-screened, populations. As a result, most of the interventions were pharmacotherapy treatments among treatment-seeking patients. Our current review applied strict inclusion criteria to ensure that the evidence applied to a screen-detected population and thus, only carried forward one trial that was previously included.[81] Likewise, because pharmacotherapy (medication-assisted therapy) is only approved for use among adults with opioid use disorders, these therapies were considered out-of-scope for this review. Other existing systematic reviews have found these treatments to be effective in ameliorating opioid withdrawal and assisting with detoxification.[118] Lastly, the previous review only included evidence related to the use of illicit opiates, cocaine, and cannabis (or those targeting all drugs) whereas our update included any psychoactive drug used for nonmedical purposes. Despite the differences in our criteria, this did not result in material differences given that all our included intervention trials targeted any drug use, cannabis, or cocaine and heroin, specifically.

Comparison with Other Reviews

We are unaware of any existing systematic reviews that have synthesized the performance of screening instruments for unhealthy drug use among primary care-relevant populations. The findings from our review with respect to intervention effectiveness are generally concordant with those of Young and colleagues' 2014 systematic review[119] (k=5) on the effectiveness of the SBIRT model for reducing nonmedical use of psychoactive substances. Young and colleagues' review limited interventions to those following the SBIRT model, while our review allowed for

variation in intervention approach and the length and number of contacts. Moreover, our review included studies with at least 3 months of followup, while Young and colleagues included studies with even shorter-term (1–2 months) followup. Despite these differences in scope, our review generated a similar body of evidence, with our review sharing four of the five trials included in the Young and colleagues review.[80, 81, 89, 111] Young and colleagues encountered similar limitations among their included studies, such as the lack of systematic screening for participants, heterogeneity in study characteristics, incomplete reporting, and small sample sizes. Due to these limitations, Young and colleagues concluded insufficient evidence to determine the efficacy of brief interventions to reduce drug use among nontreatment seeking, screen-detected populations. Our review is also similar with that of Farr and colleagues[120] with both reviews finding mixed effects of brief interventions on drug use among pregnant and postpartum women in the short-term (<3 months).

Applicability

Despite inclusion criteria designed to result in the selection of studies highly applicable to U.S. primary care, many of the screening studies were conducted in populations with high prevalence of drug use. As such, the tool accuracy reported in the included studies may not reflect the accuracy for all U.S. primary care settings. Additionally, some of the larger studies were conducted among non-clinic-based samples (e.g., national random samples) and results may not be generalizable to the primary care setting. Likewise, given the research context of these studies, in most cases participants' screening responses were anonymous and were not shared with the patients' personal clinicians. As a result, tool accuracy may be overestimated and may not accurately reflect responses that would be given if the patient knew their results would be shared with their clinician. In any case, given the potentially low PPV for detecting drug use that requires provision or referral for psychosocial interventions or other treatments, further assessment to define patients' risk level, such as the procedure recommended by the National Institute on Drug Abuse (NIDA) may help.[121] NIDA recommends referring patients for a full assessment if a problem is indicated by the screen or through discussion with the patient. Specifically, for adults age 18 or older they recommend first using the NIDA Quick Screen (adapted from the Smith et al.[45] study included in this review), which assesses previous-year use of alcohol, tobacco, prescription drugs for nonmedical reasons, and illegal drugs. If the patient answers "never" for all drugs, abstinence should be reinforced. If the patient says "yes" (at any frequency) to use of illegal or prescription drugs for nonmedical reasons, they then recommend beginning the NIDA-Modified ASSIST (an 8-item tool based on the ASSIST as tested in this review). For each substance used, a score is calculated based on frequency of use in the previous 3 months and problems related to use that helps to identify a patient's risk level and to determine further steps such as offering continuing support, considering whether to make a referral for further diagnostic assessment or treatment based on clinical judgment, or directly arranging such referrals.

By design, this review focused on primary care-relevant interventions to reduce drug use among screen-detected drug users. The findings presented here do not reflect the totality of evidence for treating drug use or drug use disorders. Like the screening evidence, while all of the included evidence reflected patients seen in primary care in the United States, they all generally targeted particular settings that resulted in samples with a higher prevalence of drug use and drug use

disorders than national data. Most participants in the two studies among adolescents were black and had previous-year cannabis use. The five trials among young adults were mostly white college students with various frequency of cannabis use. The thirteen studies among adults, in contrast, represented higher-risk adults, including majority black adults with severe socioeconomic disadvantage and high rates of comorbid mental health conditions. As a result, across the body of evidence, there was a wide range in the severity and types of drug use addressed—from occasional cannabis use to those with diagnosed cocaine use disorders. All the interventions were quite similar, generally consisting of one personalized counseling session based on principles of motivational interviewing with or without a booster session or telephone call. These brief interventions were provided either by trained behavioral or mental health specialists or self-administered electronically. In only two trials did primary care providers administer the intervention.

Limitations of the Review

This review was not intended to be a comprehensive review on the evidence for treating drug use or drug use disorders. It was designed, rather, to address outcomes related to screening (vs. no screening) for drug use, the accuracy with which drug screening instruments can identify unhealthy use or use disorders, and potential benefits and harms of providing counseling about reducing drug use among those who have been identified by screen detection. Therefore, we included only trials of interventions among screen-detected populations that were applicable to primary care. There are several other systematic reviews, however, related to nonpharmacologic interventions and pharmacologic treatments for drug dependence or drug use disorders among non-screen detected persons (i.e., treatment seeking or otherwise mandated/identified) or those conducted in settings not as applicable to primary care (e.g., school-based interventions) that show efficacy for reducing drug use.[118, 120, 122-131]

For KQ 4, we included studies reporting drug use outcomes at 3 months or longer followup. Many studies, including some of our included trials,[94, 103-105, 107] have shown effectiveness of brief interventions in reducing drug use or drug-related consequences in the short term (i.e., 1 to 3 months), [87, 89, 132] but not longer-term (i.e., 6 months or greater). It may be unreasonable to expect long-lasting effects (>3 months) of a single short feedback session in reducing drug use. Over time, effects of these interventions may wear off as motivations inspired by the interventions become less salient. This might suggest a need for more intensive multisession approaches, the addition of one or more booster sessions, or other brief interventions or referral to treatment. In addition, we only included randomized controlled trials and excluded observational designs which may have led to the exclusion of other relevant evidence. For example, in the observational study by Madras and colleagues,[133] rates of illicit drug use were compared before screening and 6 months after screening, brief intervention, and referral to treatment services were provided across six states. Among those reporting baseline illicit drug use, rates of self-reported drug use at 6-month followup were statistically significantly lower following treatment.

Because this review focused on screening and subsequent psychosocial interventions for drug use, we did not include questions or evidence related to preventing misuse of prescription opioids or detecting misuse of prescription opioids among those on chronic opioid therapy. Most

of our included screening instruments assessing drug use and several of the brief interventions, however, did address misuse of prescription drugs. Given the rise in opioid prescribing[134] and the immense burden of opioid-related morbidity and mortality, particularly overdose deaths,[134] it is clear that continued efforts to change prescribing practices (e.g., policies to reduce inappropriate opioid prescribing, requiring clinicians to review prescription drug monitoring program data) and monitor and treat prescription misuse are warranted. Clinical instruments have been designed for predicting opioid abuse or misuse prior to opioid therapy initiation, including the Screening and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) tool, the Opioid Risk Tool (ORT), and the Brief Risk Interview, although results on the accuracy of these tools are very limited and inconsistent.[135]

Limitations of the Studies and Future Research Needs

Several limitations related to the included studies should be noted and point to needs for future research. First, more research and replication are needed to test the performance and accuracy of brief screening instruments relevant for primary care implementation. Additional studies that focus on possible harms of screening are needed to elucidate factors that may deter acceptance of screening by providers and patients or discourage honest responses on screening tools. These harms may relate to concerns about documenting screening results and sharing them with referral providers, relatives, insurers, health authorities, and other entities needed for obtaining consent for treatment, authorizing payment for diagnostic or treatment services, or complying with mandatory reporting requirements. The current studies show promise for brief frequency-based screeners as well as risk assessment instruments, but they should be evaluated in more studies across more primary care populations. Future studies of screening instruments should examine their accuracy and impacts on clinical workflow and resources when they are implemented in primary care. Computer self-administered screening conducted prior to the medical visit is increasingly being used for other conditions and deserves further study as an approach to screening for drug use. Studies limited to young adults, who have the highest rates of drug use, are particularly warranted. Additionally, further understanding the social and legal context and consequences related to screening for drug use in pregnant and postpartum women is necessary.

Second, the body of evidence for the effectiveness of interventions among screen-detected populations is still relatively small and has important limitations. Few interventions were conducted in primary care settings or included involvement of the primary care provider. Thus, the feasibility and effectiveness of these interventions when delivered in primary care settings remains unclear given very limited encounter times, lack of trained interventionists, and uncertainty whether involving primary care providers in intervention delivery would influence patient drug use. In addition, some, but not all,[103, 104] of the studies had modest sample sizes, which may have limited their power to detect significant changes. Many of the included studies were framed as feasibility or pilot trials and included recommendations to conduct full-scale trials of the tested interventions. Few addressed potential harms of participating in interventions such as labeling or discrimination or loss of time from work, school or other important pursuits. Larger sample sizes would allow for meaningful subgroup analyses to evaluate how important characteristics of the population might modify effectiveness of the interventions. Additionally, in most cases, drug use outcomes were based on self-report and did not include biological confirmation. Most of the studies included steps to increase the validity of self-report including

self-administration or blinding of assessors and assurances of confidentiality. However, introducing biological measures could provide important validation. In one of our included trials that included both self-report and biochemical measures, self-report of improvements in drug use was shown to be highly inflated.[81] At baseline, there was good agreement between self-report and hair samples for current cocaine and/or heroin use; however, there was substantial under-reporting of cocaine and/or heroin use at followup (45% of participants reported no cocaine/heroin use, but only 18% tested negative for both substances), although there were no differences in this disagreement between intervention and control group participants. Research suggests self-report is both over- and underreported depending on several factors, including recency of use, reporting period, and amount used. While biologic measures may assist in determining *any* drug use, such measures are not sensitive in detecting unhealthy use – a construct that may be particularly important for drugs that are legal to use (e.g., marijuana, prescription opioids). Also, biological testing only assesses selected drugs and the length of detection time varies by drug.

Additionally, there was considerable variability in the measures used to detect change in drug use which precluded robust synthesis and comprehensive pooled analyses. Many of the measures, which generally focused on frequency of drug use, may not be as sensitive to change as other possible measures, including quantity of drugs used or number of times used on the days the drug is used. Continuing to include measures related to the consequences of drug use and other health, legal, and social outcomes is also important, especially tracking how many patients continue to substance use treatment or other referred services following brief intervention.

The control groups in most of the intervention trials included usual care or minimal interventions (i.e., at least a written referral list). The lack of differences seen between groups in these trials may be different if compared with controls under actual conditions of clinical practice rather than research structures. Assessment reactivity alone (introspective thinking about one's drug use that is prompted by an assessment) may have minimized the effect sizes for the interventions with participants (both intervention and control participants) thinking introspectively about their drug use, thereby serving as a brief intervention or increasing social desirability bias in their self-reports of use. Alternative study designs such as stepped-wedge cluster randomized trials, sequential, multiple assignment, randomized trials (SMART), and micro-randomized trials should be considered in this field to determine real-world effectiveness and where interventions may need to be adaptive and equally provided to all participants throughout a study.

Given these limitations and an apparent lack of effectiveness of brief interventions for drug use, many in this field have proclaimed a need to consider evaluating alternatives to screening and brief interventions for reducing drug use in primary care such as those that apply different counseling strategies or multidisciplinary approaches or involve more or longer sessions.[136, 137] It is clear that primary care clinicians need to address the burden of drug use, but such a complex problem will likely require more complex solutions. Studies of new intervention models are needed including varied counseling approaches, multiple contact and longer sessions, team-based collaborative care approaches, and screening and interventions integrated into primary care and including the primary care provider. Additionally, more research on interventions that concurrently address common comorbidities such as unhealthy alcohol use, anxiety, and depression among primary care patients with unhealthy drug use are warranted.

Many ongoing studies (**Appendix H**) may address some of these research gaps. None of these ongoing studies, however, appear to address the overarching question related to the benefits and harms of screening for drug use.

Conclusion

Several screening instruments with acceptable sensitivity and specificity have been developed to screen for drug use and drug use disorders in primary care, although in general, the accuracy of each tool has not been evaluated in more than one study and there is no evidence on the benefits or harms of screening versus no screening for drug use. Brief interventions for reducing the use of illicit drugs or the nonmedical use of prescription drugs in screen-detected primary care patients are unlikely to be effective for decreasing drug use or drug use consequences. Given the burden of drug use, more research is needed on approaches to identify and effectively intervene with patients exhibiting risky patterns of drug use in primary care.

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Figure 1. Analytic framework

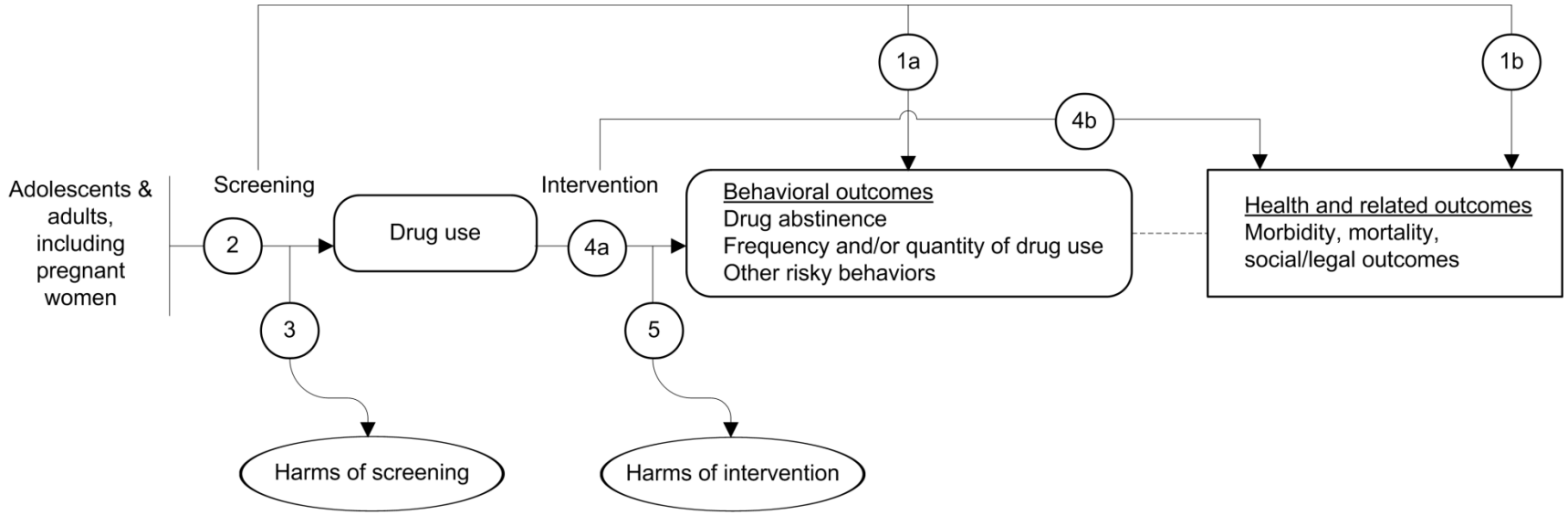
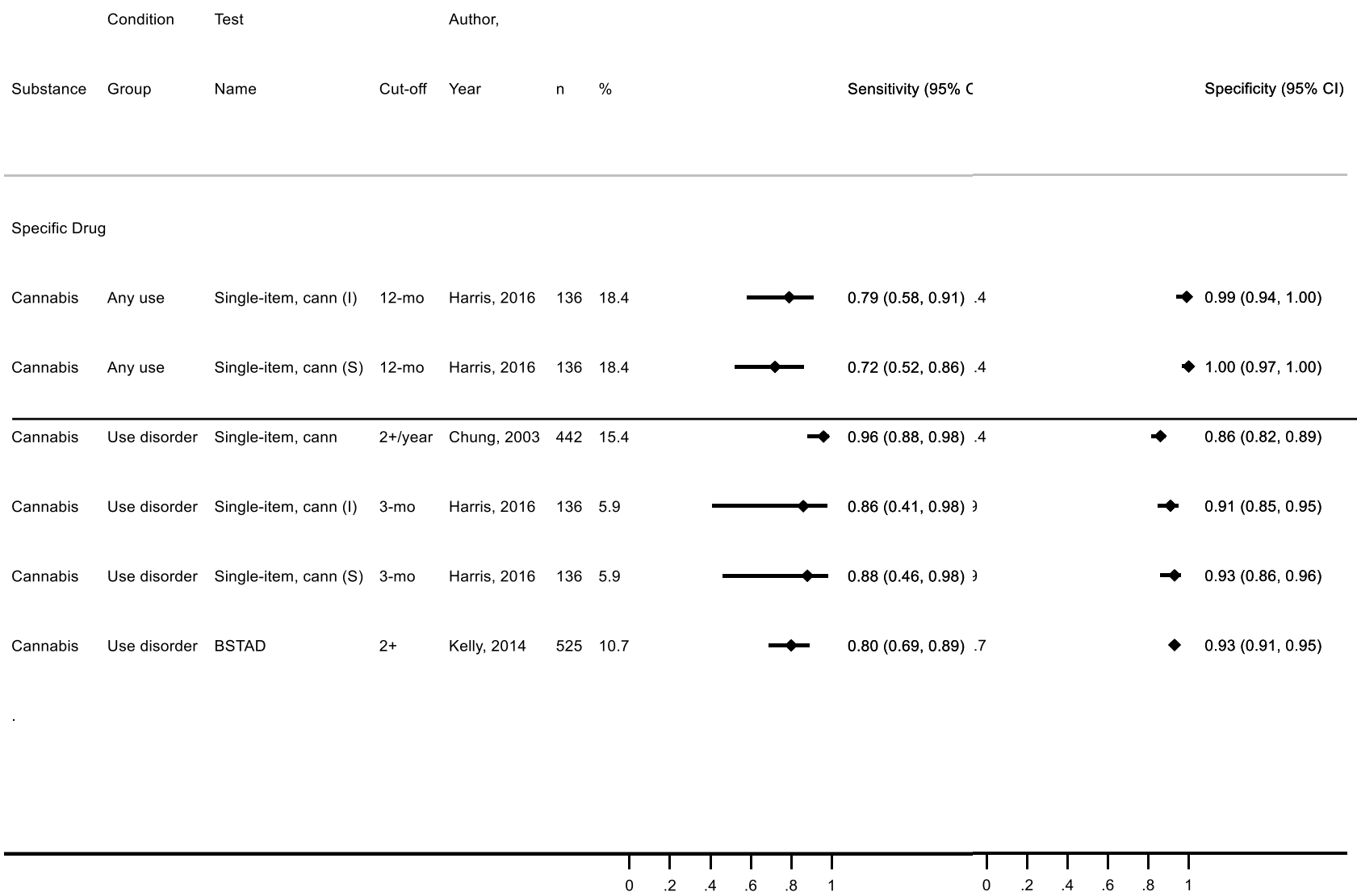
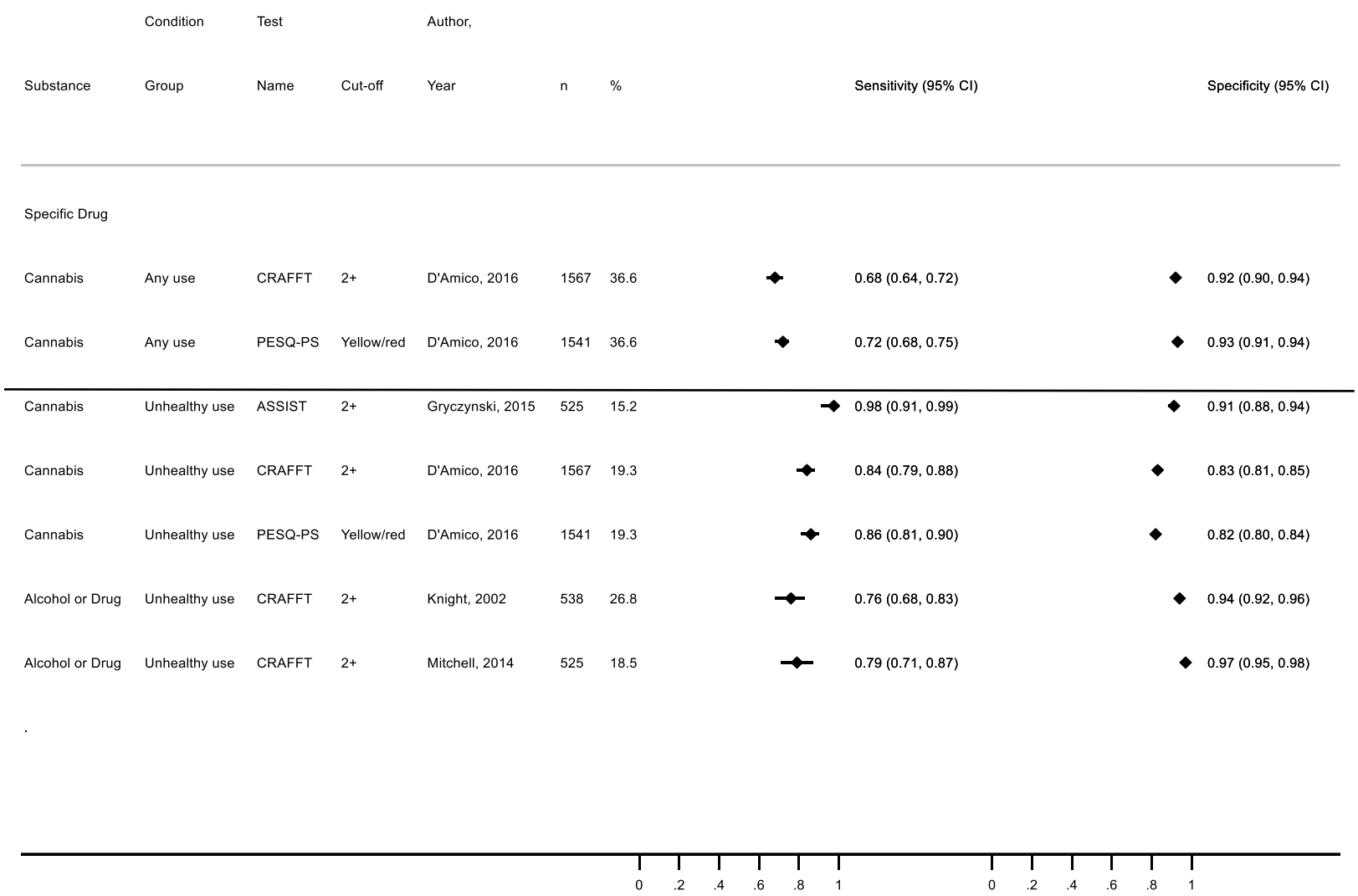


Figure 2. Accuracy of frequency-based screening tools in detecting specific drug use among adolescents



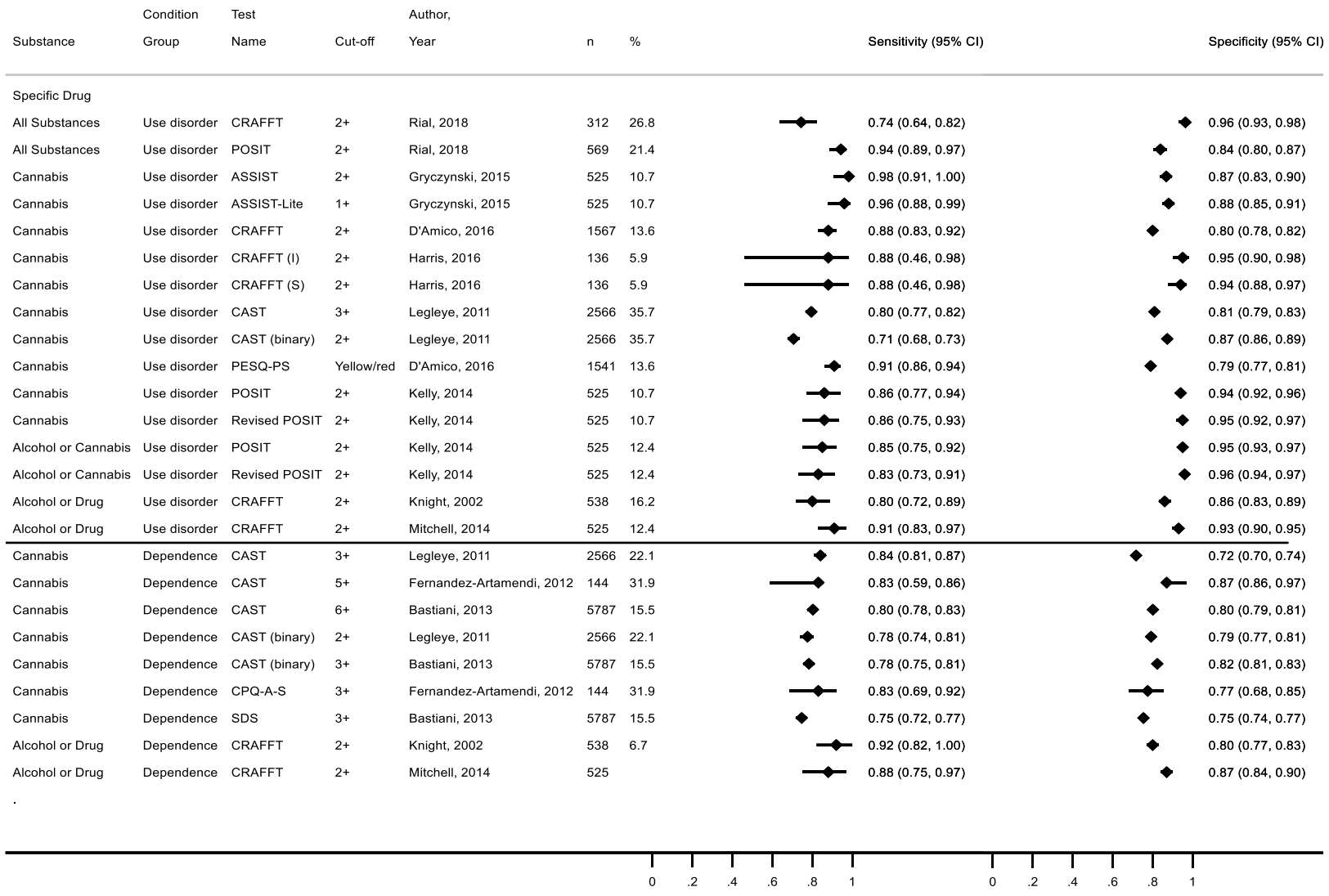
Abbreviations: BSTAD = Brief Screener for Tobacco, Alcohol, and Other Drugs; cann = cannabis; CI = confidence interval; I = interviewer-administered; mo = months; n = number of participants screened; S = self-administered

Figure 3. Accuracy of risk assessment screening tools in detecting any drug use or unhealthy drug use among adolescents



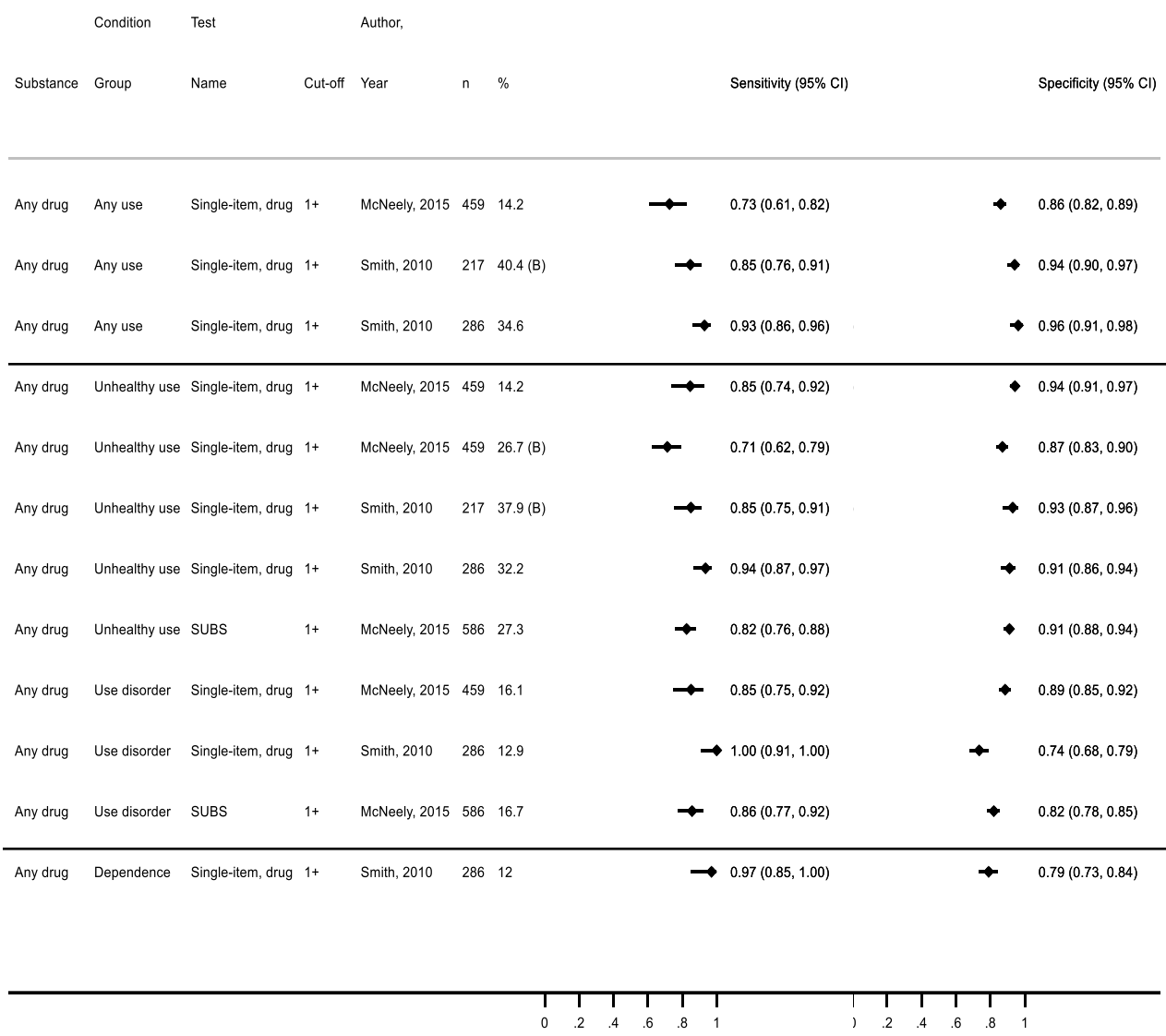
Abbreviations: ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; CAST = Cannabis Abuse Screening Test; CI = confidence interval; CRAFFT = Car Relax Alone Forget Family/Friends Trouble; n = number of participants screened; PESQ-PS = Personal Experience Screening Questionnaire

Figure 4. Accuracy of risk assessment screening tools in detecting drug use disorder among adolescents



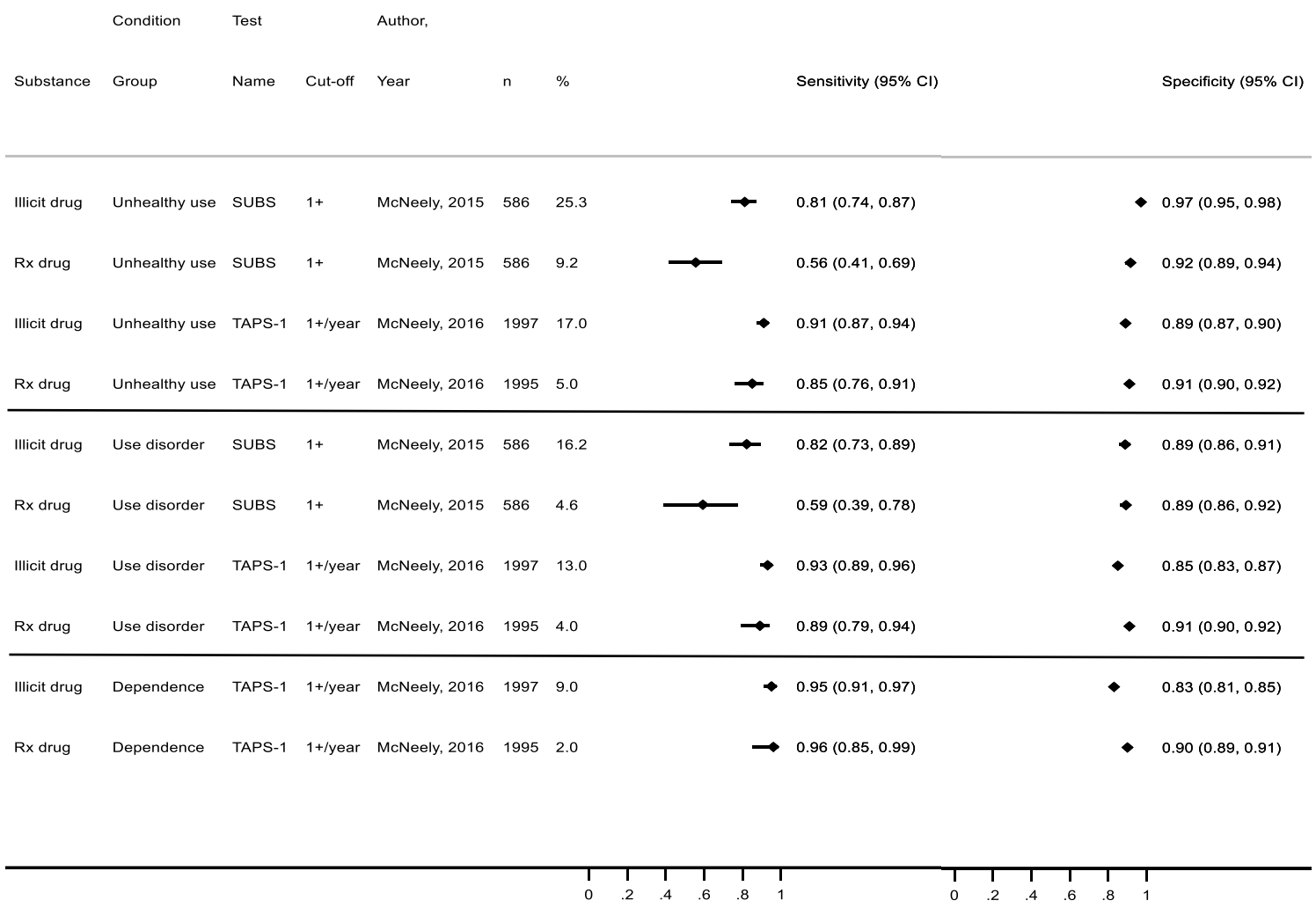
Abbreviations: ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; CAST = Cannabis Abuse Screening Test; CI = confidence interval; CPQ-A-S = Cannabis Problems Questionnaire for Adolescents Shortened; CRAFFT = Car Relax Alone Forget Family/Friends Trouble; I = interviewer-administered; n = number of participants screened; PESQ-PS = Personal Experience Screening Questionnaire; POSIT = Problem Oriented Screening Instrument for Teenagers; S = self-administered; SDS = Severity of Dependence Scale

Figure 5. Accuracy of frequency-based screening tools in detecting any drug use among adults



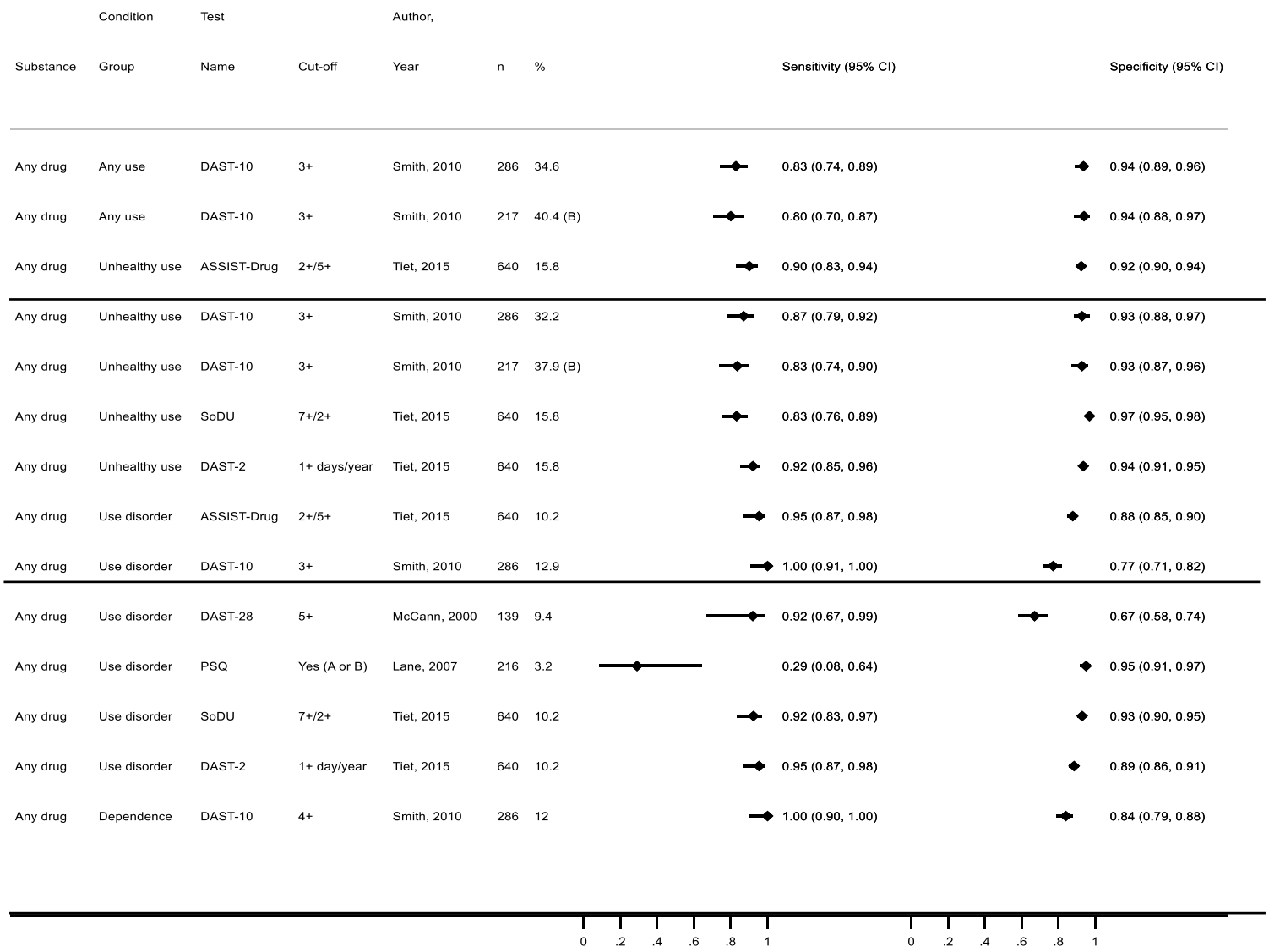
Abbreviations: B = reference standard included biologic confirmation; CI = confidence interval; n = number of participants screened; SUBS = Substance Use Brief Screen

Figure 6. Accuracy of frequency-based screening tools in detecting specific drug use among adults



Abbreviations: CI = confidence interval; n = number of participants screened; Rx = prescription; SUBS = Substance Use Brief Screen; TAPS-1 = Tobacco, Alcohol, Prescription Medication, and Other Substance Use first-stage screening component

Figure 7. Accuracy of risk assessment screening tools in detecting any drug use among adults



Abbreviations: ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; B = reference standard included biologic confirmation; CI = confidence interval; DAST-2 = 2-Item Drug-Abuse Screening Test; DAST-10 = 10-Item Drug-Abuse Screening Test; DAST-28 = 28-Item Drug-Abuse Screening Test; PSQ = Parent Screening Questionnaire; n = number of participants screened; S = self-administered; SoDU = Screen of Drug Use

Figure 8. Accuracy of risk assessment screening tools in detecting specific drug use among adults

Substance	Condition Group	Test Name	Cut-off	Author, Year	n	%	Sensitivity (95% CI)	Specificity (95% CI)
Cannabis	Any use	ASSIST	2+	Kumar, 2016	399	14.0	0.95 (0.85, 0.99)	0.82 (0.77, 0.86)
Cocaine	Any use	ASSIST	2+	Kumar, 2016	399	9.0	0.86 (0.70, 0.95)	0.84 (0.80, 0.88)
Cannabis	Unhealthy use	TAPS (I)	1+	McNeely, 2016	1996	11.6	0.82 (0.76, 0.87)	0.93 (0.91, 0.94)
Cannabis	Unhealthy use	TAPS (S)	1+	McNeely, 2016	1997	11.6	0.79 (0.73, 0.84)	0.93 (0.91, 0.94)
Cocaine/Meth	Unhealthy use	TAPS (I)	1+	McNeely, 2016	1995	6.0	0.68 (0.59, 0.77)	0.99 (0.98, 0.99)
Cocaine/Meth	Unhealthy use	TAPS (S)	1+	McNeely, 2016	1996	6.0	0.73 (0.64, 0.80)	0.99 (0.98, 0.99)
Heroin	Unhealthy use	TAPS (I)	1+	McNeely, 2016	1994	3.4	0.78 (0.67, 0.87)	1.00 (0.99, 1.00)
Heroin	Unhealthy use	TAPS (S)	1+	McNeely, 2016	1995	3.4	0.77 (0.65, 0.86)	1.00 (0.99, 1.00)
Rx opioid	Unhealthy use	TAPS (I)	1+	McNeely, 2016	1995	3.0	0.71 (0.58, 0.82)	0.99 (0.98, 0.99)
Rx opioid	Unhealthy use	TAPS (S)	1+	McNeely, 2016	1995	3.0	0.61 (0.47, 0.73)	0.98 (0.97, 0.98)
Rx opioid	Unhealthy use	PDUQp	10	Beaudoin, 2016	112	38.4	0.44 (0.35, 0.53)	0.79 (0.71, 0.86)
Rx sedative	Unhealthy use	TAPS (I)	1+	McNeely, 2016	1995	2.0	0.63 (0.47, 0.78)	0.99 (0.98, 0.99)
Rx sedative	Unhealthy use	TAPS (S)	1+	McNeely, 2016	1995	2.0	0.66 (0.49, 0.80)	0.97 (0.96, 0.98)
Cannabis	Use disorder	ASSIST	4+	Kumar, 2016	399	7.3	0.83 (0.64, 0.94)	0.83 (0.79, 0.87)
Cannabis	Use disorder	CAST	3+	Legleye, 2015	550	28.9	0.81 (0.74, 0.86)	0.75 (0.70, 0.79)
Cannabis	Use disorder	TAPS (I)	2+	McNeely, 2016	1996	7.4	0.71 (0.63, 0.79)	0.95 (0.94, 0.96)
Cannabis	Use disorder	TAPS (S)	2+	McNeely, 2016	1997	7.4	0.70 (0.62, 0.77)	0.95 (0.94, 0.96)
Cocaine	Use disorder	ASSIST	4+	Kumar, 2016	399	7.3	0.90 (0.73, 0.98)	0.87 (0.83, 0.90)
Cocaine/Meth	Use disorder	TAPS (I)	2+	McNeely, 2016	1995	5.4	0.57 (0.47, 0.67)	0.99 (0.99, 1.00)
Cocaine/Meth	Use disorder	TAPS (S)	2+	McNeely, 2016	1996	5.4	0.60 (0.50, 0.69)	0.99 (0.99, 0.99)
Heroin	Use disorder	TAPS (I)	2+	McNeely, 2016	1994	3.2	0.66 (0.53, 0.77)	1.00 (1.00, 1.00)
Heroin	Use disorder	TAPS (S)	2+	McNeely, 2016	1995	3.2	0.66 (0.53, 0.77)	1.00 (0.99, 1.00)
Rx opioid	Use disorder	TAPS (I)	2+	McNeely, 2016	1995	2.4	0.48 (0.33, 0.63)	1.00 (0.99, 1.00)
Rx opioid	Use disorder	TAPS (S)	2+	McNeely, 2016	1995	2.4	0.48 (0.33, 0.63)	0.99 (0.98, 0.99)
Rx opioid	Use disorder	PDUQp	10	Beaudoin, 2016	112	58.9	0.38 (0.29, 0.47)	0.81 (0.74, 0.88)
Rx sedative	Use disorder	TAPS (I)	2+	McNeely, 2016	1995	1.4	0.54 (0.34, 0.72)	0.99 (0.98, 0.99)
Rx sedative	Use disorder	TAPS (S)	2+	McNeely, 2016	1995	1.4	0.54 (0.34, 0.72)	0.98 (0.97, 0.99)
Cannabis	Dependence	CAST	5+	Legleye, 2015	550	12.6	0.81 (0.70, 0.89)	0.79 (0.75, 0.82)
Cannabis	Dependence	CAST	5+	Legleye, 2018	1351	16.0	0.87 (0.81, 0.90)	0.78 (0.76, 0.81)
Rx opioid	Dependence	PDUQp	10	Beaudoin, 2016	112	16.1	0.56 (0.46, 0.65)	0.75 (0.67, 0.83)

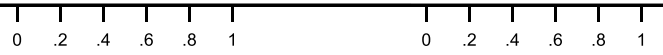
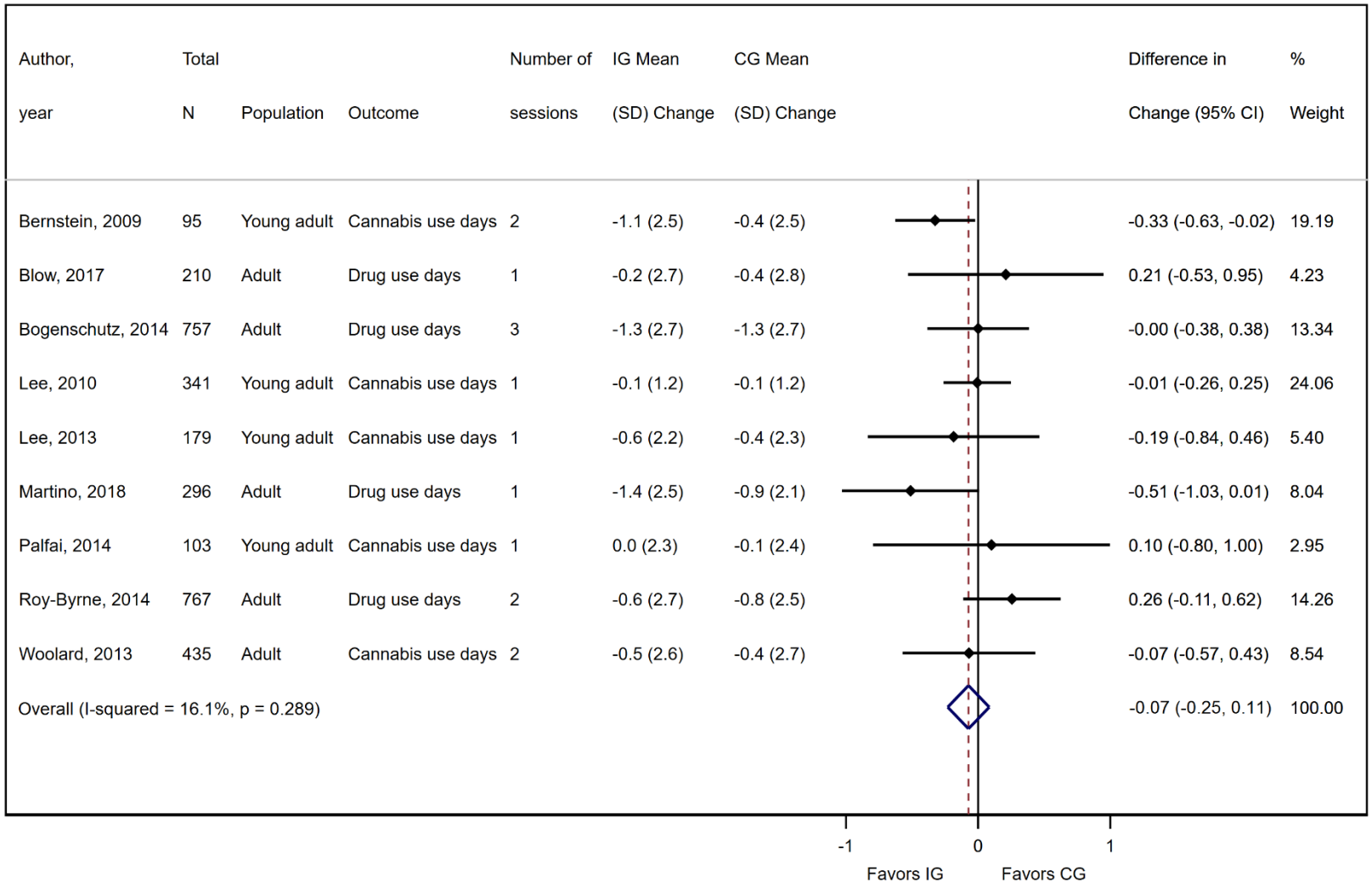


Figure 8. Accuracy of risk assessment screening tools in detecting specific drug use among adults

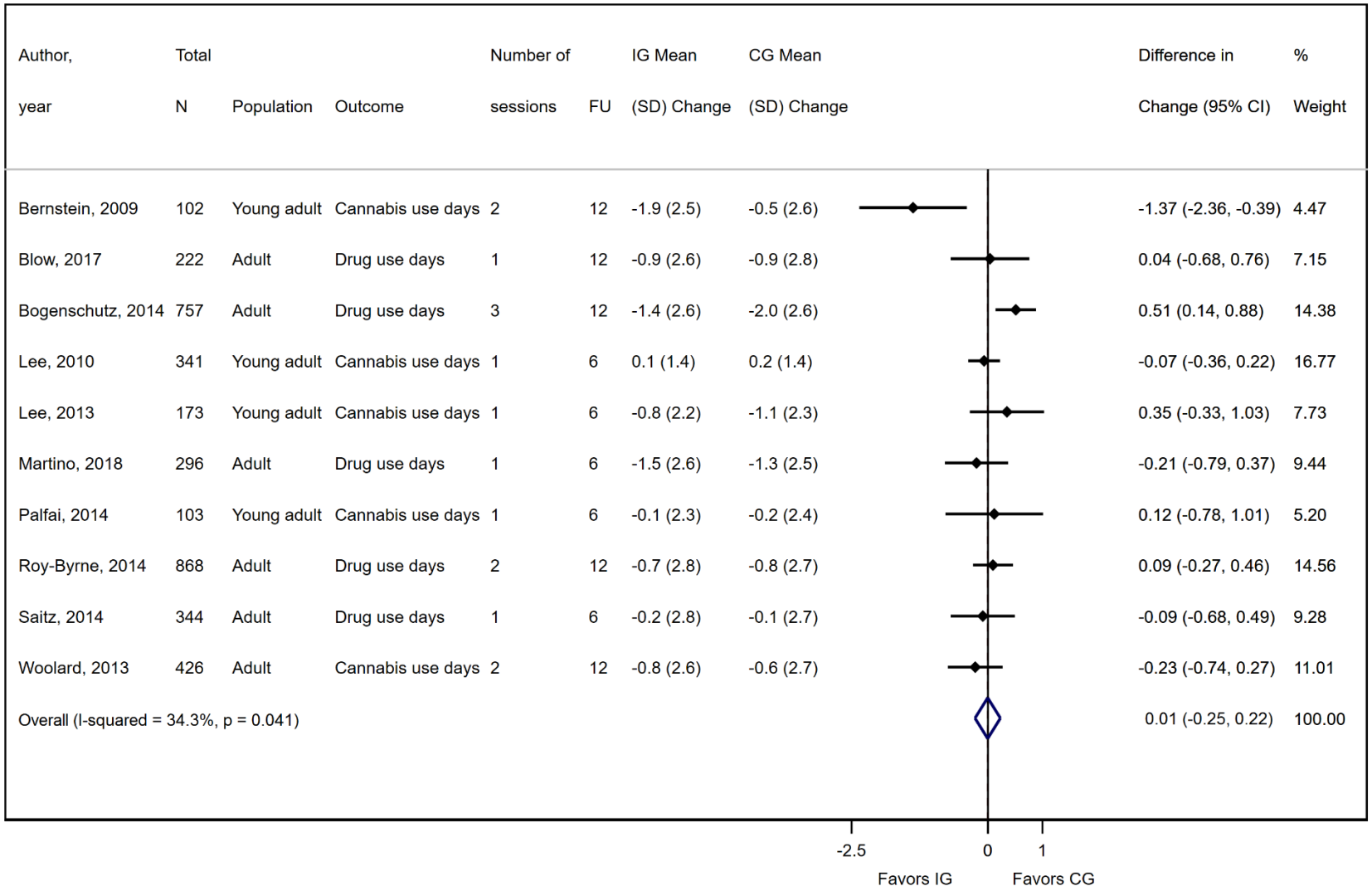
Abbreviations: ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; CAST = Cannabis Abuse Screening Test; CI = confidence interval; I = interviewer-administered; n = number of participants screened; PDUQp = Prescription Drug Use Questionnaire Patient Version; Rx = prescription; S = self-administered; TAPS = Tobacco, Alcohol, Prescription Medication, and Other Substance Use

Figure 9. Pooled analysis of days used drugs in the past 7 days (KQ 4a), mean difference in change between brief interventions and control groups at 3 months followup



Abbreviations: CG = control group; CI = confidence interval; IG = intervention group; N = number of participants analyzed; SD = standard deviation

Figure 10. Pooled analysis of days used drugs in the past 7 days (KQ 4a), mean difference in change between brief interventions and control groups at 6 to 12 months followup



Abbreviations: CG = control group; CI = confidence interval; FU = followup; IG = intervention group; N = number of participants analyzed; SD = standard deviation

Table 1. Current (previous month) illicit drug use,* 2017 National Survey on Drug Use and Health12

Substance	All (12 years or older)	Adolescents (12-17 years)	Young adults (18-25 years)	Adults (26 years or older)
Any illicit drug	11.2 (0.19)	7.9 (0.26)	24.2 (0.47)	9.5 (0.22)
Marijuana	9.6 (0.18)	6.5 (0.24)	22.1 (0.46)	7.9 (0.20)
Use/misuse of prescription psychotherapeutics†	2.2 (0.08)	1.5 (0.11)	4.5 (0.22)	1.9 (0.09)
Cocaine	0.8 (0.05)	0.1 (0.03)	1.9 (0.14)	0.7 (0.06)
Hallucinogens	0.5 (0.03)	0.6 (0.08)	1.7 (0.14)	0.3 (0.03)
Inhalants	0.2 (0.02)	0.6 (0.07)	0.5 (0.06)	0.1 (0.02)
Heroin	0.2 (0.02)	0.0 (0.01)	0.3 (0.06)	0.2 (0.03)
Binge alcohol use	24.5 (0.27)	5.3 (0.22)	36.9 (0.57)	24.7 (0.32)
Tobacco	22.4 (0.26)	4.9 (0.21)	29.1 (0.48)	23.4 (0.31)

* All values in table are percent (standard error)

† Includes pain relievers, tranquilizers, stimulants (methamphetamine), sedatives

Table 2. Recommendations on screening for drug use

Organization	Year	Recommendation
American Academy of Family Physicians (AAFP)	2014	Adopts the 2008 and 2014 USPSTF recommendation on screening adolescents, adults, and pregnant women for illicit drug use[138] and primary care-based behavioral interventions to prevent or reduce illicit drug use in children and adolescents.[139]
Department of Veterans Affairs (VA)	2015	Adopts the 2008 USPSTF recommendation on screening adolescents, adults, and pregnant women for illicit drug use.[140] For patients with substance use disorders, there is insufficient evidence to recommend for or against using a standardized assessment that would determine initial intensity and setting of substance use disorder care rather than the clinical judgment of trained providers.
American Academy of Pediatrics (AAP)	2016	Recommends that pediatricians should increase their capacity in substance use detection, assessment, and intervention; and become familiar with adolescent SBIRT practices and their potential to be incorporated into universal screening and comprehensive care of adolescents in the medical home.[141]
American College of Obstetricians and Gynecologists (ACOG)	2012 (Reaffirmed 2014)	Recommends that all women should be routinely asked about their use of drugs, including prescription drugs used nonmedically, both before pregnancy and early in pregnancy, provided counseling when substance use is suspected or identified, and referred to treatment when drug dependence is apparent.[142, 143] (committee opinion)

Abbreviations: SBIRT = Screening, brief intervention, and/or referral to treatment

Table 3. Study and population characteristics, by subpopulation (KQ 2)

Target pop	Author, year	Quality rating	Country	Recruitment setting	Brief population description	N screened	Age, mean	Female, %	Race/ ethnicity, %	Socioeconomic status	Screening tests
Adolescents	Bastiani, 2013[57]	Fair	ITA	High School	Adolescents, aged 15-19 years, using cannabis in previous year	5787	17.0	50.8	NR	NR	SDS CAST CAST (binary)
	Chung, 2003[66]	Fair	US	ED	Adolescents age 13-19 years	442	15.7	40.3	White: 67.6 Black: 7.9 Hispanic: 16.7	50% with high school-educated parent	AUDIT AUDIT-C Single question, cannabis
	D'Amico, 2016[64]	Good	US	Primary care	Adolescents, aged 12-18 years	1573	15.5	57.5	White: 14.7 Black: 26.7 Hispanic: 51.4	NR	CRAFFT AUDIT NIAAA Youth Screen PESQ-PS
	Fernandez-Artamendi, 2012[59]*	Fair	ESP	High School	Students, 16-20 years, using cannabis in the past month	144	17.4	28.5	NR	2.1% living in residential care facility	CAST CPQ-A-S
	Gryczynski, 2015[54]	Fair	US	Primary care	Adolescents, aged 12-17 years	525	NR	54	White: <1 Black: 93 Hispanic: 3	3% in college or not enrolled in high school	ASSIST ASSIST-Lite
	Harris, 2016[52]	Good	US	Primary care	Adolescents, aged 12-17 years	136	15.0	54.4	White: 18.4 Black: 27.9 Hispanic: 24.3	58% with college graduate parent(s)	CRAFFT Single question, cannabis

Table 3. Study and population characteristics, by subpopulation (KQ 2)

Target pop	Author, year	Quality rating	Country	Recruitment setting	Brief population description	N screened	Age, mean	Female, %	Race/ ethnicity, %	Socioeconomic status	Screening tests
Adolescents	Kelly, 2014[42]	Fair	US	Primary care	Adolescents, aged 12-17 years	525	NR	54.5	White: 0.8 Black: 92.8 Hispanic: NR	2.5% not enrolled in school	BSTAD POSIT POSIT revised
	Knight, 2002[46]	Good	US	Primary care	Adolescents aged 14-18 years	538	NR	68.4	White: 24.2 Black: 50.6 Hispanic: 18.8	NR	CRAFFT
	Legleye, 2011[60]	Good	FRA	Community-based	Adolescents, currently using cannabis	2566	17.0	41.9	NR	5.1% not enrolled in school	CAST CAST (binary)
	Mitchell, 2014[56]	Fair	US	Primary care	Adolescents, aged 12-17 years	525	NR	54.5	White: NR Black: 92 Hispanic: NR	13% not enrolled in school	CRAFFT
	Rial, 2018[67]	Fair	ESP	High School	Adolescents attending secondary education	569	14.7	42.9	NR	NR	CRAFFT POSIT
Adults	Beaudoin, 2016[65]	Good	US	ED	Adults 50 years or older using prescription opioids in the past 30 days	112	NR	52.7	White: 72.1 Black: 18.0 Hispanic: 9.8	79.5% HS grad or more	PDUQp
	Brown, 2001[48]	Good	US	Primary care	Adults, aged 18-59 years	702	NR	67.9	White: 83.3 Black: 12.1 Hispanic: 1.8	87% HS grad or more	TICS

Table 3. Study and population characteristics, by subpopulation (KQ 2)

Target pop	Author, year	Quality rating	Country	Recruitment setting	Brief population description	N screened	Age, mean	Female, %	Race/ ethnicity, %	Socioeconomic status	Screening tests
Adults	Dawson, 2010[61]	Fair	US	Community-based	Adults, aged ≥18 years	42923	NR	NR	NR	NR	Single-item alcohol HED
	Kumar, 2016[51]	Good	US	Primary care	Adults ≥18 years	399	46.8	48.4	White: 19.8 Black: 47.9 Hispanic: NR	82% HS grad or more	ASSIST
	Lane, 2007[62]	Fair	US	Primary care	Caregivers of children aged under 6 years	216	25.2	94.0	NR	65% HS grad or more	PSQ
	Legleye, 2015†[55]	Fair	FRA	Community-based	Adolescents and adults, aged 15-64 years, using cannabis in the past year	550	29.0	32.9	NR	NR	CAST
	Legleye, 2018[68‖]	Good	FRA	Community-based	Adolescents and adults, aged 15-64 years, using cannabis in the past year	1351	NR	44.0	NR	NR	CAST
	McCann, 2000[49]	Fair	US	Other medical	Adults seeking evaluation for ADHD	139	36.4	30.9	White: 95.7 Black: NR Hispanic: NR	NR	DAST-28

Table 3. Study and population characteristics, by subpopulation (KQ 2)

Target pop	Author, year	Quality rating	Country	Recruitment setting	Brief population description	N screened	Age, mean	Female, %	Race/ ethnicity, %	Socioeconomic status	Screening tests
Adults	McNeely, 2016[50]	Fair	US	Primary care	Adults, aged ≥18 years	2057	46.0	56.2	White: 33.4 Black: 55.6 Hispanic: NR	81% HS grad or more	TAPS TAPS-1
	McNeely, 2015[43, 70]	Good	US	Primary care	Adults, aged 21-65 years	586	46.0	49.8	White: 18.7 Black: 50.2 Hispanic: 21.7	84% HS grad or more	SUBS Single-item drug frequency question, drug‡
	Smith, 2010[45, 69]	Good	US	Primary care	Adults, aged ≥18 years	286	49.0	54.2	White: 17.1 Black: 62.6 Hispanic: 16.1	72% HS grad or more	DAST-10 Single-item drug frequency question§ Single-item alcohol HED
	Tiet, 2015[44, 72]	Fair	US	Primary care	VA adults	640	62.6	4.7	White: 57.5 Black: NR Hispanic: NR	76% HS grad or more	ASSIST-Drug SoDU DAST-2

Table 3. Study and population characteristics, by subpopulation (KQ 2)

Target pop	Author, year	Quality rating	Country	Recruitment setting	Brief population description	N screened	Age, mean	Female, %	Race/ ethnicity, %	Socioeconomic status	Screening tests
Pregnant/ Postpartum women	Chasnoff, 2007[47]	Fair	US	Primary care	Pregnant women, aged ≥18 years	228	NR	100	NR, target population was 80% Black and 20% Hispanic	NR, 40% of residents were under 185% of the poverty level at the time of the 1990 census. Medicaid or a Medicaid-managed care plan covered all the patients	4P's Plus
	Harrison, 2012[63]	Fair	US	Primary care	Pregnant women	745	23.0	100	White: 10.2 Black: 58.7 Hispanic: 7.9		PRO
	Lam, 2015[53]	Fair	HKG	Primary care	Pregnant women (<20 wks gestation)	1082	31.0	100	NR	2.4% on public financial assistance	DAST-10
	Grekin, 2010[15]	Fair	US	Hospital	Postpartum women in post-delivery recovery	274	NR	100	White: NR Black: 90.3 Hispanic: NR	68% HS grad or more 84.5% receiving some form of public assistance	DAST-10
	Ondersma, 2012[58]	Good	US	Hospital	Postpartum women in post-delivery recovery	100	NR	100	White: NR Black: 94 Hispanic: NR	72% HS grad or more 86% receiving some form of public assistance	ASSIST-2 (modified) DAST-10 WIDUS

* Includes young adults, but the study sample mean age was 17 years
† Includes adolescents, but the study sample mean age was 29 years

Table 3. Study and population characteristics, by subpopulation (KQ 2)

‡ How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons (for example, because of the experience or feeling it caused)?
§ How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?
‖ Includes adolescents, but assume the majority of the sample was adults

Abbreviations: ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; AUDIT = Alcohol Use Disorders Identification Test; AUDIT-C = Alcohol Use Disorders Identification Test - Consumption ; BSTAD = Brief Screener for Tobacco, Alcohol, and Other Drugs; CAST = Cannabis Abuse Screening Test; CPQ-A-S = Cannabis Problems Questionnaire for Adolescents Shortened; CRAFFT = Car Relax Alone Forget Family/Friends Trouble; DAST-2 = 2-Item Drug-Abuse Screening Test; DAST-10 = 10-Item Drug-Abuse Screening Test; DAST-28 = 28-Item Drug-Abuse Screening Test; ED = emergency department; ESP = Spain; FRA = France; HED = heavy episodic drinking; HKG = Hong Kong; HS = high school; ITA = Italy; KQ = key question; NR = not reported; PDUQp = Prescription Drug Use Questionnaire Patient Version; PESQ-PS = Personal Experience Screening Questionnaire; pop = population; PRO = Prenatal Risk Overview; PSQ = Parent Screening Questionnaire; SDS = Severity of Dependence Scale; SES = socioeconomic status; SoDU = Screen of Drug Use; SUBS = Substance Use Brief Screen; TAPS = Tobacco, Alcohol, Prescription Medication, and Other Substance Use; TICS = Two-Item Conjoint Screen; US = United States; WIDUS = Wayne Indirect Drug Use Screener; wks = weeks

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Frequency-based	ASSIST-2 (modified)	Alcohol, Smoking and Substance Involvement Screening Test (First 2 items of standard ASSIST, modified)*	2	Tobacco, Alcohol, Cannabis, Cocaine, Amphetamines, Inhalants, Sedatives, Hallucinogens, Opioids, Other (nonspecified)	1. In your life, which of the following substances have you ever used?* 2. In the past 3 months, how often have you used the substances you mentioned?	Self, electronic	Pregnant women (Ondersma, 2012[58])
	BSTAD	Brief Screener for Tobacco, Alcohol, and Other Drugs	6	Tobacco, Alcohol, drugs†	1. Do you have friends who smoked cigarettes or used other tobacco products in the past year? 2. Do you have friends who drank beer, wine, or any drink containing alcohol in the past year? 3. Do you have friends who in the past year sniffed or huffed anything; took illegal drugs like marijuana, cocaine, etc.; took prescription medications that were not prescribed for them; or took prescription or over-the-counter medications and took more than they were supposed to take? 4. In the past year have you smoked cigarettes or used other tobacco products in the past year? 5. In the past year have you drank beer, wine, or any drink containing alcohol in the past year? 6. In the past year have you sniffed or huffed anything; taken illegal drugs like marijuana, cocaine, etc.; taken prescription medications that were not prescribed for them; or taken prescription or over-the-counter medications and took more than you were supposed to take? a. In the past 30 days, on how many days have you used SPECIFIC SUBSTANCE? b. In the past 90 days, on how many days have you used SPECIFIC SUBSTANCE? c. In the past year, on how many days have you used SPECIFIC SUBSTANCE?	Self, electronic Interviewer, face-to-face	Adolescents (Kelly, 2014[42])

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Frequency-based	Single-item cannabis frequency		2	Marijuana	1. During the past 12 months, did you ever use any marijuana? 2. During the past 3 months, about how often did you use marijuana?	Self, electronic Interviewer, face-to-face	Adolescents (Harris, 2016[52], Chung, 2003[66])
	Single-item drug frequency	NA	1	Illegal drugs, prescription medication	1. How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons (for example, because of the experience or feeling it caused)?	Interviewer, face-to-face Self, electronic	Adults (McNeely, 2015[43, 70],Smith, 2010[45, 73])
	SUBS	Substance Use Brief Screen	4	Tobacco, Alcohol, Illegal drug (including marijuana), recreational prescription medications†	1. In the past 12 months, on how many days did you use tobacco? 2. In the past 12 months, on how many days did you have 4 or more alcohol drinks in a day, including wine or beer? 3. In the past 12 months, on how many days did you use any illegal drug, including marijuana? 4. In the past 12 months, on how many days did you use any prescription medication "recreationally" (just for the feeling, or using more than prescribed)?	Self, electronic	Adults (McNeely, 2015[43])
	TAPS-1	Tobacco, Alcohol, Prescription Medication, and Other Substance use – rapid screener	4	Tobacco, Alcohol, Illegal drug (including marijuana), prescription medications	In the past 12 months, how often have you: 1. Used any tobacco product (for example, cigarettes, e-cigarettes, cigars, pipes, or smokeless tobacco)? 2. Had 5/4 (M/F) or more drinks containing alcohol in one day? 3. Used any drugs including marijuana, cocaine or crack, heroin, methamphetamine (crystal meth), hallucinogens, ecstasy (MDMA)? 4. Used any prescription medications just for the feeling, more than prescribed, or that were not prescribed for you? (Prescription medications that may be used in this way include: opioid pain relievers (e.g., Oxycontin, Vicodin, Percocet, methadone), medications for anxiety or sleeping (e.g., Xanax, Ativan, Klonopin), medications for ADHD (e.g., Adderall or Ritalin)	Self, electronic Interviewer, face-to-face	Adults (McNeely, 2016)[50, 74]

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Risk assessment	ASSIST	Alcohol, Smoking and Substance Involvement Screening Test	8‡	Tobacco, Alcohol, Cannabis, Cocaine, Amphetamines, Inhalants, Sedatives, Hallucinogens, Opioids, Other (nonspecified)	1. In your life, which of the following substances have you ever used? 2. In the past 3 months, how often have you used the substances you mentioned? 3. During the past 3 months, how often have you had a strong desire or urge to use the substance? 4. During the past 3 months, how often has your use of the substance led to health, social, legal, or financial problems? 5. During the past 3 months, how often have you failed to do what was normally expected of you because of your use of the substance? 6. Has a friend or relative or anyone else ever expressed concern about your use? 7. Have you ever tried and failed to control, cut down, or stop using? 8. Have you ever used any drug by injection? (Includes opening question to assess use)	Interviewer, face-to-face Self, electronic	Adolescents (Gryczynski, 2015[54]) Adults (Kumar, 2016[51])
	ASSIST-Drug	Alcohol, Smoking and Substance Involvement Screening Test - Drug	2	Drugs	1. How many days in the past 12 months have you used drugs? 2. How many days in the past 12 months have you had a strong desire or urge to use drugs?	Interviewer, face-to-face	Adults (Tiet, 2015[44, 72])
	ASSIST-Lite (Cannabis)	Alcohol, Smoking and Substance Involvement Screening Test Lite (for Cannabis)	3	Cannabis	1. Did you use cannabis in the past 3 months? 2. Have you had a strong desire or urge to use cannabis at least once a week or more often? 3. Has anyone expressed concern about your cannabis use?	Interviewer, face-to-face	Adolescents (Gryczynski, 2015[54])

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Risk assessment	CAST	Cannabis Abuse Screening Test	6	Cannabis	1. Have you smoked cannabis before midday? 2. Have you smoked cannabis when you were alone? 3. Have you had memory problems when you smoked cannabis? 4. Have friends or family members told you that you should reduce or stop your cannabis consumption? 5. Have you tried to reduce or stop your cannabis use without succeeding? 6. Have you had problems because of your cannabis use (argument, fight, accident, poor results at school, etc.)?	Interviewer, phone Self, paper-pencil Self, electronic	Adolescents (Bastiani, 2013[57], Legleye, 2011[60], Fernandez-Artamendi, 2012[59]) Adults (Legleye, 2015,[55] Legleye, 2018[68])
	CPQ-A-S	Cannabis Problems Questionnaire for Adolescents Shortened	12	Cannabis	1. Have you tended to smoke more on your own than you used to? 2. Have you worried about meeting people you don't know when you are stoned? 3. Have you spent more time with smoking friends than other kinds of friends? 4. Have your friends criticized you for smoking too much? 5. Have you found yourself worried about the amount of money you have been spending on cannabis? 6. Have you been in trouble with the police due to your smoking? 7. Have you been physically sick after smoking? 8. Have you passed out after a smoking session? 9. Have you had pains in your chest or lungs after a smoking session? 10. Have you had a persistent chest infection or cough? 11. Have you felt paranoid or antisocial after a smoking session? 12. Have you worried about getting out of touch with friends or family?	Self, electronic	Adolescents (Fernandez-Artamendi, 2012[59])

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Risk assessment	CRAFFT	Car Relax Alone Forget Friends Trouble	6	Alcohol, drugs	1. Have you ever ridden in a CAR driven by someone (including yourself) who was "high" or had been using alcohol or drugs? 2. Do you ever use alcohol or drugs to RELAX, feel better about yourself, or fit in? 3. Do you ever use alcohol/drugs while you are by yourself, ALONE? 4. Do you ever FORGET things you did while using alcohol or drugs? 5. Do your family or FRIENDS ever tell you that you should cut down on your drinking or drug use? 6. Have you gotten into TROUBLE while you were using alcohol or drugs? (Includes opening question to assess use)	Interviewer, face-to-face Self, electronic Self, paper-pencil	Adolescents (Knight, 2002[46], Harris, 2016[52], Mitchell, 2014[56], D'Amico, 2016,[64] Rial, 2018[67, 77])
	DAST-2	Drug Abuse Screening Test-2 items	2	Drugs	1. How many days in the past 12 months have you felt bad or guilty about your drug use? 2. How many days in the past 12 months have you used drugs other than those required for medical reasons?	Interviewer, face-to-face	Adults (Tiet, 2015[44, 75])

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Risk assessment	DAST-10	Drug Abuse Screening Test-10 items	10	Drugs	1. Have you used drugs other than those required for medical reasons? 2. Do you abuse more than one drug at a time? 3. Are you always able to stop using drugs when you want to? 4. Have you had "blackouts" or "flashbacks" as a result of drug use? 5. Do you ever feel bad or guilty about your drug use? 6. Does your spouse (or parents) ever complain about your involvement with drugs? 7. Have you neglected your family because of your use of drugs? 8. Have you engaged in illegal activities in order to obtain drugs? 9. Have you ever experienced withdrawal symptoms (felt sick) when you stopped taking drugs? 10. Have you had medical problems as a result of your drug use (e.g., memory loss, hepatitis, convulsions, bleeding, etc.)?	Interviewer, face-to-face Self, paper-pencil Self, electronic	Adults (Smith, 2010[45]) Pregnant women (Lam, 2015[53], Ondersma, 2012[58], Grekin, 2010[15])

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Risk assessment	DAST-28	Drug Abuse Screening Test-28 items	28	Drugs	1. Have you used drugs other than those required for medical reasons? 2. Have you abused prescription drugs? 3. Do you abuse more than one drug at a time? 4. Can you get through the week without using drugs (other than those required for medical reasons)? 5. Are you always able to stop using drugs when you want to? 6. Do you abuse drugs on a continuous basis? 7. Do you try to limit your drug use to certain situations? 8. Have you had "blackouts" or "flashbacks" as a result of drug use? 9. Do you ever feel bad about your drug abuse? 10. Does your spouse (or parents) ever complain about your involvement with drugs? 11. Do your friends or relatives know or suspect you abuse drugs? 12. Has drug abuse ever created problems between you and your spouse? 13. Has any family member ever sought help for problems related to your drug use? 14. Have you ever lost friends because of your use of drugs? 15. Have you ever neglected your family or missed work because of your use of drugs? 16. Have you ever been in trouble at work because of drug abuse? 17. Have you ever lost a job because of drug abuse? 18. Have you gotten into fights when under the influence of drugs? 19. Have you ever been arrested because of unusual behavior while under the influence of drugs? 20. Have you ever been arrested for driving while under the influence of drugs? 21. Have you engaged in illegal activities to obtain drugs? 22. Have you ever been arrested for possession of illegal drugs? 23. Have you ever experienced withdrawal symptoms as a result of heavy drug intake? 24. Have you had medical problems as a result of your drug use (e.g., memory loss, hepatitis, convulsions, or bleeding)? 25. Have you ever gone to anyone for help for a drug problem? 26. Have you ever been in hospital for medical problems related to your drug use? 27. Have you ever been involved in a treatment program specifically related to drug use? 28. Have you been treated as an outpatient for problems related to drug abuse?	Interviewer, face-to-face	Adults (McCann, 2000[49])

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Risk assessment	PESQ-PS	Personal Experience Screening Questionnaire Problem Severity Scale	18	Alcohol, drugs	How often have you used alcohol or other drugs: 1. At home 2. At places on the street where adults hang around 3. With older friends 4. At the homes of friends or relatives 5. At school activities, such as dances or football games 6. At work 7. When skipping school 8. To enjoy music or colors, or feel more creative How often have you: 9. Made excuses to your parents about your alcohol or drug use 10. Gotten drugs from a dealer 11. Used alcohol or drugs secretly, so no one would know you were using 12. Made excuses to teachers about your alcohol or drug use 13. Been upset about other people talking about your using or drinking When using alcohol or other drugs, how often have you: 14. Spilled things, bumped into things, fallen down, or had trouble walking around 15. Seen, felt, or heard things that were not there 16. Spent money on things you wouldn't normally buy 17. Found out things you said or did while using or drinking that you did not remember In order to get or pay for alcohol or other drugs, how often have you: 18. Sold drugs	Self, paper-pencil	Adolescents (D'Amico, 2016[64])

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Risk assessment	POSIT Substance Use and Abuse Subscale	Problem Oriented Screening Instrument for Teenagers, Substance Use and Abuse Subscale	17	Alcohol, drugs	1. Do you get into trouble because you use drugs or alcohol at school? 2. Have you accidentally hurt yourself or someone else while high on alcohol or drugs? 3. Do you miss out on activities because you spend too much money on drugs or alcohol? 4. Do you ever feel you are addicted to alcohol or drugs? 5. Have you started using more and more drugs or alcohol to get the effect you want? 6. Do you ever leave a party because there is no alcohol or drugs? 7. Do you have a constant desire for alcohol or drugs? 8. During the past month have you driven a car while you were drunk or high? 9. Have you had a car accident while high on drugs or alcohol? 10. Do you forget things you did while drinking or using drugs? 11. Does alcohol or drug use cause your moods to change quickly like from happy to sad or vice versa? 12. Do your family or friends ever tell you that you should cut down on your drinking or drug use? 13. Do you have serious arguments with friends or family members because of your drinking or drug use? 14. Does your alcohol or drug use ever make you do something you would not normally do, like breaking rules, missing curfew, breaking the law or having sex with someone? 15. Do you miss school or arrive late for school because of your alcohol or drug use? 16. Do you have trouble getting along with any of your friends because of your alcohol or drug use? 17. Do you ever feel you can't control your drug use?	Interviewer, face-to-face	Adolescents (Rial, 2018,[67, 77] Kelly, 2014[42, 76])

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Risk assessment	POSIT revised	Problem-Oriented Screening Instrument for Teenagers, revised	11	Alcohol, drugs	1. Do you ever feel you are addicted to drugs? 2. Have you started using more and more drugs or alcohol to get the effect you want? 3. Does your alcohol or drug use ever make you want to do something you would not normally do – like breaking rules, missing curfew, breaking the law, or having sex with someone? 4. Do you forget things you did while drinking or using drugs? 5. Do your family and friends ever tell you that you should cut down on your drinking or drug use? 6. Do you have a constant desire for alcohol or drugs? 7. Do you ever feel you can't control your alcohol or drug use? 8. Do you have serious arguments with friends or family members because of your drinking or drug use? 9. Do you miss out on activities because you spend too much money on drugs or alcohol? 10. Does alcohol or drug use cause your moods to change quickly like form happy to sad or vice versa? 11. Have you accidentally hurt yourself or someone else while high on alcohol or drugs?	Self, NR	Adolescents (Kelly, 2014[42, 76])
	PRO	Prenatal Risk Overview-Drug Use	3	Drugs	1. During the 12 months before you knew you were pregnant, on how many days did you use marijuana or any other drug not prescribed for you by your doctor? 2. During the past 12 months, have you neglected your responsibilities because of drug use? 3. Since you have known you were pregnant, on how many days did you use marijuana or any other drug not prescribed for you by your doctor?	Interviewer, face-to-face	Pregnant women (Harrison, 2012[63])
	PSQ	Parent Screening Questionnaire	2	Alcohol, drugs	1. In the past year, have you or your partner had a problem with drugs or alcohol? 2. In the past year, have you or your partner felt the need to cut back on drinking or drug use?	Self, electronic	Adults (Lane, 2007[62])

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Risk assessment	PDUQp	Prescription Drug Use Questionnaire, patient version	31	Prescription opioids	1. Do you have more than one painful condition? 2. Are you disabled by pain (unable to work or participate fully in activities)? 3. Are you receiving any disability payments (such as SSI, or VA disability)? 4. Do you have any current lawsuits or claims related to your pain problem? 5. Have you tried any non-medication treatments for your pain problem (such as physical therapy, TENS, biofeedback) 6. Has your pain been adequately treated over the past 6 months? 7. Do you feel at all angry or mistrustful toward your previous doctors? 8. Have you been given pain medications from more than one clinic over the past 6 months? 9. Have you ever been or do you think you might currently be addicted to pain medications? 10. Has a doctor ever told you that you were addicted to pain medications? 11. Have you had to increase the amount of pain medications you take over the past 6 months? 12. Have you had to call in for more pain medications because your prescription ran out? 13. Have you used the pain medications to help other symptoms such as problems sleeping, anxiety, or depression? 14. Do you save up unused medications in case you might need them in the future? 15. Do you ever use alcohol to help relieve some of the pain? 16. Do you think certain pain medications (such as vicodin, codeine, or percocet) work better for you and you prefer to take them and not others? 17. Have you ever lost your pain medications and needed them replaced? 18. Have you had to visit the emergency room in the past 6 months because of your pain problem? 19. Have you ever had to buy pain medications on the street? 20. Have doctors ever refused to give you the pain medications you felt you needed because of fear that you might abuse them? 21. Is anyone in your family or among your friends concerned that you might be addicted to pain medications? 22. Do any of your family members disagree with your use of pain medications? 23. Does anyone in your family help to take care of you due to your pain problem?	Self, electronic	Adults (Beaudoin, 2016[65])

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Risk assessment					24. Does your spouse or significant other have problems with drugs or alcohol? 25. Have those in your family or among your friends ever obtained pain medications for you? 26. Have you ever borrowed pain medications from a friend or family member? 27. Has anyone in your immediate family (father, mother, siblings) ever had a problem with drugs or alcohol? 28. Has anyone in your immediate family (father, mother, siblings) ever had a problem with chronic pain? 29. Have you ever had an alcohol or drug addiction problem? 30. Have you ever been treated for an alcohol or drug abuse problem? 31. Have you ever been taken partially or completely off pain medications to decrease your tolerance?		
	SDS	Severity Dependence Scale	5	Cannabis	During the past year: 1. Did you think your use of cannabis was out of control? 2. Did the prospect of missing a dose of cannabis makes you anxious or worried? 3. Did you worry about your use of cannabis? 4. Did you wish you could stop the use of cannabis? 5. How difficult did you find it to stop, or go without cannabis?	Self, paper-pencil	Adolescents (Bastiani, 2013[57])
	SoDU	Screen of Drug Use	2	Drugs	1. How many days in the past 12 months have you used drugs other than alcohol? 2. How many days in the past 12 months have you used drugs more than you meant to?	Interviewer, face-to-face	Adults (Tiet, 2015[44, 72])

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Risk assessment	TAPS	Tobacco, Alcohol, Prescription Medication, and Other Substance Use	5-26§	Marijuana, cocaine or crack, heroin, methampheta mine, hallucinogens, ecstasy/MDMA , prescription medications†	1. In the past 12 months, how often have you used any drugs, including marijuana, cocaine or crack, heroin, methamphetamine (crystal meth), hallucinogens, or ecstasy/MDMA? a. In the past 3 months, did you use SPECIFIC SUBSTANCE? i. In the past 3 months, have you had a strong desire or urge to use SPECIFIC SUBSTANCE at least once a week or more often? ii. In the past 3 months, has anyone expressed concern about your use of SPECIFIC SUBSTANCE? 2. In the past 12 months, how often have you used any prescription medications (opiate pain reliever/medication for anxiety or sleep/medication for ADHD) just for the feeling, more than prescribed, or that were not prescribed for you? a. In the past 3 months, did you use SPECIFIC SUBSTANCE not as prescribed or that was not prescribed for you? i. In the past 3 months, have you tried and failed to control, cut down, or stop using SPECIFIC SUBSTANCE? ii. In the past 3 months, has anyone expressed concern about your use of SPECIFIC SUBSTANCE? 3. Any drugs or prescription medications a. In the past 3 months, did you use any other illegal or recreational drug (for example, ecstasy, molly, GHB, poppers, LSD, mushrooms, special K, bath salts, synthetic marijuana (”spice”), whip-its, etc.)? (no = 0, yes = 1) b. In the past 3 months, what were the other drug(s) you used? (fill in response)	Self, electronic Interviewer, face-to-face	Adults (McNeely, 2016[50])
	TICS	Two-Item Conjoint Screen	2	Alcohol, drugs	1. In the last year, have you ever drunk or used drugs more than you meant to? 2. Have you felt you wanted or needed to cut down on your drinking or drug use in the last year?	Interviewer, face-to-face	Adults (Brown, 2001[48])

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Indirect[¶]	AUDIT-C	Alcohol Use Disorders Identification Test - Consumption	3	Alcohol	1. How often do you have a drink containing alcohol? 2. How many drinks containing alcohol do you have on a typical day when you are drinking? 3. How often do you have 6 or more drinks on one occasion?		Adolescents (Chung, 2003[66])
	AUDIT	Alcohol Use Disorders Identification Test	10	Alcohol	1. How often do you have a drink containing alcohol? 2. How many drinks containing alcohol do you have on a typical day when you are drinking? 3. How often do you have 6 or more drinks on one occasion? 4. How often during the last year have you found that you were not able to stop drinking once you had started? 5. How often during the last year have you failed to do what was expected of you because of drinking? 6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session? 7. How often during the last year have you had a feeling of guilt or remorse after drinking? 8. How often during the last year have you been unable to remember what happened the night before because of your drinking? 9. Have you or someone else been injured because of your drinking? 10. Has a relative, friend, or doctor, or other health care worker been concerned about your drinking or suggested you cut down? (Includes opening question to assess use)	Interviewer, face-to-face Self, electronic	Adolescents (D'Amico, 2016[64] Chung, 2003[66])
	NIAAA Youth Screen	National Institute on Alcohol Abuse and Alcoholism Screening Guide	2	Alcohol	1. In the past year, on how many days have you had more than a few sips of beer, wine, or any drink containing alcohol? Do any of your friends drink alcohol?[‖]	Interviewer, face-to-face	Adolescents (D'Amico, 2016[64])
	Single-item HED frequency	NA	1	Alcohol	1. How many times in the past year have you had 5/4 (male/female) or more drinks in a day? (Often includes opening question to assess use)	Interviewer, face-to-face	Adults (Dawson, 2010[61], Smith, 2010[45, 69, 73])

Table 4. Properties of screening instruments (KQ 2)

Tool type	Tool name	Full name	No. of items	Substances addressed	Questions	Admin methods	Population addressed (Authors)
Indirect¶	WIDUS	Wayne Indirect Drug Use Screener	6	Cigarettes	1. I am currently married 2. In the past year I have been bothered by pain in my teeth or mouth 3. I have smoked at least 100 cigarettes in my entire life 4. Most of my friends smoke cigarettes 5. There have been times in my life, for at least 2 weeks straight, where I felt like everything was an effort 6. I get mad easily and feel a need to blow off some steam	Self, electronic	Pregnant women (Ondersma, 2012[58])
	4P's Plus	Parents Partner Past Pregnancy	5	Alcohol, tobacco#	1. Did either of your parents ever have a problem with alcohol or drugs? 2. Does your partner have a problem with alcohol or drugs? 3. Have you ever drunk beer, wine, or liquor? 4. In the month before you knew you were pregnant, how many cigarettes did you smoke? 5. In the month before you knew you were pregnant, how many beers/how much wine/how much liquor did you drink?	Interviewer, face-to-face	Pregnant women (Chasnoff, 2007[47])

* Specific modifications not reported by study
† Tobacco and alcohol were included in the screening test, but those questions were not used to determine who screened
‡ Questions 1-7 of the ASSIST each contain specific questions regarding up to 10 substance classes. The number of items delivered depends on the responses given to Question 1 and Question 2
§ Five initial questions for specific substance groups followed by 3-4 optional questions for each substance that are asked only if one of the first 5 questions is answered affirmatively
‖ Order of questions varied depending on age
¶ Targets only substances other than drugs (like alcohol or tobacco) and/or other social factors associated with drug use
# Parents' and partners' alcohol and drug use were assessed in addition to participant's use of alcohol and tobacco

Abbreviations: Admin = administration; ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; AUDIT = Alcohol Use Disorders Identification Test; BSTAD = Brief Screener for Tobacco, Alcohol, and Other Drugs; CAST = Cannabis Abuse Screening Test; CPQ-A-S = Cannabis Problems Questionnaire for Adolescents Shortened; CRAFFT = Car Relax Alone Forget Family/Friends Trouble; DAST-10 = 10-Item Drug-Abuse Screening Test; DAST-28 = 28-Item Drug-Abuse Screening Test; HED = heavy episodic drinking; No. = number; PESQ-PS = Personal Experience Screening Questionnaire; PRO = Prenatal Risk Overview; PSQ = Parent Screening Questionnaire; SDS = Severity of Dependence Scale; SoDU = Screen of Drug Use; SUBS = Substance Use Brief Screen; TAPS = Tobacco, Alcohol, Prescription Medication, and Other Substance Use; TICS = Two-Item Conjoint Screen; WIDUS = Wayne Indirect Drug Use Screener

Table 5. Results of screening accuracy studies among adolescents (KQ 2), by tool type and specific test

Tool type	Tool name	Tool cutoff*	Author, year	Reference standard	Condition	Condition, %	Total n	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
Frequency-based	BSTAD	2+[†]	Kelly, 2014[42]	CIDI-2	Cannabis use disorder	10.7	525	0.80 (0.69, 0.89)	0.93 (0.91, 0.95)	0.87 (NR)
	Single-item frequency, cannabis	2+/year	Chung, 2003[66]	DISC	Cannabis abuse or dependence	15.4	442	0.96 (0.88, 0.98)	0.86 (0.82, 0.89)	NR
	Single-item frequency, cannabis (self-administered)	12-month use	Harris, 2016[52]	TLFB	Cannabis use in past year	18.4	136	0.72 (0.52, 0.86)	1.00 (0.97, 1.00)	NR
	Single-item frequency, cannabis (interviewer-administered)	12-month use	Harris, 2016[52]	TLFB	Cannabis past year use	18.4	136	0.79 (0.58, 0.91)	0.99 (0.94, 1.00)	NR
	Single-item frequency, cannabis (self-administered)	3-month use	Harris, 2016[52]	ADI	Cannabis abuse or dependence	5.9	136	0.88 (0.46, 0.98)	0.93 (0.86, 0.96)	NR
	Single-item frequency, cannabis (interviewer-administered)	3-month use	Harris, 2016[52]	ADI	Cannabis abuse or dependence	5.9	136	0.86 (0.41, 0.98)	0.91 (0.85, 0.95)	NR
Risk assessment	ASSIST	2+	Gryczynski, 2015[54]	CIDI-2	Cannabis unhealthy use[‡]	15.2	525	0.975 (0.91, 0.98)	0.912(0.88, 0.94)	0.94 (NR)
	ASSIST	2+	Gryczynski, 2015[54]	CIDI-2	Cannabis use disorder	10.7	525	0.982 (0.91, 1.0)	0.868 (0.83, 0.90)	0.93 (NR)
	ASSIST	7+	Gryczynski, 2015[54]	CIDI-2	Cannabis moderate-severe use disorder	NR	525	1.0 (NR[§])	0.92 (NR[§])	0.96 (NR)

Table 5. Results of screening accuracy studies among adolescents (KQ 2), by tool type and specific test

Tool type	Tool name	Tool cutoff*	Author, year	Reference standard	Condition	Condition, %	Total n	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
Risk assessment	ASSIST-Lite	1+	Gryczynski, 2015[54]	CIDI-2	Cannabis use disorder	10.7	525	0.96 (0.88, 0.99)	0.88 (0.85, 0.91)	0.92 (NR)
	CAST	3+	Legleye, 2011[60]	M-CIDI	Cannabis abuse or dependence‖	35.7	2566	0.795 (0.77, 0.82)	0.809 (0.79, 0.83)	0.877 (NR)
	CAST	6+	Bastiani, 2013[57]	M-CIDI	Cannabis dependence¶	15.5	5787	0.803 (0.78, 0.83)	0.801 (0.79, 0.81)	0.875 (0.861, 0.888)
	CAST	5+	Fernandez-Artamendi, 2012[59]	NSDUH	Cannabis dependence	31.9	144	0.83 (0.589, 0.857)	0.87 (0.858, 0.971)	0.929 (NR)
	CAST	3+	Legleye, 2011[60]	M-CIDI	Cannabis dependence‖	22.1	2566	0.841 (0.81, 0.87)	0.717 (0.70, 0.74)	0.854 (NR)
	CAST (binary)	2+	Legleye, 2011[60]	M-CIDI	Cannabis abuse or dependence‖	35.7	2566	0.706 (0.68, 0.73)	0.873 (0.86, 0.89)	0.859 (NR)
	CAST (binary)	3+	Bastiani, 2013[57]	M-CIDI	Cannabis dependence¶	15.5	5787	0.783 (0.75, 0.81)	0.823 (0.81, 0.83)	0.869 (0.855, 0.883)
	CAST (binary)	2+	Legleye, 2011[60]	M-CIDI	Cannabis dependence	22.1	2566	0.776 (0.74, 0.81)	0.792 (0.77, 0.81)	0.849 (NR)
	CPQ-A-S	3+	Fernandez-Artamendi, 2012[59]	NSDUH	Cannabis dependence	31.9	144	0.83 (0.686, 0.922)	0.775 (0.680, 0.854)	0.881 (NR)
	CRAFFT	2+	Knight, 2002[46]	ADI + POSIT	Alcohol or drug unhealthy use#	26.8	538	0.76 (0.68, 0.83)	0.94 (0.92, 0.96)	0.92 (NR)
	CRAFFT	2+	Mitchell, 2014[56]	CIDI-2	Alcohol or drug unhealthy use**	18.5	525	0.79 (0.71, 0.87)	0.97 (0.95, 0.98)	0.93 (NR)
	CRAFFT	2+	Knight, 2002[46]	ADI	Alcohol or drug abuse or dependence	16.2	538	0.80 (0.72, 0.89)	0.86 (0.83, 0.89)	0.90 (NR)
	CRAFFT	2+	Mitchell, 2014[56]	CIDI-2	Alcohol or drug abuse or dependence	12.4	525	0.91 (0.83, 0.97)	0.93 (0.90, 0.95)	0.97 (NR)
	CRAFFT	2+	Rial, 2018[67, 77]	ADI	All substances use disorder	26.8	312	0.744 (0.64, 0.82)	0.964 (0.93, 0.98)	0.946 (NR)

Table 5. Results of screening accuracy studies among adolescents (KQ 2), by tool type and specific test

Tool type	Tool name	Tool cutoff*	Author, year	Reference standard	Condition	Condition, %	Total n	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
Risk assessment	CRAFFT	2+	Mitchell, 2014[56]	CIDI-2	Alcohol or drug moderate-severe use disorder	NR	525	0.88 (0.75, 0.97)	0.87 (0.84, 0.90)	0.95 (NR)
	CRAFFT	2+	Knight, 2002[46]	ADI	Alcohol or drug dependence	6.7	538	0.92 (0.82, 1.00)	0.80 (0.77, 0.83)	0.93 (NR)
	CRAFFT	2+	D'Amico, 2016[64]	DISC-IV	Cannabis past year use	36.6	1567	0.68 (0.64, 0.72)	0.92 (0.90, 0.94)	NR
	CRAFFT	2+	D'Amico, 2016[64]	DISC-IV	Cannabis unhealthy use††	19.3	1567	0.84 (0.79, 0.88)	0.83 (0.81, 0.85)	NR
	CRAFFT (self-administered)	2+	D'Amico, 2016[64]	DISC-IV	Cannabis use disorder	13.6	1567	0.88 (0.83, 0.92)	0.80 (0.78, 0.82)	NR
	CRAFFT (self-administered)	2+	Harris, 2016[52]	ADI	Cannabis abuse or dependence	5.9	136	0.88 (0.46, 0.98)	0.94 (0.88, 0.97)	NR
	CRAFFT (interviewer-administered)	2+	Harris, 2016[52]	ADI	Cannabis abuse or dependence	5.9	136	0.88 (0.46, 0.98)	0.95 (0.90, 0.98)	NR
	PESQ-PS	Yellow or Red Flag	D'Amico, 2016[64]	DISC-IV	Cannabis use in past year	36.6	1541	0.72 (0.68, 0.75)	0.93 (0.91, 0.94)	NR
	PESQ-PS	Yellow or Red Flag	D'Amico, 2016[64]	DISC-IV	Cannabis unhealthy use††	19.3	1541	0.86 (0.81, 0.90)	0.82 (0.80, 0.84)	NR
	PESQ-PS	Yellow or Red Flag	D'Amico, 2016[64]	DISC-IV	Cannabis use disorder	13.6	1541	0.91 (0.86, 0.94)	0.79 (0.77, 0.81)	NR
	POSIT	2+	Rial, 2018[67, 77]	ADI	All substances use disorder	21.4	569	0.943 (0.89, 0.97)	0.839 (0.80, 0.87)	0.953 (NR)
	POSIT	2+	Kelly, 2014[42, 76]	CIDI	Alcohol or cannabis use disorder	12.4	525	0.85 (0.75, 0.92)	0.95 (0.93, 0.97)	0.90 (0.85, 0.95)

Table 5. Results of screening accuracy studies among adolescents (KQ 2), by tool type and specific test

Tool type	Tool name	Tool cutoff*	Author, year	Reference standard	Condition	Condition, %	Total n	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
Risk assessment	POSIT	2+	Kelly, 2014[42, 76]	CIDI	Cannabis use disorder	10.7	525	0.86 (0.77, 0.94)	0.94 (0.92, 0.96)	0.91 (0.86, 0.96)
	POSIT, revised	2+	Kelly, 2014[42, 76]	CIDI	Alcohol or cannabis use disorder	12.4	525	0.83 (0.73, 0.91)	0.96 (0.94, 0.97)	0.90 (0.84, 0.95)
	POSIT, revised	2+	Kelly, 2014[42, 76]	CIDI	Cannabis use disorder	10.7	525	0.86 (0.75, 0.93)	0.95 (0.92, 0.97)	0.90 (0.85, 0.95)
	SDS	3+	Bastiani, 2013[57]	M-CIDI	Cannabis dependence¶	15.5	5787	0.747 (0.72, 0.77)	0.754 (0.74, 0.77)	0.828 (0.813, 0.844)
Indirect	AUDIT	3	Chung, 2003[66]	DISC	Cannabis abuse or dependence	15.4	442	0.70 (0.59, 0.80)	0.82 (0.78, 0.86)	NR
	AUDIT	8+	D'Amico, 2016[64]	DISC-IV	Cannabis use in past year	36.6	1569	0.20 (0.17, 0.24)	0.99 (0.98, 0.99)	NR
	AUDIT	8+	D'Amico, 2016[64]	DISC-IV	Cannabis unhealthy use††	19.3	1569	0.29 (0.24, 0.34)	0.97(0.96, 0.98)	NR
	AUDIT	8+	D'Amico, 2016[64]	DISC-IV	Cannabis use disorder	13.6	1569	0.32 (0.26, 0.39)	0.96 (0.94, 0.97)	NR
	AUDIT-C	2	Chung, 2003[66]	DISC	Cannabis abuse or dependence	15.4	442	0.62 (0.50, 0.72)	0.85 (0.81, 0.88)	NR
	NIAAA Youth Screen	Moderate or high risk	D'Amico, 2016[64]	DISC-IV	Cannabis use in past year	36.6	1573	0.39 (0.35, 0.44)	0.93 (0.92, 0.95)	NR
	NIAAA Youth Screen	Moderate or high risk	D'Amico, 2016[64]	DISC-IV	Cannabis unhealthy use††	19.3	1573	0.48 (0.42, 0.54)	0.88 (0.87, 0.90)	NR
	NIAAA Youth Screen	Moderate or high risk	D'Amico, 2016[64]	DISC-IV	Cannabis use disorder	13.6	1573	0.54 (0.47, 0.60)	0.87 (0.85, 0.89)	NR

* Study-reported or reviewer-determined optimal cut-off
† 2 days in past 12 months
‡ Past year cannabis use and ≥1 DSM-5 criteria for cannabis
§ Could not be calculated
ǁ Included withdrawal as criterion for dependence

Table 5. Results of screening accuracy studies among adolescents (KQ 2), by tool type and specific test

¶ Dependence was based on 4/7 criteria and included withdrawal as criterion
# POSIT score ≥2 or DSM-IV abuse or dependence for alcohol and drugs
** ≥1 DSM-5 criterion for alcohol and drugs
†† ≥2 instances of cannabis use/days used

Abbreviations: ADI = Adolescent Diagnostic Interview; ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; AUC = area under the curve; AUDIT = Alcohol Use Disorders Identification Test; BSTAD = Brief Screener for Tobacco, Alcohol, and Other Drugs; CAST = Cannabis Abuse Screening Test; CI = confidence interval; CPQ-A-S = Cannabis Problems Questionnaire for Adolescents Shortened; CRAFFT = Car Relax Alone Forget Family/Friends Trouble; DISC-IV = Diagnostic Interview for Children Version IV; M-CIDI = Munich-Composite International Diagnostic Interview; n = number; NIAAA = National Institute on Alcohol Abuse and Alcoholism; NSDUH = National Survey on Drug Use and Health; PESQ-PS = Personal Experience Screening Questionnaire; SDS = Severity of Dependence Scale

Table 6. Results of screening accuracy studies among adults (KQ 2), by tool type and specific test

Tool type	Tool name	Tool cutoff*	Author, year	Reference standard	Condition	Condition, %	Total n	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
Frequency-based	Single-item drug frequency	1+	McNeely, 2015[43]	TLFB, Oral fluid	Drug use in past month	14.2	459	0.726 (0.609, 0.824)	0.860 (0.821, 0.893)	0.79 (0.74, 0.85)
	Single-item drug frequency	1+	Smith, 2010[45]	CIDI	Drug use in past year	34.6	286	0.929 (0.861, 0.965)	0.941 (0.898, 0.967)	0.93 (NR)
	Single-item drug frequency	1+	Smith, 2010[45]	CIDI, Oral Fluid	Drug use in past year	40.4	217	0.847 (0.756, 0.908)	0.962 (0.914, 0.984)	0.92 (NR)
	Single-item drug frequency	1+	McNeely, 2015[43, 70]	MINI Plus, SIP	Drug unhealthy use†	14.2	459	0.846 (0.735, 0.924)	0.870 (0.833, 0.902)	0.86 (0.81, 0.91)
	Single-item drug frequency	1+	McNeely, 2015[43, 70]	MINI Plus, SIP, TLFB, Oral Fluid§	Drug unhealthy use‡	26.7	459	0.713 (0.624, 0.791)	0.943 (0.913, 0.966)	0.83 (0.79, 0.87)
	Single-item drug frequency	1+	Smith, 2010[45]	CIDI, SIP-DU	Drug unhealthy use‖	32.2	286	0.935 (0.865, 0.970)	0.912 (0.864, 0.945)	0.90 (NR)
	Single-item drug frequency	1+	Smith, 2010[45]	CIDI, Oral Fluid, SIP-DU	Drug unhealthy use¶	37.9	217	0.85 (0.75, 0.91)	0.93 (0.87, 0.96)	0.89 (NR)
	Single-item drug frequency	1+	McNeely, 2015[43, 70]	MINI Plus	Drug abuse or dependence	16.1	459	0.851 (0.750, 0.923)	0.886 (0.850, 0.916)	0.87 (0.83, 0.91)
	Single-item drug frequency	1+	Smith, 2010[45]	CIDI	Drug abuse or dependence	12.9	286	1.00 (0.906, 1.00)	0.735 (0.677, 0.786)	NR
	Single-item drug frequency	1+	Smith, 2010[45]	CIDI	Drug dependence	12	286	0.97 (0.85, 0.999)	0.79 (0.73, 0.84)	0.93 (NR)
	SUBS	1+	McNeely, 2015[43]	MINI-Plus, ASSIST, TLFB, Oral Fluid§	Drug unhealthy use#	27.3	586	0.825 (0.757, 0.880)	0.911 (0.879, 0.936)	0.87 (0.84, 0.90)
	SUBS	1+	McNeely, 2015[43]	MINI-Plus, ASSIST, TLFB, Oral Fluid§	Illicit drug unhealthy use**	25.3	586	0.811 (0.738, 0.870)	0.970 (0.949, 0.984)	0.89 (0.86, 0.92)
	SUBS	1+	McNeely, 2015[43]	MINI Plus, ASSIST, TLFB, Oral Fluid§	Prescription drug unhealthy use**	9.2	586	0.556 (0.414, 0.691)	0.916 (0.889, 0.938)	0.74 (0.67, 0.80)
Frequency	SUBS	1+	McNeely, 2015[43]	MINI Plus	Drug abuse or dependence	16.7	586	0.857 (0.772, 0.920)	0.820 (0.782, 0.853)	0.84 (0.80, 0.88)

Table 6. Results of screening accuracy studies among adults (KQ 2), by tool type and specific test

Tool type	Tool name	Tool cutoff*	Author, year	Reference standard	Condition	Condition, %	Total n	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
	SUBS	1+	McNeely, 2015[43]	MINI Plus	Illicit drug abuse or dependence	16.2	586	0.821 (0.729, 0.892)	0.888 (0.856, 0.914)	0.85 (0.81, 0.90)
	SUBS	1+	McNeely, 2015[43]	MINI Plus	Prescription drug abuse or dependence	4.6	586	0.593 (0.388, 0.776)	0.892 (0.863, 0.916)	0.74 (0.65, 0.84)
	TAPS-1	1+/year	McNeely, 2016[50, 74]	CIDI	Illicit drug problem use or higher††	17.0	1997	0.91 (0.87, 0.94)	0.89 (0.87, 0.90)	0.90 (NR)
	TAPS-1	1+/year	McNeely, 2016[50, 74]	CIDI	Illicit drug use disorder	13.0	1997	0.93 (0.89, 0.96)	0.85 (0.83, 0.87)	0.89 (NR)
	TAPS-1	1+/year	McNeely, 2016[50, 74]	CIDI	Illicit drug moderate-severe use disorder	9.0	1997	0.95 (0.91, 0.97)	0.83 (0.81, 0.85)	0.89 (NR)
	TAPS-1	1+/year	McNeely, 2016[50, 74]	CIDI	Prescription drug use problem use or higher††	5.0	1995	0.85 (0.76, 0.91)	0.91 (0.90, 0.92)	0.88 (NR)
	TAPS-1	1+/year	McNeely, 2016[50, 74]	CIDI	Prescription drug use disorder	4.0	1995	0.89 (0.79, 0.94)	0.91 (0.90, 0.92)	0.90 (NR)
	TAPS-1	1+/year	McNeely, 2016[50, 74]	CIDI	Prescription drug use moderate-severe disorder	2.0	1995	0.96 (0.85, 0.99)	0.90 (0.89, 0.91)	0.93 (NR)
Risk assessment	ASSIST	2+	Kumar, 2016[51]	MINI Plus	Cannabis use in past yea	14.0	399	0.946 (0.851, 0.989)	0.816 (0.771, 0.856)	0.83 (NR)
	ASSIST	2+	Kumar, 2016[51]	MINI Plus	Cocaine use in past year	9.0	399	0.861 (0.705, 0.953)	0.840 (0.798, 0.876)	0.85 (NR)
	ASSIST	4+	Kumar, 2016[51]	MINI Plus	Cannabis abuse or dependence	7.3	399	0.828 (0.642, 0.942)	0.832 (0.790, 0.874)	0.83 (NR)
	ASSIST	4+	Kumar, 2016[51]	MINI Plus	Cocaine abuse or dependence	7.3	399	0.897 (0.726, 0.978)	0.868 (0.829, 0.900)	0.88 (NR)

Table 6. Results of screening accuracy studies among adults (KQ 2), by tool type and specific test

Tool type	Tool name	Tool cutoff*	Author, year	Reference standard	Condition	Condition, %	Total n	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
Risk assessment	ASSIST-Drug	2+ days (Q1) and/or 5+ days (Q2)	Tiet, 2015[44, 72]	InDUC	Drug unhealthy use‡‡	15.8	640	0.901 (0.827, 0.945)	0.924 (0.898, 0.943)	0.91 (NR)
	ASSIST-Drug	2+ days (Q1) and/or 5+ days (Q2)	Tiet, 2015[44, 72]	MINI	Drug abuse or dependence	10.2	640	0.954 (0.873, 0.984)	0.878 (0.849, 0.903)	0.92 (NR)
	CAST	3+	Legleye, 2015[55]	M-CIDI	Cannabis abuse or dependence	28.9	550	0.805 (0.737, 0.859)	0.749 (0.704, 0.790)	0.851 (0.814, 0.887)
	CAST	5+	Legleye, 2018[68]	M-CIDI	Cannabis moderate-severe use disorder	16.0	1351	0.866 (0.81, 0.90)	0.782 (0.76, 0.81)	0.91 (0.89, 0.93)
	CAST	5+	Legleye, 2015[55]**	M-CIDI	Cannabis dependence	12.6	550	0.812 (0.704, 0.886	0.790 (0.73, 0.84)	0.868 (0.823, 0.913)
	CAST	8+	Legleye, 2018[68]	M-CIDI	Cannabis severe use disorder	5.5	1351	0.86 (0.77, 0.92)	0.867 (0.85, 0.88)	0.94 (0.92, 0.96)
	DAST-2	1+ day/ year	Tiet, 2015[44, 72, 75]	InDUC	Drug unhealthy use‡‡	15.8	640	0.921 (0.851, 0.959)	0.934 (0.911, 0.953)	0.93 (NR)
	DAST-2	1+ day/ year	Tiet, 2015[44, 72, 75]	MINI	Drug abuse or dependence	10.2	640	0.954 (0.873, 0.984)	0.885 (0.857, 0.909)	0.92 (NR)
	DAST-10	3+	Smith, 2010[45]	CIDI	Drug use in past year	34.6	286	0.828 (0.742, 0.890)	0.936 (0.891, 0.963)	0.89 (NR)
	DAST-10	3+	Smith, 2010[45]	CIDI, Oral Fluid	Drug use in past year	40.4	217	0.800 (0.703, 0.871)	0.939 (0.885, 0.969)	0.89 (NR)
	DAST-10	3+	Smith, 2010[45]	CIDI, SIP-DU	Drug unhealthy use§§	32.2	286	0.870 (0.786, 0.924)	0.928 (0.885, 0.969)	0.88 (NR)
	DAST-10	3+	Smith, 2010[45]	CIDI, Oral Fluid, SIP-DU	Drug unhealthy use¶	37.9	217	0.835 (0.738, 0.901)	0.928 (0.872, 0.960)	NR
	DAST-10	3+	Smith, 2010[45]	CIDI	Drug abuse or dependence	12.9	286	1.0 (0.906, 1.0)	0.771 (0.715, 0.819)	NR

Table 6. Results of screening accuracy studies among adults (KQ 2), by tool type and specific test

Tool type	Tool name	Tool cutoff*	Author, year	Reference standard	Condition	Condition, %	Total n	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
Risk assessment	DAST-10	4+	Smith, 2010[45]	CIDI	Drug dependence	12	286	1.0 (0.90, 1.0)	0.84 (0.79, 0.88)	0.96 (NR)
	DAST-28	5+	McCann, 2000[49]	Structured clinical interview	Drug abuse or dependence	9.4	139	0.92 (0.667, 0.986)	0.67 (0.58, 0.74)	NR
	PDUQp	10	Beaudoin, 2016[65]	NESARC	Prescription opioid unhealthy use[lll]	38.4	112	0.442 (0.350, 0.533)	0.786 (0.710, 0.861)	0.61 (0.49, 0.72)
	PDUQp	10	Beaudoin, 2016[65]	AUDADIS	Prescription opioid use disorder	58.9	112	0.379 (0.289, 0.468)	0.809 (0.736, 0.881)	0.64 (0.53, 0.74)
	PDUQp	10	Beaudoin, 2016[65]	AUDADIS	Prescription opioid moderate-severe use disorder	16.1	112	0.556 (0.464, 0.647)	0.747 (0.667, 0.828)	0.71 (0.56, 0.86)
	PSQ	NA[¶¶]	Lane, 2007[62]	CIDI	Drug abuse	3.2	216	0.29 (0.082, 0.641)	0.95 (0.91, 0.97)	NR
	PSQ	NA[¶¶]	Lane, 2007[62]	CIDI	Alcohol or drug abuse	15.7	216	0.15 (0.064, 0.301)	0.96 (0.92, 0.98)	NR
	SoDU	7+ (Q1), 2+ (Q2)	Tiet, 2015[44, 72]	MINI	Drug abuse or dependence	10.2	640	0.9231 (0.8322, 0.9667)	0.9287 (0.9047, 0.9470)	0.93 (NR)
	SoDU	7+ (Q1), 2+ (Q2)	Tiet, 2015[44, 72]	InDUC	Drug unhealthy use[‡‡]	15.8	640	0.8317 (0.7569, 0.8922)	0.9685 (0.9501, 0.9802)	0.90 (NR)
	TAPS (self-administered)	1+	McNeely, 2016[50]	CIDI	Cannabis unhealthy use[##]	11.6	1997	0.79 (0.73, 0.84)	0.93 (0.91, 0.94)	NR
	TAPS (interviewer-administered)	1+	McNeely, 2016[50]	CIDI	Cannabis unhealthy use[##]	11.6	1996	0.82 (0.76, 0.87)	0.93 (0.91, 0.94)	NR
	TAPS (self-administered)	1+	McNeely, 2016[50]	CIDI	Cocaine or methampheta mine unhealthy use[##]	6.0	1996	0.73 (0.64, 0.80)	0.99 (0.98, 0.99)	NR
	TAPS (interviewer-administered)	1+	McNeely, 2016[50]	CIDI	Cocaine or methampheta mine unhealthy use[##]	6.0	1995	0.68 (0.59, 0.77)	0.99 (0.98, 0.99)	NR

Table 6. Results of screening accuracy studies among adults (KQ 2), by tool type and specific test

Tool type	Tool name	Tool cutoff*	Author, year	Reference standard	Condition	Condition, %	Total n	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
Risk assessment	TAPS (self-administered)	1+	McNeely, 2016[50]	CIDI	Heroin unhealthy use[##]	3.4	1995	0.77 (0.65, 0.86)	1.00 (0.99, 1.00)	NR
	TAPS (interviewer-administered)	1+	McNeely, 2016[50]	CIDI	Heroin unhealthy use[##]	3.4	1994	0.78 (0.67, 0.87)	1.00 (0.99, 1.00)	NR
	TAPS (self-administered)	1+	McNeely, 2016[50]	CIDI	Prescription opioid unhealthy use[##]	3.0	1995	0.61 (0.47, 0.73)	0.98 (0.97, 0.98)	NR
	TAPS (interviewer-administered)	1+	McNeely, 2016[50]	CIDI	Prescription opioid unhealthy use[##]	3.0	1995	0.71 (0.58, 0.82)	0.99 (0.98, 0.99)	NR
	TAPS (self-administered)	1+	McNeely, 2016[50]	CIDI	Prescription sedative unhealthy use[##]	2.0	1995	0.66 (0.49, 0.80)	0.97 (0.96, 0.98)	NR
	TAPS (interviewer-administered)	1+	McNeely, 2016[50]	CIDI	Prescription sedative unhealthy use[##]	2.0	1995	0.63 (0.47, 0.78)	0.99 (0.98, 0.99)	NR
	TAPS (self-administered)	2+	McNeely, 2016[50]	CIDI	Cannabis use disorder	7.4	1997	0.70 (0.62, 0.77)	0.95 (0.94, 0.96)	NR
	TAPS (interviewer-administered)	2+	McNeely, 2016[50]	CIDI	Cannabis use disorder	7.4	1997	0.71 (0.63, 0.79)	0.95 (0.94, 0.96)	NR

Table 6. Results of screening accuracy studies among adults (KQ 2), by tool type and specific test

Tool type	Tool name	Tool cutoff*	Author, year	Reference standard	Condition	Condition, %	Total n	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
Risk assessment	TAPS (self-administered)	2+	McNeely, 2016[50]	CIDI	Cocaine or methamphetamine use disorder	5.4	1996	0.60 (0.50, 0.69)	0.99 (0.99, 0.99)	NR
	TAPS (interviewer-administered)	2+	McNeely, 2016[50]	CIDI	Cocaine or methamphetamine use disorder	5.4	1996	0.57 (0.47, 0.67)	0.99 (0.99, 1.00)	NR
	TAPS (self-administered)	2+	McNeely, 2016[50]	CIDI	Heroin use disorder	3.2	1995	0.66 (0.53, 0.77)	1.00 (0.99, 1.00)	NR
	TAPS (interviewer-administered)	2+	McNeely, 2016[50]	CIDI	Heroin use disorder	3.2	1995	0.66 (0.53, 0.77)	1.00 (1.00, 1.00)	NR
	TAPS (self-administered)	2+	McNeely, 2016[50]	CIDI	Prescription opioid use disorder	2.4	1995	0.48 (0.33, 0.63)	0.99 (0.98, 0.99)	NR
	TAPS(interviewer-administered)	2+	McNeely, 2016[50]	CIDI	Prescription opioid use disorder	2.4	1995	0.48 (0.33, 0.63)	1.00 (0.99, 1.00)	NR
	TAPS (self-administered)	2+	McNeely, 2016[50]	CIDI	Prescription sedative use disorder	1.4	1995	0.54 (0.34, 0.72)	0.98 (0.97, 0.99)	NR

Table 6. Results of screening accuracy studies among adults (KQ 2), by tool type and specific test

Tool type	Tool name	Tool cutoff*	Author, year	Reference standard	Condition	Condition, %	Total n	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
Risk assessment	TAPS (interviewer-administered)	2+	McNeely, 2016[50]	CIDI	Prescription sedative use disorder	1.4	1995	0.54 (0.34, 0.72)	0.99 (0.98, 0.99)	NR
	TICS	NA***	Brown, 2001[48]	CIDI	Alcohol or drug abuse or dependence †††	21.4	702	0.780 (0.707, 0.839)	0.763 (0.73, 0.80)	NR
Indirect	Single-item alcohol HED	1+	Dawson, 2010[61]	NESARC	Drug use in past year	5.7	42923	0.633 (0.614, 0.652)	0.789 (0.785, 0.793)	0.799 (NR)
	Single-item alcohol HED	1+	Smith, 2010[45, 69, 73]	CIDI, Oral Fluid	Drug use in past year	40.4	217	0.588 (0.476, 0.694)	0.803 (0.725, 0.867)	0.70 (NR)
	Single-item alcohol HED	1+	Smith, 2010[45, 69, 73]	CIDI	Drug use in past year	34.6	286	0.626 (0.523, 0.722)	0.727 (0.658, 0.790)	0.67 (NR)
	Single-item alcohol HED	1+	Dawson, 2010[61]	NESARC	Cannabis use in past year	3.8	42923	0.727 (0.704, 0.748)	0.784 (0.780, 0.788)	0.839 (NR)
	Single-item alcohol HED	7+	Dawson, 2010[61]	NESARC	Cocaine use in past year	0.5	42923	0.776 (0.714, 0.825)	0.845 (0.842, 0.848)	0.893 (NR)
	Single-item alcohol HED	1+	Dawson, 2010[61]	NESARC	Prescription drug use in past year	2.9	42923	0.565 (0.537, 0.593)	0.774 (0.77, 0.778)	0.748 (NR)
	Single-item alcohol HED	1+	Smith, 2010[45, 69]	CIDI, SIP-DU	Drug unhealthy use‖	32.2	286	0.602 (0.501, 0.697)	0.721 (0.650, 0.785)	0.66 (NR)
	Single-item alcohol HED	1+	Smith, 2010[45, 69]	CIDI, Oral Fluid, SIP-DU	Drug unhealthy use¶	37.9	217	0.608 (0.491, 0.716)	0.797 (0.720, 0.861)	NR
	Single-item alcohol HED	1+	Smith, 2010[45]	CIDI	Drug abuse or dependence	12.9	286	0.676 (0.502, 0.820)	0.647 (0.584, 0.706)	0.58 (NR)
	Single-item alcohol HED	1+	Dawson, 2010[61]	NESARC	Drug abuse or dependence	1.8	42923	0.719 (0.686, 0.749)	0.773 (0.769, 0.777)	0.833 (NR)
	Single-item alcohol HED	1+	Dawson, 2010[61]	NESARC	Cannabis abuse or dependence	1.3	42923	0.770 (0.734, 0.804)	0.771 (0.767, 0.775)	0.854 (NR)
	Single-item alcohol HED	7+	Dawson, 2010[61]	NESARC	Cocaine abuse or dependence	0.2	42923	0.760 (0.669, 0.836)	0.843 (0.84, 0.846)	0.897 (NR)

Table 6. Results of screening accuracy studies among adults (KQ 2), by tool type and specific test

Tool type	Tool name	Tool cutoff*	Author, year	Reference standard	Condition	Condition, %	Total n	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
Indirect	Single-item alcohol HED	1+	Dawson, 2010[61]	NESARC	Prescription drug abuse or dependence	0.5	42923	0.601 (0.539, 0.663)	0.765 (0.761, 0.769)	0.766 (NR)
	Single-item alcohol HED	1+	Smith, 2010[45, 69, 73]	CIDI	Drug dependence	12	286	0.676 (0.495, 0.826)	0.643 (0.580, 0.702)	0.57 (NR)
	Single-item alcohol HED	1+	Dawson, 2010[61]	NESARC	Drug dependence	0.6	42923	0.724 (0.667, 0.778)	0.766 (0.762, 0.77)	0.826 (NR)
	Single-item alcohol HED	1+	Dawson, 2010[61]	NESARC	Cannabis dependence	0.3	42923	0.783 (0.702, 0.842)	0.765 (0.76, 0.77)	0.851 (NR)
	Single-item alcohol HED	12+	Dawson, 2010[61]	NESARC	Cocaine dependence	0.1	42923	0.760 (0.619, 0.854)	0.860 (0.857, 0.863)	0.887 (NR)
	Single-item alcohol HED	1+	Dawson, 2010[61]	NESARC	Prescription drug dependence	0.2	42923	0.603 (0.498, 0.698)	0.764 (0.760, 0.768)	0.764 (NR)

* Study-reported or systematic reviewer-determined optimal cutoff
† Any drug use in past 30 days with self-reported consequence of use
‡ Any drug use in past 30 days with or without self-reported consequence of use, or DSM-IV abuse or dependence
§ Oral fluid testing only for participants at New York site
‖ Past 12-month use and ≥1 positive response on the SIP-DU or DSM-IV drug abuse or dependence
¶ Past 12-month use confirmed through oral fluid testing and ≥1 positive response on the SIP-DU or DSM-IV drug abuse or dependence
# Any use of an illicit drug or nonmedical use of a prescription drug (TLFB, oral fluid), moderate- or high-risk use (ASSIST), or a positive response on unhealthy drug use (MINI question J1)
** Any illicit *or* nonmedical use of a prescription drug (TLFB, oral fluid), moderate- or high-risk use (ASSIST), or a positive response on unhealthy drug use (MINI question J1)
†† 1+ DSM-5 criterion
‡‡ Negative consequences of drug use in past 12 months
§§ Past 12-month use and ≥1 positive response on the SIP-DU or DSM-IV drug abuse or dependence
‖‖ Defined as the use of prescription opioids outside of their prescribed indications (i.e., pain), self-escalating doses of these medications, or giving to or receiving prescription opioid medications from others within the past 30 days.
¶¶ Positive response to either question
Any DSM-5 criterion
*** Positive response to either question
††† DSM-III-R abuse or dependence

Abbreviations: ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; AUC = area under the curve; CAST = Cannabis Abuse Screening Test; CI = confidence interval; CIDI = Composite International Diagnostic Interview; DAST-10 = 10-Item Drug-Abuse Screening Test; DAST-28 = 28-Item Drug-Abuse Screening Test; DSM = Diagnostic and Statistical Manual of Mental Disorders; HED = heavy episodic drinking; InDUC = Inventory of Drug Use Consequences; MINI = Multi International

Table 6. Results of screening accuracy studies among adults (KQ 2), by tool type and specific test

Neuropsychiatric Interview-plus; n = number; NESARC = National Epidemiologic Survey on Alcohol and Related Conditions; PDUQp = Prescription Drug Use Questionnaire, patient version; PSQ = Parent Screening Questionnaire; SIP-DU = The Short Inventory of Problems—Modified for Drug Use; SoDU = Screen of Drug Use; SUBS = Substance Use Brief Screen; TAPS = Tobacco, Alcohol, Prescription Medication, and Other Substance Use; TICS = Two-Item Conjoint Screen; TLFB = Timeline Followback

Table 7. Results of screening accuracy studies among pregnant and postpartum women (KQ 2), by tool type and specific test

Tool type	Tool name	Tool cutoff*	Author, year	Reference standard	Condition	Condition, %	Total n	Sensitivity (95% CI)	Specificity (95% CI)
Frequency -based	ASSIST-2 (modified)‡	Any use	Ondersma, 2012[58]†	Hair and urine analyses	Any drug use during prenatal period	41	100	0.41 (0.28, 0.57)	0.83 (0.72, 0.91)
Risk assessment	DAST-10	1+	Grekin, 2010[15]†	Hair and urine analyses	Any cannabis use during prenatal period	NR	274	0.53 (NR‡)	0.82 (NR‡)
			Grekin, 2010[15]†	Hair and urine analyses	Any drug use in the last trimester	24	274	0.47 (0.35, 0.59)	0.82 (0.76, 0.87)
			Ondersma, 2012[58]†	Hair and urine analyses	Any drug use during prenatal period	41	100	0.37 (0.24, 0.52)	0.83 (0.72, 0.91)
			Lam, 2015[53]§	Urinalysis	Any drug use in the last trimester	1.2	1082	0.692 (0.424, 0.873)	0.700 (0.672, 0.726)
			Grekin, 2010[15]†	Hair and urine analyses	Any noncannabis use during prenatal period	NR	274	0.32 (NR‡)	0.77 (NR‡)
	PRO	Mod+	Harrison, 2012[63]§	SCID	Drug abuse or dependence	7.0	745	0.885 (0.77, 0.946)	0.743 (0.709, 0.774)
	WIDUS/ ASSIST-2 (modified)‖	3+/Any use	Ondersma, 2012[58]†	Hair and urine analyses	Any drug use during prenatal period	41	100	0.76 (0.61, 0.86)	0.68 (0.55, 0.78)
Indirect	4P's Plus	Any cigarette or alcohol use	Chasnoff, 2007[47]§	Structured clinical interview	Any alcohol or drug use in the month prior to knowledge of pregnancy or after	13.6	228	0.87 (0.71, 0.95)	0.76 (0.70, 0.82)
	WIDUS	3+	Ondersma, 2012[58]†	Hair and urine analyses	Any drug use during prenatal period	41	100	0.68 (0.53, 0.80)	0.69 (0.57, 0.80)

* Study-reported or reviewer-determined optimal cut-off
† Postpartum
‡ Could not be calculated
§ Pregnant
‖ Specific modifications not reported by the study

Table 7. Results of screening accuracy studies among pregnant and postpartum women (KQ 2), by tool type and specific test

Abbreviations: ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; CI = confidence interval; DAST-10 = 10-Item Drug-Abuse Screening Test; n = number; N = no; NR = not reported; PRO = Prenatal Risk Overview; SCID = Structured Clinical Interview for the DSM; WIDUS = Wayne Indirect Drug Use Screener; Y = yes

Table 8. Trial and population characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year Study name	QR	Country	Target subs	n rand	Brief population description	Mean age, yrs	Female, %	Race/ ethnicity, %	SES variables	Outcomes reported
Adolescents	D'Amico, 2018[78]	Fair	US	Cannabis, Alcohol	294	Adolescents aged 12-18 yrs	16.0	56.8	White: 11.6 Black: 16.7 Hisp: 66.3 Other: 5.4		Health, Beh
	Mason, 2015[96]	Fair	US	Alcohol, All drugs	119	Adolescents aged 14-18 yrs	16.4	71.0	Black: 84.0 Other: 16.0		Beh
	Walton, 2013[107] Project Chill	Fair	US	Cannabis	328	Adolescents aged 12-18 yrs	16.3	66.5	Black: 60.7 Hisp: 11.0	Dropped out of school: 5.8%	Health, Beh
Young adults	Bernstein, 2009[80]	Fair	US	Cannabis	139†	Adolescents and young adults aged 14-21 yrs	NR‡	66.2	White: 5.7 Black: 80.6 Hisp: 12.9 Other: 0.7		Health, Beh
	Lee, 2010[93]	Fair	US	Cannabis	341	Incoming college students aged 17-19 yrs	18.0	54.6	White: 68.3 Black: 1.5 Hisp: 6.2 Asian: 16.2 AI/NA: 0.9 Other: 7.0		Health, Beh, Harms
	Lee, 2013[94]	Fair	US	Cannabis	212	College students aged 18-25 yrs	20.0	45.3	White: 74.8 Hisp: 5.7 Asian: 10.5 Other: 14.7		Health, Beh, Harms
Young adults	Palfai, 2014[101] eCHECKUP TO GO	Fair	US	Cannabis	123	Undergraduate students	19.7	57.7	White: 87.0 Black: 2.4 Hisp: 17.0 Asian: 5.7 AI/NA: 1.6		Health, Beh

Table 8. Trial and population characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year Study name	QR	Country	Target subs	n rand	Brief population description	Mean age, yrs	Female, %	Race/ ethnicity, %	SES variables	Outcomes reported
	Stein, 2011[105]	Fair	US	Cannabis	332	Women aged 18-24 yrs	20.5	100	White: 67.8 Black: 10.5 Hisp: 11.5 Other: 10.2	Some college or degree: 69.9%	Health, Beh
Adults	Bernstein, 2005[81§]	Fair	US	Cocaine, Heroin	1175	Adults aged ≥18 yrs	37.9	29.4	White: 14.2 Black: 62.0 Hisp: 23.2 Other: 0.06	Educ <HS: 37.8% Working: 42.9% Homeless: 45.8%	Beh
	Blow, 2017[82] HealthiER You	Good	US	All drugs	387	Adults aged 18-60 yrs	31.2	55.5	White: 39.2 Black: 52.2 Hisp: 6.0 Other: 8.6	Educ <HS: 64% Unemployed: 74%	Beh
	Bogenschutz, 2014[83] SMART-ED (Screening, Motivational Assessment, Referral, and Treatment in Emergency Departments)	Fair	US	All drugs	854[‖]	Adults aged ≥18 yrs	36.0	31.0	White: 48.8 Black: 34.9 Asian: 1.0 AI/AN: 2.3 Other: 9.5	Educ <HS: 30.6% Unemployed in past 30 days: 41.7% Household income ≤$15,000: 62.2%	Beh
	Gelberg, 2015[87] Project QUIT (Quit Using Drugs Intervention Trial)	Fair	US	All drugs	334	Adults aged ≥18 yrs	41.7	37.1	White: 37.7 Black: 22.8 Hisp: 33.8 Other: 5.7	Educ ≥12 yrs: 83.8% U.S. born: 87.2% Homelessness: 61.0% Income ≤ $500/month: 58.0%	Health, Beh
Adults	Gelberg, 2017[88] Project QUIT pilot replication	Fair	US	All drugs	65	Adults aged ≥18 yrs	30.8	41.5	Hispanic: 93.9	Education ≥12 yrs: 83.1% U.S. born: 87.5% Homelessness: 34.4% Income ≤$500/month: 75.0%	Beh

Table 8. Trial and population characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year Study name	QR	Country	Target subs	n rand	Brief population description	Mean age, yrs	Female, %	Race/ ethnicity, %	SES variables	Outcomes reported
	Gryczynski, 2016[112]	Fair	US	All drugs	80	Adults aged ≥18 yrs	35.2	52.5	White: 86.2 Hisp: 42.5	NR	Beh
	Humeniuk, 2012[89]	Fair	Australia, Brazil, India, US[¶]	All drugs	389	Adolescents and adults aged 16-62 yrs	31.4[#]	44.2	NR	Employed: 59.8%	Beh
	Martino, 2018[95]	Good	US	Alcohol, All drugs	439	Pregnant and nonpregnant women aged ≥18 yrs	34.2	100	White: 13.2 Black: 66.7 Hisp: 14.8 Other: 5.2	Educ <HS: 33.4% Employed: 33.7%	Health, Beh
	Poblete, 2017[102]	Fair	Chile	Alcohol, All drugs	806	Adults aged 19-55 yrs	29.2	21.8	NR	Employed: 67.4%	Beh
	Roy-Byrne, 2014[103]	Good	US	All drugs	868	Adults aged ≥18 yrs	47.8	30.0	White: 45.0 Black: 37.0 Hisp: 9.0 Other: 18.0	Educ <HS: 19% Working: 9% Homeless: 30%	Health, Beh
	Saitz, 2014[104] ASPIRE	Good	US	All drugs	528	Adults aged ≥18 yrs	41.3	30.1	White: 20.2 Black: 68.8 Hisp: 9.6 Other: 1.4	HS grad: 69.9% Medicaid/ Medicare: 81.3% No insurance: 5.7%	Health, Beh
	Watkins, 2017[108] SUMMIT (Substance Use Motivation and Medication)	Fair	US	Alcohol, Opioids	397	Adults aged ≥18 yrs	42.0	20.4	White: 43.8 Black: 13.3 Asian: 0.8 AI/AN: 1.3 Hisp: 31.0 Other: 40.3	<HS: 27.9% HS grad: 31.0% >HS: 41.1% Homeless: 49.3%	Health, Beh
Adults	Woolard, 2013[109] Project Reduce	Fair	US	Alcohol, Cannabis	515	Adults aged ≥18 yrs	28.4	16.5	White: 68.0 Hisp: 17.0	Mean educ, yrs: 12.4	Health, Beh

Table 8. Trial and population characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year Study name	QR	Country	Target subs	n rand	Brief population description	Mean age, yrs	Female, %	Race/ ethnicity, %	SES variables	Outcomes reported
	Zahradnik, 2009[111]	Fair	DEU	Prescription drugs	126	Adults aged 18-69 yrs	55.1	61.9	NR	Educ >10 yrs: 13.5% Employed: 12.7%	Beh
Postpartum women	Ondersma, 2007[99]	Fair	US	All drugs	107	Postpartum women in post-delivery recovery aged ≥18 yrs	25.1	100	Black: 97.2	<HS: 41.1% Employed full-time: 29.0% Public assistance: 88.8%	Beh
	Ondersma, 2014[98]	Fair	US	All drugs	143	Postpartum women in post-delivery recovery aged ≥18 yrs	26.6	100	White: 5.8 Black: 90.6 Hisp: 1.5 Other: 3.6	Food assistance: 90.0% HS grad or higher: 58.7% Currently married: 7.1% Work for pay: 44.8%	Beh, Harms
	Ondersma, 2018[100]	Fair	US	All drugs	502	Postpartum women in post-delivery recovery aged 18-45 yrs	24.6	100	White: 2.6 Black: 73.2 Hisp: 3.6 Other: 24.2	Employed: 35.2% Food assistance: 83.4%	Beh, Harms
Pregnant women	Tzilos Wernette, 2017[106]	Fair	US	Alcohol, Cannabis	50	Pregnant women (<5 months gestation)	24.4	100	White: 30.0 Black: 26.0 Asian: 0 AI/AN: 4.0 Hisp: 32.0 Other: 40.0	HS grad: 28.0% ≥ Some college: 34% Unemployed: 44.0% Single: 48.0% Public assistance: 62.0%	Beh
	Yonkers, 2012[110]	Fair	US	Alcohol, All drugs	183	Pregnant women (<28 wks gestation), aged ≥16 yrs	NR**	100	White: 22.0 Black: 53.0 Hisp: 23.0 Other: 2.0	Mean educ (yrs): <12: 34.0 12: 40.0 13-15: 22.0 16+: 4.0	Health, Beh

* As available or reported by study
† Full study randomized N = 210. The nonassessed control group was not included in this report.
‡ ≤ 17 years: 29.5%; ≥ 18 years: 70.5%
§ In previous review
‖ Full study randomized N = 1285. Minimal screening only group was not included in this report given no baseline measures for outcome variables.
¶ Country-specific data for only Australia and the US reported where available. Full N randomized=731; Australia N=171; US N=218

Table 8. Trial and population characteristics, by subpopulation (KQ 4 and KQ 5)

Mean age of full sample (N= 731)
** <20: 17%; 20-34: 75%; 35+: 8%

Abbreviations: Beh = behavioral; educ = education; Hisp = Hispanic; HS = high school; n = number; NR = not reported; QR = quality rating; pop = population; n rand = number of participants randomized; SES = socioeconomic status; subs = substance; target subs = specific substance(s) targeted by the intervention; wks = weeks; yrs = years

Table 9. Trial recruitment methods and baseline substance-related variables, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year Study name	Recruitment method	Screener	Substance use eligibility criteria	Screen pos, %	n rand	FU, mos	FU, %*	Baseline substance use-related characteristics (mean, sd)
Adolescents	D'Amico, 2018[78]	Primary care visit	NIAAA SG	Any past-year drinking ≥1 day (for 12-15 yrs), ≥6 days (for 16-17 yrs), or ≥12 days (for 18 yrs)	18.7	294	3, 6, 12	80.3	Cannabis use in past 12 months: 77% Cannabis use disorder: 38.4%
	Mason, 2015[96]	Primary care visit	CRAFFT	CRAFFT score of 2 or 3 (at risk for substance use disorder)†	15.8	119	1, 3, 6	98.3	Cannabis use in past 30 days‡: 1.4 (1.3) Intentions to use cannabis in next 90 days§: 1.9 (1.3)
	Walton, 2013[107] Project Chill	Primary care visit	Add Health	Any cannabis use in past year	25.8	328	3, 6, 12	83.8	Cannabis use in past 90 days‖: 3.2 (1.9)
Young adults	Bernstein, 2009[80]	Pediatric ED visit	Youth and Young Adult Health and Safety Needs Survey	Smoked marijuana ≥3 times in the past 30 days or risky behavior related to marijuana use	NR	139	3, 12	73.4	Days used cannabis in past 30 days: 17.1 (10.5)
	Lee, 2010[93]	Direct mailing	GAIN-I	Any cannabis use in the past 3 months	17.4	341	3, 6	94.4	Days used cannabis in past 90 days: 9.9 (16.0)
	Lee, 2013[94]	Direct mailing	NR	Cannabis use ≥5 days in the past month	14.1	212	3, 6	82.5	Days used cannabis in past 30 days: 16.1 (10) Number of joints smoked in typical week: 8.9 (9.7)
	Palfai, 2014[101] eCHECKUP TO GO	Primary care visit	ASSIST	At least monthly cannabis use in past 3 months¶	19.4	123	3, 6	83.7	Days used cannabis in past 90 days: 35.0 (28.4) ASSIST score: 11.9 (6.5) Readiness to change#: 1.34 (2.3)

Table 9. Trial recruitment methods and baseline substance-related variables, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year Study name	Recruitment method	Screener	Substance use eligibility criteria	Screen pos, %	n rand	FU, mos	FU, %*	Baseline substance use-related characteristics (mean, sd)
Young adults	Stein, 2011[105]	Generic advertising for health study	NR	Cannabis use ≥3 times in past 3 months**	29.8	332	1, 3, 6	78.9	Proportion of days used cannabis, in past 90 days: 0.57 (0.34) Years of regular cannabis use: 3.9 (2.6) Cannabis dependence: 39.5% Desire to quit using cannabis: 60.2%
Adults	Bernstein, 2005[81††]	Primary care visit	DAST-10	Cocaine and/or heroin use in last 30 days and DAST-10 score ≥ 3 (moderate-to-severe problems related to drug use)	5.2	1175	6	66.2	Cocaine use: 92.5% Heroin use: 44.9% Readiness to change‡‡: 7.0 ≥1 prior admission for detox or substance abuse treatment: 46.4%
	Blow, 2017[82]	ED visit	ASSIST	ASSIST score ≥4 (past 3-month use of illicit drugs or misuse or prescription drugs)	22.0	387	3, 6, 12	85.3	Cannabis use: 91.0% Cannabis use problem (ASSIST≥4): 88.0% Prescription drug misuse: 20.0%
	Bogenschutz, 2014[83]	ED visit	DAST-10	At least one day of drug use in past 30 days and DAST-10 score ≥ 3 (moderate-to-severe problems related to drug use)	15.3	854	3,6, 12	80.3	Drug use days in past 30 days: 16.2 (11.6) Prevalence of drug use§§: Cannabis: 44% Cocaine: 27% Street opioids: 17% Prescription opioids: 5% Methamphetamine: 4%

Table 9. Trial recruitment methods and baseline substance-related variables, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year Study name	Recruitment method	Screener	Substance use eligibility criteria	Screen pos, %	n rand	FU, mos	FU, %*	Baseline substance use-related characteristics (mean, sd)
Adults	Gelberg, 2015[87]	Primary care visit	ASSIST	ASSIST score 4 to 26 (Moderate risk for drug use)	10.5	334	3	79.0	ASSIST score§§: 14.5 (range 4-26) Duration of drug use, yrs‡‡: 20.4 (13.4) Prevalence of drug use‡‡: Cannabis: 51.8% Cocaine/crack: 20.1% Amphetamines: 12.3% Sedatives: 8.7% Opiates: 6.6% Other (inhalants, hallucinogens): 0.6%
	Gelberg, 2017[88]	Primary care visit	ASSIST	ASSIST score 4 to 26 (Moderate risk for drug use)	7.6	65	3	78.5	ASSIST score§§: 14.4 (6.2) Duration of drug use, yrs§§: 12.9 (12.9) Prevalence of drug use§§: Cannabis: 67.7% Cocaine/crack: 9.2% Amphetamines: 7.7% Sedatives: 3.1% Opiates: 12.3% Other (inhalants, hallucinogens): 0.0%
	Gryczynski, 2016[112]	Community health center	ASSIST	ASSIST score 4 to 26 (Moderate risk for drug use)	14.4	80	3	88.8	Moderate risk (ASSIST score 4-26): Cannabis: 90.0% Cocaine: 5.0% Amphetamines16.2% Opioids: 23.8%

Table 9. Trial recruitment methods and baseline substance-related variables, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year Study name	Recruitment method	Screener	Substance use eligibility criteria	Screen pos, %	n rand	FU, mos	FU, %*	Baseline substance use-related characteristics (mean, sd)
Adults	Humeniuk, 2012[89]	University-affiliated community clinic, walk-in health clinic, walk-in sexually transmitted disease clinic visit	ASSIST	ASSIST score 4 to 26 (Moderate risk for cannabis, cocaine, amphetamine-type stimulant, or opioid use†††)	NR	389	3	85.1	Moderate risk (ASSIST score 4-26)§§‖‖: Cannabis: 54.0% Cocaine: 12.9% Amphetamines: 21.2% Opioids: 12.7%
	Martino, 2018[95]	Reproductive health clinic visit	ASSIST	ASSIST score 4 to 26 (Moderate risk for drug use) or ≥11 for nonpregnant women and ≥6 for pregnant women for alcohol	NR	439	1, 3, 6	87.9	ASSIST score§§: 22.5 (8.1) Cannabis use disorder: 33.7% Other illicit drug use disorder: 20.2%
	Poblete, 2017[102]	Primary care, ED, or police station visit	ASSIST, Chilean version	ASSIST score 11 to 20 for alcohol or ASSIST score 4 to 20 for drug use (moderate risk)	15.8	806	3	61.7	ASSIST (Chilean) score: 26.8 (9.5) Moderate risk (ASSIST score 4-20): Cannabis: 49% Cocaine: 19% Sedatives: 5% Other drug: 5%

Table 9. Trial recruitment methods and baseline substance-related variables, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year Study name	Recruitment method	Screener	Substance use eligibility criteria	Screen pos, %	n rand	FU, mos	FU, %*	Baseline substance use-related characteristics (mean, sd)
Adults	Roy-Byrne, 2014[103]	Primary care visit	NR	Any illegal drug or nonprescribed medication use at least once in the past 3 months	15.7	868	3, 6, 9, 12	89.5	Days used most frequently used drug in past 30 days: 13.8 (11.0) Past 30 day use: Cannabis: 76% Stimulants: 42% Cocaine: 37% Amphetamines: 7% Opiates: 26% Heroin: 7% Methadone and other opiates/analgesics nonprescribed: 24% Sedatives/hypnotics/tranquilizers: 8%
	Saitz, 2014[104] ASPIRE	Primary care visit	ASSIST	ASSIST score ≥4 (drug use weekly or more in past 3 months or less frequent use but with consequences)	68.1	528	6	97.9	Days used most frequently used drug past 30 days: 14.4 (11.5) Main drug: Opioid (including prescription): 17.1% Prescription opioid only: 5.7% Cocaine: 18.6% Cannabis: 62.7%
	Watkins, 2017[108] SUMMIT	Primary care visit	NIDA Quick Screen	Probable opioid or alcohol use disorder	61.2	397	6	69.2	Alcohol abuse or dependence only: 54% Heroin abuse or dependence with or without cooccurring alcohol or prescription opioid abuse or dependence: 31% Prescription opioid abuse or dependence with or without cooccurring alcohol abuse or dependence: 16%
	Woolard, 2013[109]	ED visit	10-item wellness questionnaire	Any past month alcohol use and past year marijuana use	14.0	515	12	82.7	AUDIT score: 10.9 (1.4) Cannabis use days in past 30 days: 12.6

Table 9. Trial recruitment methods and baseline substance-related variables, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year Study name	Recruitment method	Screener	Substance use eligibility criteria	Screen pos, %	n rand	FU, mos	FU, %*	Baseline substance use-related characteristics (mean, sd)
Adults	Zahradnik, 2009[111]	Admission to internal, surgical, or gynecological ward of hospital	QPM, SDS	Prescription drug use¶¶ >60 days in past 3 months or PD abuse or dependence	18.0	126	3, 12	88.9	PD misuse: 17.5% PD dependence: 43.6%
Postpartum women	Ondersma, 2007[99]	Inpatient hospitalization for childbirth	Single question	Any illicit drug use in the month before becoming pregnant	NR	107	4	71.0	Daily or weekly cannabis use in 3 months prior to pregnancy: 62.6% Drug use other than cannabis in 3 months prior to pregnancy: 12.1%
	Ondersma, 2014[98]	Inpatient hospitalization for childbirth	Single question	Any illicit drug use in the month before becoming pregnant	25.7	143	3, 6	65.9	≥ ASSIST scores for moderate risk[##]: Cannabis: 76.9% Cocaine: 11% Opiates: 9.1% Daily/near daily cannabis use[##]: 86.5%
	Ondersma, 2018[100]	Inpatient hospitalization for childbirth	WIDUS	WIDUS score ≥3	NR	502	3, 6	65.3	Pre-pregnancy opioid misuse: 12.0%***
Pregnant women	Tzilos Wernette, 2017[106]	Obstetrics visit	T-ACE or SURP-P	Current alcohol or drug use or at -risk for prenatal alcohol/drug use (positive score on T-ACE or SURP-P)	NR	50	4	98.0	Reported alcohol or marijuana use: 70%

Table 9. Trial recruitment methods and baseline substance-related variables, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year Study name	Recruitment method	Screener	Substance use eligibility criteria	Screen pos, %	n rand	FU, mos	FU, %*	Baseline substance use-related characteristics (mean, sd)
Pregnant women	Yonkers, 2012[110]	Obstetrics visit	TWEAK	Any use of alcohol or illicit drug use (excluding opiates) in last 30 days or TWEAK score ≥3	NR	183	1, 3	91.8	Past month use: Alcohol: 52% Heroin: 2% Methadone: 8% Opiates (excl methadone): 6% Barbiturates: 0 Sedatives: 4% Cocaine: 11% Amphetamines: 1% Cannabis: 44% Hallucinogens: 2% Inhalants: 0

* At longest followup time point
† Those endorsing ≥4 were excluded and were encouraged to talk with a social worker or doctor
‡ Scale 0-7 where 0 = 0 days, 1 = 1-2 days, 2 = NR, 3 = 3-5 days, 4 = 6-9 days, 5 = 10-19 days, 6 = 20-29 days, and 7 = all 30 days
§ Scale 0-4 where 0 = definitely no, 1 = probably no, 2 = unsure, 3 = probably yes, and 4 = definitely yes
‖ Scale 0-6 where 0 = never, 1= 1–2 days, 2 = once a month or less, 3= 2–3 days per month, 4 = 1–2 days per week, 5 = 3–5 days per week, and 6 = every day or almost every day
¶ Persons with ASSIST score >27 for cannabis at baseline (indicating a high likelihood of substance dependence) were excluded
# Computed by subtracting the mean precontemplation score from the sum of the contemplation and action scores, range not reported
** Those meeting criteria for drug dependence, other than cannabis dependence, were excluded
†† In previous review
‡‡ Range 1-10 where 0-3 = not ready, 4-6 = unsure, 7-10 = ready to change
§§ For primary drug
‖‖ For full sample. Proportion of participants at moderate risk for each drug class not reported by country.
¶¶ Includes opioids, anxiolytics, hypnotics, sedative, and caffeine with addiction potential
Baseline measures referred to use in the three months prior to pregnancy
***Use of other drugs not reported at baseline
††† Those scoring >27 or who had frequently injected drugs in the last 3 months were referred to specialist drug and alcohol treatment services.

Abbreviations: Add Health = National Longitudinal Study of Adolescent Health; ASPIRE = The Assessing Screening Plus Brief Intervention's Resulting Efficacy to Stop Drug Use; ASSIST = Alcohol, Smoking, and Substance Involvement Screening Test; BL = baseline; CRAFFT = Car, Relax, Alone, Forget, Friends, Trouble; DAST-10 = The Drug Abuse Screening Test-10 item; ED = emergency department; excl = excluding; FU = followup; GAIN-I = The Global Appraisal of Individual Needs-Initial; n rand = number of participants randomized to the trial; NIAAA SG = National Institute of Alcohol Abuse and Alcoholism Screening Guide; NR = not reported; PD = prescription drugs; pop = population; pos = positive; QPM = questionnaire for prescription drug misuse; sd = standard deviation; SDS = Severity of dependence scale; SURP-P = Substance Use Risk Profile-Pregnancy scale; TWEAK = Tolerance, Worried, Eye-opener; Amnesia; K/Cut Down; WIDUS = Wayne Indirect Drug Use Screener

Table 10. Intervention characteristics of all trials, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	Intensity category*	Brief description	Setting	CBT	ME	MI	PNF	Refer	Provider	CG
Adolescents	D'Amico, 2018[78]	Cannabis, Alcohol	IG1	In-person brief intervention	Extended single	One 15-20-min individual counseling session	Primary care			X	X		Trained facilitator	UC
	Mason, 2015[96]	Alcohol, all drugs	IG1	Peer network counseling	Extended single	One 20-min individual counseling session	Primary care		X	X	X		Mental or behavioral health specialists	AC
	Walton, 2013[107]	Cannabis	IG1	In-person personalized feedback	Very brief†	One personalized feedback session (min NR)	Primary care			X	X		Mental or behavioral health specialists	UC
		Cannabis	IG2	Computer-based personalized feedback	Very brief†	One computerized feedback session (min NR)	Primary care			X	X		Self-directed	UC
Young adults	Bernstein, 2009[80]	Cannabis	IG1	In-person brief intervention	Extended multi-contact	One 20-30-min brief individual counseling session and one 5-10-min booster phone call	ED			X			Lay counselors	UC
	Lee, 2010[93]	Cannabis	IG1	Computer-based personalized feedback	Very brief	One computerized, personalized feedback session with access to feedback for 3 months	Home				X		Self-directed	None
Young adults	Lee, 2013[94]	Cannabis	IG1	In-person personalized feedback	Extended single	One 60-min in-person personalized feedback session	NR		X	X	X		NR	None

Table 10. Intervention characteristics of all trials, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	Intensity category*	Brief description	Setting	CBT	ME	MI	PNF	Refer	Provider	CG
	Palfai, 2014[101]	Cannabis	IG1	Computer-based personalized feedback (eCHECKUP TO GO)	Brief single	One web-based personalized feedback session (min NR)	College health clinic				X		Self-directed	AC
	Stein, 2011[105]	Cannabis	IG1	Motivational interviewing	Extended multi-contact	Two 45-min motivational interviewing sessions	Research clinic			X	X		Mental or behavioral health specialists	None
Adults	Bernstein, 2005[81]	Cocaine, heroin	IG1	Motivational interviewing + telephone booster session	Extended multi-contact	One 10-45 min motivational interview interviewing session followed by one 5-10 min phone call	Primary care			X			Peers	Minimal
Adults	Blow, 2017[82]	All drugs	IG1	Therapist delivered brief intervention	Extended single	One 30-min in-person brief intervention session	ED			X			Behavioral health specialist	UC
			IG2	Computer-delivered brief intervention	Extended	One 30-min computerized brief intervention session	ED			X			Self-directed	UC
Adults	Bogenschutz, 2014[83]	All drugs	IG1	Brief intervention + telephone booster sessions	Brief multi-contact	One brief intervention and two telephone booster calls	ED		X	X		X	Research staff	Minimal

Table 10. Intervention characteristics of all trials, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	Intensity category*	Brief description	Setting	CBT	ME	MI	PNF	Refer	Provider	CG
	Gelberg, 2015[87]	All drugs	IG1	Brief intervention + telephone coaching sessions	Extended multi-contact	One 3-4-min brief intervention followed by two 20-30 min phone calls	Primary care	X		X			PCP, lay counselors	AC
	Gelberg, 2017[88]	All drugs	IG1	Brief intervention + telephone coaching sessions	Extended multi-contact	One 3-4 min brief intervention followed by two 20-30 min phone calls	Primary care	X		X			PCP, lay counselors	AC
	Gryczynski, 2016[112]	All drugs	IG1	Computer-based brief intervention	Brief single	One 10 min computerized brief session	Community health center			X	X		Self-directed	WL
	Humenuik, 2011[89]	All drugs	IG1	Brief intervention	Brief single	One 15 min brief intervention session	Primary care			X			Research staff	WL
	Martino, 2018[95]	Alcohol, All drugs	IG1	In-person brief intervention	Extended single	One 20 min brief intervention session	Primary care			X		X	Research nurse, social workers, PCP	UC
			IG2	Computer-based brief intervention	Extended single	One 20 min brief intervention session	Primary care			X		X	Self-directed	UC
Adults	Poblete, 2017[102]	Alcohol, All drugs‡	IG1	Brief intervention based on FRAMES	Extended single	One 18 min brief individual counseling session	Primary care, ED, police station						Social workers, psychologists	UC

Table 10. Intervention characteristics of all trials, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	Intensity category*	Brief description	Setting	CBT	ME	MI	PNF	Refer	Provider	CG
	Roy-Byrne, 2014[103]	All drugs	IG1	In-person personalized feedback + telephone booster session	Extended multi-contact	One 30 min personalized feedback session and one 10-min booster call	Primary care			X	X	X	Social workers	UC
	Saitz, 2014[104]	All drugs	IG1	Brief negotiated interview	Brief single	One 10-15 min brief negotiated interviewing session	Primary care			X	X		Health educators	Minimal
		All drugs	IG2	Motivational interviewing + telephone booster session	Extended multi-contact	One 30-45 min motivational interviewing session and one optional 20-30 min booster followup session	Primary care			X	X		Mental or behavioral health specialists	Minimal
Adults	Watkins, 2017[108]	Alcohol, Opioids	IG1	Collaborative care	Extended multi-contact	Collaborative care (registry, regular assessment, adherence support) plus training for behavioral therapists and doctors for medication-assisted treatment	Primary care	X		X			PCP, mental or behavioral health specialists, social workers	UC

Table 10. Intervention characteristics of all trials, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	Intensity category*	Brief description	Setting	CBT	ME	MI	PNF	Refer	Provider	CG
	Woolard, 2013[109]	Alcohol, Cannabis	IG1	Motivational interviewing	Extended multi-contact	Two 15-60 min individual counseling sessions	ED, behavioral /mental health clinic		X	X			Research staff	UC
	Zahradnik, 2009[111]	Prescrip-tion drugs	IG1	Motivational interviewing	Extended multi-contact	One 35-min in-person MI session, one phone MI session, and one individualized feedback letter	Hospital			X	X		Psychologist	UC
Postpartum women	Ondersma, 2007[99]	All drugs	IG1	Computer-based brief intervention	Extended single	One 20 min computer-delivered brief intervention session and two non-tailored mailings	Hospital			X	X	X	Self-directed	None
Postpartum women	Ondersma, 2014[98]	All drugs	IG1	Computer-based personalized feedback (eCHECKUP TO GO)	Extended single	One 20 min interactive computer-based personalized feedback session	Hospital			X			Self-directed	AC
	Ondersma, 2018[100]	All drugs	IG1	Computer-based brief intervention focused on parenting	Brief single	One brief computer-based session and personalized feedback report	Hospital			X			Self-directed	AC
Pregnant wome	Tzilos Wernette, 2017[106]	Alcohol, Cannabis	IG1	Health Checkup for Expectant Moms	Extended multi-contact	One 60-min computer-delivered MI session and one	Ob/Gyn clinic			X			Self-directed	AC

Table 10. Intervention characteristics of all trials, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	Intensity category*	Brief description	Setting	CBT	ME	MI	PNF	Refer	Provider	CG
				computerized program§		15-min computer-delivered booster session								
	Yonkers, 2012[110]	Alcohol, all drugs (except opioids)	IG1	MET-CBT	Extended multi-contact	Six 30 min MET + CBT sessions	Ob/Gyn clinic		X				Research nurses	UC

***** Intensity categories defined as: Very brief = single contact, ≤5 min; Brief = singe contact, ≤15 min; Extended = single contact, ≥15 min; Brief multi-contact = multiple contacts, ≤15 min each; Extended multi-contact = multiple contacts, ≥15 min each

‡ 48% received alcohol-related brief intervention, 36% received a cannabis-related brief intervention, 12% received a cocaine-related brief intervention, and 4% received a brief intervention for other substances.

§ Intervention addressed both STI/HIV and alcohol/drug risk

Abbreviations: AC = attention control; CBT = cognitive behavioral therapy; CG = control group; ED = emergency department; FRAMES = Feedback, Responsibility, Advice, Menu Options, Empathy and Self-Efficacy; IG = intervention group; Int = intervention; MET = motivational enhancement therapy; MI = motivational interviewing; min = minute; None = assessment only; NR = not reported; PCP = primary care provider; PNF = personalized normative feedback; self-admin = self-administered; subs = substance; target subs = substance(s) targeted by the intervention; UC = usual care; WL = waitlist

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Adolescents	D'Amico, 2018[78]	Cannabis, Alcohol	IG1	In-person brief intervention	Participants received a 15-20 minute in-person brief motivational interviewing intervention that focused on assessing motivation for change. Participants discussed their personal pros and cons of alcohol or drug (AOD) use and determined what their friends thought about AOD use, and how that might affect their own use. The facilitator provided normative information on AOD use and participants were asked to discuss what they thought might happen if they continued to use AOD in the same way. Depending on participants' motivation to change their behavior, a discussion that addresses their willingness and confidence to cut back and/or stop their use followed. Finally, if participants were willing, they discussed a plan to prepare for high-risk situations where AOD might be present and how they could make a healthy choice in those situations.	92.8% received intervention as assigned	UC: During their primary care appointment, participants received a brochure developed by the project team with information on the effects of AOD use, how to prepare for risky situations, and online and telephone resources to obtain additional information.

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Adolescents	Mason, 2015[96]	Alcohol, all drugs	IG1	Peer network counseling	Participants received a 20-min Peer Network Counseling intervention guided by five key motivational interviewing (MI) clinical issues: rapport, acceptance, collaboration, reflections, and nonconfrontation. Therapists used baseline data from participants' screening surveys to show graphic displays of substance use and peer network characteristics during the counseling session. The intervention followed Motivational Enhancement procedures with age-matched substance use normative data presented as feedback. The intervention was structured into four component parts each lasting for 5 minutes: (a) rapport building and laptop presentation of substance use feedback in simple graphic form, (b) discussion of substance use likes/dislikes and discrepancies, (c) introduction of peer network information and graphical feedback, and (d) summary, change talk, and plans. The rapport building and feedback component was used to establish a nonjudgmental relationship and to present the participant with a graphical display of their substance use compared to national normative data. During the likes/dislikes discussion, participants' baseline responses were then reflected back to the teen, highlighting goals and values in order to have the participant identify and articulate discrepancies between current use and future goals and values. The peer network component began by introducing the concept of peer network and its influence on health using the laptop to illustrate the concept. The participants' peer network is reviewed for risks, protection, support, prosocial activities, and encouragement for healthful behavior as well as for substance use, influence/offers to use substance, and risky/dangerous activities. Participants were encouraged to reflect on their network and to consider making small modifications, such as adjusting the amount of time spent with particular peers as well as time spent at particular locations in order to support participants' willingness for peer network adjustment. The summary, change, talk and plans component summarized the session with appreciation of the client's honesty, and pays particular attention to underscoring discrepancies and reflecting on client-generated change talk. If the adolescent has articulated a change plan, this is reviewed, encouraged, and supported. If the teen has not made a specific change plan, the counselor encourages personal reflection on what was discussed.	100% received intervention	AC: Participants reviewed an informational handout with the therapist which covered several topics related to health behaviors such as exercise, nutrition/weight management, and life skills. These sessions lasted 20 minutes, matching the experimental condition in length.

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Adolescents	Walton, 2013[107]	Cannabis	IG1	In-person personalized feedback	The intervention, delivered by a therapist and facilitated by a computer, incorporated motivational interviewing, including tailored, parallel content: (1) goals/values; (2) feedback for cannabis, alcohol and other drug use, including consequences and DUI; (3) decisional balance exercise about cannabis; (4) tricky situations (e.g., role plays) including refusal skills for cannabis and other drug use, safe ways to get home/prevent driving high/drunk, dealing with peer pressure for delinquency (e.g., stealing a car/joy riding), coping with negative affect such as boredom, anger or sadness, and consequences (i.e., problem identification, getting help); and 5) the control brochure. The therapist used an elicit-provide-elicit framework when reviewing tailored feedback, using summaries and open-ended questions to evoke change talk. During role plays, therapists elicited tools to reduce use and avoid consequences.	NR	UC: Participants handed a brochure containing warning signs of cannabis problems, resources (substance use treatment, suicide hotlines, employment services, leisure activities), and cannabis information websites.
			IG2	Computer-based personalized feedback	The CBI was a stand-alone interactive animated program administered with a touch screen tablet and incorporated motivational interviewing, including tailored, parallel content: (1) goals/values; (2) feedback for cannabis, alcohol and other drug use, including consequences and DUI; (3) decisional balance exercise about cannabis; (4) tricky situations (e.g., role plays) including refusal skills for cannabis and other drug use, safe ways to get home/prevent driving high/drunk, dealing with peer pressure for delinquency (e.g., stealing a car/joy riding), coping with negative affect such as boredom, anger or sadness, and consequences (i.e., problem identification, getting help); and 5) the control brochure. Research staff handed a tablet to participants, and showed them how to adjust the audio. A virtual buddy guided participants through the program and provided audio feedback (via headphones). During the roleplays, participants watched animated situations and then were asked to make a behavioral choice. If a participant chose a negative option (e.g., smoking cannabis), they were asked to consider the consequences in relation to their goals. Once a positive choice was made, the animation resumed, modeling this selection. The tailored role-plays included six characters and showed the progression in medical, social, and legal consequences for characters that did and did not use cannabis over time. At the end, the computer instructed participants to return the tablet to staff.	NR	

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Young adults	Bernstein, 2009[80]	Cannabis	IG1	Computer-based personalized feedback	After completion of their baseline surveys, participants could immediately view feedback online and could choose to print feedback to their own printer. Participants could return to view feedback on the web for 3 months. Feedback was based on a motivational interviewing approach and normative feedback and was primarily text-based, but incorporated pictures to enhance interest and appeal as well as figures and graphs representing normative information and comparisons. Participants were presented with feedback about their cannabis use (e.g., frequency and quantity of use), perceived and actual descriptive norms for cannabis use (e.g., how frequently they believe the typical student uses cannabis), and perceived pros and cons of using cannabis. Self-reported negative consequences were included in the feedback, as well as ways in which reducing or eliminating cannabis use might be associated with reduced social and academic harm and participants' own cost-benefit scale for use. Skills training tips for avoiding cannabis and making changes in one's use were provided, as well as feedback about limiting alcohol intake. Perceived high-risk contexts and alternative activities around campus and in the community, were provided.	92.5% reported receiving emails about feedback, 75.2% reported linking to and viewing feedback, and 5.6% reported printing the feedback.	None

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Young adults	Lee, 2010[93]	Cannabis	IG1	In-person brief intervention	In addition to brief written materials about risks associated with marijuana use and a list of community resources and adolescent treatment facilities, participants received a 20- to 30-minute structured intervention delivered by a peer educator. The intervention consisted of the following components: 1) obtaining engagement and permission to raise the subject; 2) establishing context (''What's a typical day in your life like?''); 3) offering brief feedback, information, and norms, specific to age and sex, and exploring pros and cons of use: eliciting ''change talk'' and using the CRAFFT questions and a Readiness to Change ruler to reinforce movement toward behavior change); 4) generating a menu of options; 5) calling up assets／instilling hope; 6) discussing the challenges of change; and ending in a 7) prescription for change, generated by the subject, and referrals to community resources and specialty drug treatment services. Participants with CRAFFT scores of >2 were advised that the score may indicate high risk and a possible need for further evaluation and treatment. Participants also received a 5- to 10-minute booster phone call during which the interventionist reviewed the elements of the change plan, inquired about any progress toward change, and offered further referrals if those originally provided had not been possible to accomplish.	NR	UC: Participants received brief written materials about risks associated with marijuana use and a list of community resources and adolescent treatment facilities.

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Young adults	Lee, 2013[94]	Cannabis	IG1	In-person personalized feedback	Participants received a 1-hour intervention designed to provide the opportunity to discuss their cannabis use and review personalized graphic feedback. Facilitators used motivational interviewing principles. The personalized graphic feedback illustrated the impact of cannabis use in multiple domains to facilitate conversations about patterns of use and related consequences, including information regarding participants' typical pattern of cannabis use (i.e., frequency, quantity, peak occasion, timing of use during the day, and perceived time spent high) and comparison to peers. Information was provided on participants' estimated spending on cannabis compared with items that could be purchased instead, followed by feedback about self-reported confidence to avoid smoking in certain situations. Participants received feedback on family history risk, alcohol use, frequency of other drug use, and instances of combining other substances with cannabis such that interaction risks could be described. The final two sections of the feedback were dedicated to exploring students' social networks and goals for the next year. Related to social networks students listed up to 6 people whom they could count on for support, considered if the person knew about their cannabis use, and considered how the person felt about their cannabis use (or would feel about it). Finally, their five most important goals were listed and students were asked to rate how cannabis use affects goal attainment and how reducing cannabis use may positively or negatively affect attainment. At the end of the feedback session, students could ask questions and discuss goals. Participants who did not attend an in-person session were offered a mailed copy of the personalized feedback with a facilitated guide to reading the feedback.	54.7% participants attended the in-person intervention. Overall, 90 (84.9%) of participants received either the in-person or mailed feedback.	None
	Palfai, 2014[101]	Cannabis	IG1	Computer-based personalized feedback (eCHECKUP TO GO)	Following assessment, participants were provided with detailed personalized feedback about their cannabis use, including costs, norm risks, consequences, and alternative activities.	NR	AC: Participants were provided minimal general health feedback regarding recommended guidelines for sleep, exercise, and nutrition.

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Young adults	Stein, 2011[105]	Cannabis	IG1	Motivational interviewing	Participants received two 45-min motivational interviewing sessions spaced 1 month apart. During the initial session, participants were informed that the goals of the session (raising awareness of the pros and cons of cannabis use, exploring any conflicting motivation governing the decision to change, and organizing strategies to deal with internal or external obstacles to achieving change goals) and assured there was no "hidden agenda" about having to quit. Interventionists engaged participants in a discussion of values and goals, thoughts about cutting back/quitting, and state of readiness to make changes and provided feedback from the research assessment materials. This discussion led to the option of generating a change plan, which could be used for any goal, such as a health behavior goal or a general life goal, in addition to or instead of a cannabis-related goal. If participants were unable to generate an idea for a goal and did not explicitly state they did not want to set a goal, common goals were offered as examples, such as increased exercise, change in diet, or change in money or time management. At the end of the session, change plan sheets and an assessment feedback report were given to participants and the next appointment date was set. The followup session occurred 1 month later and was based on the participants' goals and change plans from the initial session. MI techniques were used to review the information from the first session to reevaluate the interest in setting a cannabis-related goal. Participants were also offered suggestions about interim steps that they might consider prior to setting an abstinence goal, such as gaining knowledge about trigger situations and/or beginning to increase quality of life activities such as exercising or using stress management techniques. For participants who did not set any goals in the first session, MI techniques were used to review the information from the first session to reevaluate the interest for setting a health-related, cannabis-related risk behavior and/or cannabis-related risk behavior goal.	80.3% received both MI sessions, 9.8% received one MI session, and 9.8% received none of the MI sessions.	None

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Adults	Bernstein, 2005[81]	Cocaine, Heroin	IG1	Motivational interviewing	Participants received a semi scripted, brief (10-45 min) motivational interview delivered by a peer, a substance abuse outreach worker in recovery. The motivational interview involved the following steps: establishing rapport, asking permission to discuss drugs, exploring the pros and cons of drug use, eliciting the gap between real and desired quality of life, and assessing readiness to change on a ruler scaled from 1 (not ready) to 10 (ready). The peer interventionist negotiated an action plan based on examples of the enrollee's past successes in making behavior change. Participants also received a handout from the interventionist stating that "based on your screening responses, you would benefit from help with your drug use." This form included a list of treatment options including detox, AA/NA, acupuncture, residential treatment facilities, and harm reduction information about safe sex and needle exchange. In addition to this interview, semi-scripted and tailored to individual behavior, risks, culture, and language, participants in the intervention group received referrals if desired, and a 5-10 min telephone booster call after 10 days, during which the interventionist asked what had transpired and if any new referrals were needed.	31% could be reached for phone booster session.	MI: Participants received only a handout stating that "based on your screening responses, you would benefit from help with your drug use." This form included a list of treatment options including detox, AA/NA, acupuncture, residential treatment facilities, and harm reduction information about safe sex and needle exchange, but there was no discussion about this information.
	Blow, 2017[82]	All drugs	IG1	Therapist-delivered brief intervention	Received 30-min therapist-delivered intervention based on principles of motivational interviewing, transtheoretical model, and FRAMES during their ED visit. Therapists used a touchscreen tablet to guide the session. Throughout the intervention, therapists handed the participant the computer so that they could view and collaboratively select goals, concerns, benefits, readiness to change statements for each drug, tools to manage challenging situations, and strengths. During the feedback portion of the intervention, participants viewed a graphic depicting the local prevalence of each substance the patient reported using during screening. The final screen displayed a tailored summary which therapists used to provide a final verbal summary and which was printed and provided to the participants. At the end of the intervention, participants received a 4-page "change plan" booklet	NR	UC: Printed materials with information about community treatment resources and 3-min review of information

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Adults					containing goals, plan related to their use, benefits, tools, and strengths.		
			IG2	Computer-based brief intervention	Received 30-min computer-delivered intervention based on principles of motivational interviewing, transtheoretical model, and FRAMES during their ED visit. The intervention was delivered via touchscreen tablet computers with audio headphones. The intervention included still images of actors streamed together and interactive questions and exercises. Participants had a choice of selecting a culturally-specific virtual health counselor who introduced choices and activities on the computer. Participants watched short video vignettes featuring a recorded voice of a character telling a story of drug use. Interactive exercises during the intervention including selecting goals, concerns, benefits, change statement, challenges, tools/strategies and strengths.	NR	
	Bogenschutz, 2014[83]	All drugs	IG1	Brief intervention + telephone booster sessions	In addition to an informational pamphlet about drug use and misuse, its potential consequences, and treatment options and optional referral to addiction treatment, participants received a manual-guided brief intervention with telephone boosters (BI-B) based on motivational interviewing principles. The BI-B had content patterned based on motivational enhancement therapy, including use of feedback based on screening information and development of a change plan if indicated. Consistent with the spirit of motivational interviewing, the BI focused initially on the primary problem drug identified by the participant, but also addressed concerns about other substance use if these came up in the session. In addition, participants received up to 2 telephone "booster" sessions to check whether they had entered treatment, review change plans, and reinforce motivation. The booster calls occurred within 7 days of the ED visit if possible, but up to 1 month was allowed to complete the calls if necessary.	421 (99%) participants received the initial brief intervention, 243 (57%) received the first booster call, and 166 (39%) received the second booster call. 250 (58.5%) of participants were referred to addiction treatment	MI: Participants received an informational pamphlet about drug use and misuse, its potential consequences, and treatment options and optional referral to addiction treatment, consisting of a recommendation to seek treatment and a standardized list of available options.

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Adults	Gelberg, 2015[87]	All drugs	IG1	Brief intervention + telephone coaching sessions	Participants received a face-to-face brief intervention during their clinician visit. Clinicians followed a paper scripted protocol "Summary to Clinician" provided by research staff based on the patients' highest-scoring drug in risky range (HSD). The message covered drug addiction as a chronic brain disease, the need to quit or reduce using drugs to prevent this disease, the physical and mental consequences of drug use, and the potential accelerated progression towards severe substance use disorders caused by poly-substance use. If a participant scored in the risky range on multiple drugs, clinicians focused on the HSD, but also recommended reduction of the other drugs. If a participant scored in the risky range for a stimulant (methamphetamine, amphetamines, cocaine), clinicians focused on that stimulant even if it was not the HSD, since prior investigation found that stimulants were the most common serious drugs used illicitly by the patient population. Clinicians also told participants that they would receive telephone calls 2 and 6 weeks later from a health educator. Participants subsequently received a Drug Health Education Booklet with a Report Card for their HSD and viewed a video doctor (2 minutes) reinforcing the clinician message. The 2-week and 6-week telephone drug-use coaching sessions (20–30 minutes each) reinforced the clinicians' message, and followed a patient-centered protocol, focusing on HSD use reduction.	All 171 intervention participants received clinician brief advice, and 134 (78%) had at least 1 telephone session (93 [54%] two sessions, 41 [24%] one session).	AC: Received a video doctor and information booklet on cancer screening. At study exit, participants were given all intervention materials and, if they scored 4 or higher for nay drugs on the 3-month ASSIST, with their permission the results were given to their doctor (although brief intervention for drug use was not provided to CG participants).
	Gelberg, 2017[88]	All drugs	IG1	Brief intervention + telephone coaching sessions	Replication of Gelberg, 2015 intervention with minor modifications.	All 32 intervention participants received clinician brief advice (as reported on the clinician Intervention Plan), and 22 (69%) had at least 1 telephone session and 15 (47%) had both sessions.	AC: Participants received a video doctor and information booklet on cancer screening.

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Adults	Gryczynski, 2016[112]	All drugs	IG1	Brief computer-based session	Computerized brief intervention consisting of a short, single-session interactive program led by an animated talking avatar. Participants' choice was emphasized throughout, and participants were free to choose which substances to focus on (up to two) and what kinds of behavioral changes they were willing to make. The computer BI included questions about substance use problems, gender-specific normative feedback messaging, rating importance to change, and rating confidence (self-efficacy) to change. Participants received tailored messages and options based on their responses.	NR	WL
	Humenuik, 2011[89]	All drugs	IG1	Brief intervention	Participants received a brief intervention (BI) linked to the results of the ASSIST screening questionnaire via the use of the ASSIST Feedback Report card. The BI focused on the drug receiving the highest moderate-risk specific substance involvement score on the ASSIST (for cannabis, cocaine, amphetamine-type stimulants, or opioids). If participants scored within the moderate-risk range for two or more of the target drugs, the intervention focused on the highest scoring substance or the substance that was of most concern to the participant. Discussion of the scores and their meaning comprised a major part of the BI, and participants took the card home with them. The BI incorporated motivational interviewing (MI) techniques, and each country developed their own culturally appropriate BI based on the principles of MI. The BI also comprised a take-home guide called Self-Help Strategies for Cutting Down or Stopping Substance Use. On average, sessions lasted 13.8 minutes.	Assume 100% of participants received brief intervention	WL: Participants were invited to contact the clinical interviewer if they had concerns about their substance use and were administered the brief intervention following the intervention period.
	Martino, 2018[95]	Alcohol, All drugs	IG1	In-person brief intervention	Following screening, one 20-min intervention based on motivational interviewing to support the importance of, and a woman's confidence in, cutting down or quitting substances and obtaining treatment.	99% received the intervention	UC: Received 2-min interaction based on their ASSIST score and told about local treatments.
			IG2	Computer-based brief intervention	Following screening, one 20-min computer-based, self-directed intervention based on motivational interviewing to support the importance of, and a woman's confidence in, cutting down or quitting substances and obtaining treatment. The electronic sessions featured an interactive, 3-dimensional, mobile narrator that delivered the intervention.		

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Adults	Poblete, 2017[102]	Alcohol, All drugs	IG1	Brief intervention based on FRAMES	Participants received an ASSIST-linked brief intervention for the substance with the highest score, and the ASSIST self-help guide, with additional information regarding substances and high-risk situation management. When two substances had the same score, the participant had the choice to decide which substance to receive counseling for. The intervention was based on the FRAME (Feedback, Responsibility, Advice, Menu Options, Empathy, and Self-Efficacy) model, which provides specific feedback, offers a menu of options, and enhances motivation to change. The average intervention time, including the initial screening was 17.6 minutes.	Assume 100% of participants received brief intervention	UC: Participants received a pamphlet of their own choosing containing broad information on substance use risk and harm.
	Roy-Byrne, 2014[103]	All drugs	IG1	In-person personalized feedback + telephone booster session	Participants received a single brief (30-min) intervention in which interventionists provided feedback about their drug use screening results, explored pros and cons of drug use, increased participant confidence in their ability to change, and discussed opportunities to change. When appropriate, interventionists used an illustrated handout depicting the participant's DAST-10 score and its associated problem severity (low, intermediate, substantial/severe) to aid the discussion and provided a list of substance abuse treatment resources. Interventionists used a motivational interviewing approach and tailored the intervention to allow for flexibility as to which or how many drugs to target, as well as in how to guide the participant (e.g., specialty treatment, abstinence, harm reduction). The same interventionist attempted a follow-up telephone booster session within 2 weeks of the intervention.	97% received a brief intervention and 47% received a booster call. Brief intervention averaged 27 min.	UC: Participants received an illustrated handout depicting their DAST-10 drug problem severity score and list of substance abuse resources. Resembled the "notification and referral" strategy that might be implemented in high-quality usual care.
	Saitz, 2014[104]	All drugs	IG1	Brief negotiated interview	Participants received a single 10- to 15-minute structured interview that used some features of motivational interviewing and included feedback, review of the "pros and cons" of use, and development of a plan for change. The interview focused on the participant's main drug, but addressed alcohol and other drugs if they emerged as relevant.	All participants received intervention.	MI: Participants were given information on how to contact AA, NA, the hospital behavioral health clinic and emergency

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Adults	Saitz, 2014[104]	All drugs	IG2	Motivational interviewing	Participants received 30 to 45 minutes of motivational interviewing with an offered 20- to 30-minute booster followup session. The interview elicited possible links between drug use and health concerns, heightening discrepancies between negative drug use outcomes and valued goals, enhancing self-efficacy about behavior change, and providing options for change. The interview focused on the participant's main drug, but addressed alcohol and other drugs if they emerged as relevant.	All participants received 30-45 min motivational interviewing session, and 31% received the optional 20-30 min booster session.	team, a state hotline, a city triage line, and websites for alcohol and drug screening.
	Watkins, 2017[108]	Alcohol, All drugs	IG1	Collaborative care	The intervention included a population-based management approach, measurement-based care, and integration of addiction expertise through a RAND-based clinical psychologist affiliated with the Motivational Interviewing Network of Trainers. Along with therapy, participants had the option to use medication-assisted treatment (MAT) with sublingual buprenorphine/naloxone for opioid use or long-acting injectable naltrexone for alcohol use disorders. Care coordinators met with participants and encouraged them to meet with a therapist for evaluation and treatment planning. All participants were entered in a registry that tracked treatment progress and prompted care coordinators to reach out to patients with missed visits. Care coordinators conducted regular assessments of substance use; results were entered in the registry and reviewed during team meetings.	98% were entered into the registry, 93% met with the care coordinator, 76% scheduled an appointment with a therapist, 45% kept the appointment, and 20% had at least 1 additional psychotherapy session. Sixteen of the 24 clinicians who were trained prescribed XR-NTX and 11 of the 12 waivered prescribers prescribed BUP/NX; overall 61% prescribed MAT.	UC: Participants were told by the research team that the clinic provided opioid, alcohol, and other drug treatment and given a number for appointment scheduling and list of community referrals. They did not receive any additional outreach or contact.

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Adults	Woolard, 2013[109]	Alcohol, Cannabis	IG1	Brief motivational interviewing	Participants received two brief interventions guided by the principles of motivational interviewing. The goal of the first brief intervention was to engage the participant in reflection upon the pros and cons of alcohol and marijuana use. The intervention incorporated the following elements of motivational interviewing: 1) feedback; 2) emphasis on personal responsibility for change; 3) advice with permission; 4) a menu of alternative change options; 5) an empathic interventionist style; and 6) fostering patient self-efficacy. The interventionist provided direct feedback concerning the participant's alcohol and marijuana use compared to community norms. The participant and interventionist developed a change plan that addressed the changes the participant wanted to make, usually focused on reduction of substance use. If the participant was not ready to change substance use, the interventionist worked with the participant to increase motivation for change. The interventionists discussed with participants the pros and cons of alcohol and marijuana use and explored their conjoint use, and the effect that conjoint use had on the pros and cons. The focus of the second brief intervention session was to review and reinforce the change and create a change plan with those who had not made a change plan in the first session. In addition to the brief intervention sessions, participants received routine emergency care for their presenting medical complaint and were offered information on local treatment resources for substance misuse.	51% returned to second intervention session	UC: Participants received routine emergency care for their presenting medical complaint and were offered information on local treatment resources for substance misuse.
	Zahradnik, 2009[111]	Prescrip-tion drugs	IG1	Motivational interviewing	Participants received two motivational interviewing sessions. The first 30-45 minute session took place in the hospital; the second session, 4 weeks later, was conducted by phone. The intervention was based on the Transtheoretical Model of behavior change. Participants received an individualized feedback letter eight weeks after the first intervention. which was sent to study participants 8 weeks after the first intervention. When appropriate, strategies for improving self-efficacy and maintaining changes were included in the feedback letter. In each step of the intervention, it was pointed out that it was necessary to discontinue or reduce the medication only with help from professionals, e.g. the general practitioner or a medical specialist.	NR	UC: Informational booklet about prescription drugs.

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Postpartum women	Ondersma, 2007[99]	All drugs	IG1	Computer-based brief intervention	Participants received a 20-minute single-session computer-delivered brief intervention. The intervention consisted of three components based on motivational interviewing and brief intervention principles: (1) feedback regarding the negative consequences of drug use that the participant reported, as well as self-reported readiness to change, and drug use as compared to that of all adult women; (2) pros and cons of drug use and related change, in which the participant chose from lists of positive and negative aspects of drug use from their perspective; and (3) a summary and query regarding the participant's interest in change, followed by optional goal-setting regarding drug use. Throughout the intervention section, the animated narrator reflected back the participant's answers, emphasized that whether or not to change was up to the participant, and expressed optimism regarding the possibility of success. In addition, participants received two non-tailored mailings 4 and 9 weeks after the intervention and were offered free taxi transportation for electing to attend a treatment intake/substance abuse evaluation at a local agency.	NR	None: CG received no intervention.

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Postpartum women	Ondersma, 2014[98]	All drugs	IG1	Computer-based personalized feedback (eCHECKUP TO GO)	Participants received six 30-min individual behavioral therapy sessions that involved a combination of motivational enhancement therapy (MET) and cognitive behavioral therapy (CBT). The content included motivational enhancement, functional analysis, safe sexual behavior, communication skills, relapse prevention and problem-solving skills. Research nurse therapists had the flexibility to offer additional sessions or repeat topics if there was time and need. An unlimited number of sessions was available in pregnancy and up to 2 booster sessions after delivery although the manual included 6 total sessions.	4.3% did not receive the intervention, 23.9% received 1-2 sessions, and 60.9% received ≥3 sessions. Women in CG attended an average of 7 treatment visits while IG subjects attended an average of 5 visits. Average time in treatment was 7.12 (SD 3.57) minutes for CG and 148.17 (SD 97.34) minutes for IG participants. An average of 5.88 sessions and 3.89 sessions were received in pregnancy by the CG and IG, respectively.	UC: Participants received one minute of brief advice based on a manualized version of standard interventions offered by obstetrical doctors and nurses. The manual, used by the participant's obstetrical provider, provided guidance on the risks of substance use, the importance of abstinence, and the benefit of seeking drug and alcohol treatment outside of the prenatal setting.

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Postpartum women	Ondersma, 2018[100]	All drugs	IG1	Computer-based brief intervention focused on parenting	Participants received an indirect computerized, interactive intervention with an animated talking narrator and natural-language reflections. The intervention was patterned after motivational interviewing principles and used tailoring on multiple elements to present each participant with unique content. Participants began the intervention by completing a brief assessment of substance use, mental health, relationship safety, exposure to violence, risky sexual behaviors, ethnic identity, and religiosity. Upon completing the assessment, participants received a video-based orientation to the intervention, described as "The Parent Check-up (PCU)", which was tailored to their ethnic identity and religiosity. After the video, the intervention focused on key parenting strengths, first focusing a strength identified by participants provided during the assessment process, and then discussing the four key strengths that facilitate infant growth and development (emotional health, safety, physical health, and a healthy home). The video touched on substance use but did not focus on it exclusively. After the video, participants received a feedback report indicating which of the four strengths were already strengths, and which might be considered a growth area. Participants were asked for their thoughts regarding that feedback and were offered the option of changing in one of the four areas or ending the PCU.	100% received intervention	AC: Participants watched educational videos about infant nutrition from birth to age one (i.e., breastfeeding, formula feeding, when to introduce solids) with no mention of safety, emotional health, or substance use.

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Pregnant women	Tzilos Wernette, 2017[106]	Alcohol, Cannabis	IG1	Health Checkup for Expectant Moms computerized program	Participants interacted with a computer and were guided by an animated narrator, which engages in a motivational interviewing-consistent style, can use emotionally expressive statements and empathic reflection. Health Checkup for Expectant Moms (HCEM), a 60-minute computer-delivered session, was self-administered with the assistance of a research assistant (RA) and included a behavioral skills component, in which the RA facilitated the setup of models for male and female condom use application. This portion of HCEM included video instruction that was guided by a computer. HCEM presented information and education regarding health risks and included testimonial videos of women who were HIV positive and pictures of STIs. All participants had the option to create a personalized safety plan that was tailored and designed to increase awareness of the interconnected risk factors for STI/HIV and alcohol/drug use in the woman's life. At the 15-minute booster session, the narrator reviewed the components of the intervention session (e.g., goal-setting), and participants reviewed their personalized plan and identified any barriers to increasing safety behaviors. Participants also received brochures specifically designed to reduce risky behaviors during pregnancy	100% completed HCEM program; 97% completed booster session	AC: Participants interacted with the computer and were guided by the same narrator used for intervention group participants. Participants watched brief segments of popular television shows with subsequent questions for ratings of their subjective preference. Participants also received brochures specifically designed to reduce risky behaviors during pregnancy.

Table 11. Detailed intervention characteristics, by subpopulation (KQ 4 and KQ 5)

Target pop	Author, year	Target subs	Int arm	Intervention	IG detailed description	Intervention adherence	CG description
Pregnant women	Yonkers, 2012[110]	Alcohol, all drugs	IG1	MET-CBT	Participants completed a 20-min screening and brief intervention on tablets. The intervention comprised a mobile, 3-dimensional cartoon character capable of ≥50 animated actions that read each item for the participant, acted as narrator and guide throughout the process, and actively sought a nonjudgmental, empathic, and nonthreatening demeanor using reflections and self-deprecating humor. The experience of working with the software was intended to be highly interactive, with immediate responses to most input, occasional summaries, branching based on participant characteristics, responses, or preferences, and empathic reflection branches/approaches based on participant reports of current drug use and type of drug use, as well as on participants' stated plans regarding drug use after going home. The intervention was broken down into components focusing on (a) eliciting the participant's thoughts about change and their perceived advantages of doing so, if any; (b) reviewing feedback regarding how the participant's drug use compares to that of others, and of possible benefits of changing; and (c) optional goal-setting, including a menu of change options. The intervention allowed participant input (e.g., whether or not to see more information on a certain topic), and used different branches/approaches based on participant reports of current drug use and type of drug use, as well as on participants' stated plans regarding drug use after going home. Participants listened to the narrator via headphones to ensure privacy.	NR	AC: Participants were asked a number of questions about their preferences in music and television, were shown brief video clips consistent with their preferences, and were asked to provide feedback regarding their opinion of the various video clips.

Abbreviations: AA = Alcoholics Anonymous; AC = attention control; CBT = cognitive behavioral therapy; CG = control group; FRAMES = Feedback, Responsibility, Advice, Menu Options, Empathy and Self-Efficacy; IG = intervention group; MET = motivational enhancement therapy; MI = motivational interviewing; NA = Narcotics Anonymous; NR = not reported; target subs = substance(s) targeted by the intervention; UC = usual care; WL = waitlist

Table 12. Results for drug use (KQ 4a) for trials among adolescents

Author, year	Outcome	Scale range*	Recall (mo.)	Arm (subgrp)	FU	IG n	IG BL mean (sd)	IG FU mean (sd)	IG % mean change (sd)	CG n	CG BL mean (sd)	CG FU mean (sd)	CG mean change (sd)	Study-reported between group difference†	Study-reported p-value
D'Amico, 2018[78]	Cannabis use frequency	NA	3‡	IG1	3	153	10.02 (8.51)	6.38 (8.05)	NR	141	9.51 (8.31)	5.95 (7.58)	NR	0.00	0.99
					6	153	10.02 (8.51)	6.13 (7.9)	NR	141	9.51 (8.31)	5.07 (6.83)	NR	0.11	0.35
					12	153	10.02 (8.51)	6.76 (8.37)	NR	141	9.51 (8.31)	5.21 (7.35)	NR	0.14	0.23
	Number of times used cannabis on days used	NA	3‡	IG1	3	153	1.54 (1.15)	1.34 (1.16)	NR	141	1.51 (1.15)	1.22 (1.1)	NR	0.09	0.41
					6	153	1.54 (1.15)	1.14 (1.16)	NR	141	1.51 (1.15)	1.18 (1.16)	NR	-0.04	0.73
					12	153	1.54 (1.15)	1.18 (1.2)	NR	141	1.51 (1.15)	1.06 (1.16)	NR	0.05	0.64
Mason, 2015[96]	Cannabis use days	0-7§	1	IG1 (Males)	3	15	1.59 (NR)	1.43 (NR)	NR	20	1.11 (NR)	1.26 (NR)	NR	NR	NR
				IG1 (Females)		44	1.06 (NR)	1.10 (NR)	NR	40	1.78 (NR)	1.40 (NR)	NR	NR	NR
				IG1 (Males)	6	15	1.59 (NR)	1.28 (NR)	NR	20	1.11 (NR)	1.44 (NR)	NR	0.37	NR
				IG1 (Females)		44	1.06 (NR)	1.13 (NR)	NR	40	1.78 (NR)	1.28 (NR)	NR	NR, NS	NR
Walton, 2013[107]	Cannabis use frequency	0-6‖	3	IG1	3	118	3.14 (1.86)	2.37 (2.13)	-24.5 (≤0.01)	110	3.25 (1.87)	2.09 (2.06)	-35.7 (≤0.01)	-0.18 (0.13)	0.16
				IG2		100	3.06 (1.90)	2.05 (2.25)	-33.0 (≤0.01)	110	3.25 (1.87)	2.09 (2.06)	-35.7 (≤0.01)	-0.08 (0.15)	0.57
				IG1	6	118	3.14 (1.86)	2.40 (2.11)	-23.6 (NR)	110	3.25 (1.87)	2.04 (2.10)	-37.2 (NR)	0.25 (0.14)	0.08
				IG2		100	3.06 (1.90)	1.96 (2.05)	-35.9 (NR)	110	3.25 (1.87)	2.04 (2.10)	-37.2 (NR)	0.08 (0.16)	0.62
				IG1	12	118	3.14 (1.86)	2.63 (2.20)	-19.1 (NR)	110	3.25 (1.87)	2.14 (2.21)	-31.1 (NR)	0.15 (0.14)	0.28
				IG2		100	3.06 (1.90)	2.04 (2.20)	-32.7 (NR)	110	3.25 (1.87)	2.14 (2.21)	-31.1 (NR)	-0.03 (0.16)	0.85
	Other drug use frequency	0-6‖	3	IG1	3	118	0.47 (1.29)	0.26 (0.92)	-44.7 (≤0.05)	110	1.16 (2.71)	1.18 (4.13)	1.7 (NR)	0.61 (0.39)	0.12
				IG2		100	0.86 (3.01)	0.16 (0.62)	-81.4 (≤0.05)	110	1.16 (2.71)	1.18 (4.13)	1.7 (NR)	1.82 (0.68)	<0.01
				IG1	6	118	0.47 (1.29)	0.26 (0.93)	-44.7 (NR)	110	1.16 (2.71)	1.19 (4.64)	2.6 (NR)	-0.48 (0.42)	0.255

Table 12. Results for drug use (KQ 4a) for trials among adolescents

Author, year	Outcome	Scale range*	Recall (mo.)	Arm (subgrp)	FU	IG n	IG BL mean (sd)	IG FU mean (sd)	IG % mean change (sd)	CG n	CG BL mean (sd)	CG FU mean (sd)	CG mean change (sd)	Study-reported between group difference†	Study-reported p-value
				IG2		100	0.86 (3.01)	0.11 (0.45)	-87.2 (NR)	110	1.16 (2.71)	1.19 (4.64)	2.6 (NR)	-1.41 (0.52)	<0.01
				IG1	12	118	0.47 (1.29)	0.38 (1.70)	-19.1 (NR)	110	1.16 (2.71)	0.64 (2.12)	-39.7 (NR)	0.33 (0.51)	0.52
				IG2		100	0.86 (3.01)	0.48 (2.13)	-44.2 (NR)	110	1.16 (2.71)	0.64 (2.12)	-39.7 (NR)	0.21 (0.48)	0.66
	Frequency of cannabis DUI	0-5¶	3	IG1	3	118	0.40 (0.93)	0.20 (0.65)	-50.0 (≤0.05)	110	0.26 (0.66)	0.32 (0.83)	23.1 (NR)	0.87 (0.33)	<0.01
				IG2		100	0.48 (1.06)	0.37 (0.94)	-22.9 (NR)	110	0.26 (0.66)	0.32 (0.83)	23.1 (NR)	0.55 (0.35)	0.11
				IG1	6	118	0.40 (0.93)	0.26 (0.79)	-35.0	110	0.26 (0.66)	0.37 (0.90)	42.3	-0.68 (0.41)	0.10
				IG2		100	0.48 (1.06)	0.46 (1.05)	-4.2	110	0.26 (0.66)	0.37 (0.90)	42.3	-0.34 (0.37)	0.36
				IG1	12	118	0.40 (0.93)	0.33 (0.90)	-17.5	110	0.26 (0.66)	0.25 (0.85)	-3.8	-0.32 (0.41)	0.44
				IG2		100	0.48 (1.06)	0.45 (0.99)	-6.2	110	0.26 (0.66)	0.25 (0.85)	-3.8	-0.17 (0.44)	0.70

* Low value indicates better outcome for all scales

† D'Amico, 2018 and Mason, 2015 reported Cohen's d effect size. Walton, 2013 reported mean difference and standard error

‡ Baseline measurement reflects number of times used cannabis in the past year whereas measures at 3-, 6-, and 12-months reflect number of times used cannabis in the past 3 months

§ Categorical responses where 0 = 0 days, 1 = 1-2 days, 2 = NR, 3 = 3-5 days, 4 = 6-9 days, 5 = 10-19 days, 6 = 20-29 days, and 7 = all 30 days

‖ Categorical responses where 0 = never, 1= 1–2 days, 2 = once a month or less, 3= 2–3 days per month, 4 = 1–2 days per week, 5 = 3–5 days per week, and 6 = every day or almost every day

¶ Categorical responses (assumed) where 0 = never, 1 = 1–2 times, 2 = 3–5 times, 3 = 6–9 times, 5 = 10 or more times

Abbreviations: BL = baseline; CG = control group; DUI = driving under the influence; FU = followup; IG = intervention group; mo. = months; n = number; NR = not reported; NS = not statistically significant; recall = period of time respondents are asked to recall their substance use; sd = standard deviation; subgrp = subgroup

Table 13. Results for health, social, and legal outcomes (KQ 4b) for trials among adolescents

Author, year	Outcome	Scale range	Recall (mo.)	Arm	FU	IG n	IG BL mean (sd)	IG FU mean (sd)	IG % mean change (sd)	CG n	CG BL mean (sd)	CG FU mean (sd)	CG % mean change (sd)	Study-reported between group mean difference (se)*	Study-reported p-value
D'Amico, 2018[78]	Cannabis-related consequences	0-20†	3‡	IG1	3	153	3.58 (10.46)	1.67 (5.19)	NR	141	4.63 (12.54)	1.89 (7.19)	NR	0.01	0.93
					6	153	3.58 (10.46)	0.70 (1.54)	NR	141	4.63 (12.54)	1.46 (5.67)	NR	-0.20	0.16
					12	153	3.58 (10.46)	0.92 (3.26)	NR	141	4.63 (12.54)	2.36 (9.29)	NR	-0.28	0.04
Walton, 2013[107]	Cannabis-related consequences	0-28§	3	IG1	3	118	14.2 (15.3)	12.5 (12.5)	-11.7 (NR)	110	14.0 (15.0)	13.6 (15.1)	-2.6 (NR)	-0.18 (0.12)	0.15
				IG2		100	14.3 (15.5)	11.5 (15.0)	-19.7 (≤0.01)	110	14.0 (15.0)	13.6 (15.1)	-2.6 (NR)	-0.24 (0.12)	<0.05
				IG1	6	118	14.2 (15.3)	11.3 (12.9)	-20.4	110	14.0 (15.0)	11.0 (13.6)	-20.9	-0.08 (0.15)	0.60
				IG2		100	14.3 (15.5)	10.5 (13.6)	-26.6	110	14.0 (15.0)	11.0 (13.6)	-20.9	-0.15 (0.16)	0.37
				IG1	12	118	14.2 (15.3)	11.1 (13.0)	-21.8	110	14.0 (15.0)	11.5 (14.4)	-17.9	-0.07 (0.15)	0.62
				IG2		100	14.3 (15.5)	12.7 (13.8)	-6.7	110	14.0 (15.0)	11.5 (14.4)	-17.9	0.08 (0.17)	0.62

* D'Amico, 2018 reported Cohen's d effect size.

† Adolescents rated how often they experienced a particular negative consequence in the past year or past 3 months on a scale from 0 (never) to 7 (20 or more times). Items were rescaled to a pseudo-continuous variable ranging from 0 to 20 using the midpoint of any range as the new value (e.g., 3–5 times was recoded as 4 times) and then summed to create a total score indicating the number of negative consequences experienced

‡ Baseline measurement reflects number of times used cannabis in the past year whereas measures at 3-, 6-, and 12-months reflect number of times used cannabis in the past 3 months

§ Included 23 items from the adapted version of the Rutgers Alcohol Problems Index (Marijuana Problem Inventory) and 5 items from the Severity of Dependence Scale where endorsement of an item = 1 and no endorsement = 0. Low value indicates better outcome.

Abbreviations: BL = baseline; CG = control group; FU = followup; IG = intervention group; mo. = months; n = number; recall = period of time respondents are asked to recall their substance use; sd = standard deviation; se = standard error

Table 14. Results for drug use (KQ 4a) for trials among young adults and adults

Target pop	Author, year	Outcome	Recall (mo)	Arm	FU (mo)	IG n	IG BL mean (sd)*	IG FU mean (sd)†	CG n	CG BL mean (sd)*	CG FU mean (sd)†	Study-reported between group difference	Study-reported p-value
Young Adults	Bernstein, 2009[80]	Cannabis use days	1	IG1	3	41	19.0 (10.9)	14.2 (10.8)	54	15.3 (10.1)	13.7 (11.2)	-4.2 (-8.1 to -0.3)	0.039
					12	47	19.0 (10.9)	11.0 (10.7)	55	15.3 (10.1)	13.2 (11.7)	-5.3 (-10.0 to -0.6)	0.024
		Cannabis abstinence‡			3	42	0	6 (14.3)	54	0	7 (12.7)	OR=1.15 (0.36 to 3.73)	0.814
					12	47	0	21 (44.7)	55	0	12 (21.8)	OR=2.89 (1.22 to 6.84)	0.014
	Lee, 2010[93]	Cannabis use days	3	IG1	3	171	9.9 (15.8)	9.1 (14.1)	170	9.8 (16.2)	9.1 (15.8)	NR	NR, NS
					6		9.9 (15.8)	11.1 (18.7)		9.8 (16.2)	11.9 (19.3)	NR	NR, NS
	Lee, 2013[94]	Cannabis use days	1	IG1	3	86	16.5 (8.2)	14.1 (10.1)	93	16.5 (8.2)	14.9 (10.8)	RR=0.96 (0.80 to 1.15)§	NR, NS
					6	89	16.5 (8.2)	13.2 (10.6)	84	16.5 (8.2)	11.7 (11.1)	RR=1.11 (0.85 to 1.43)§	NR, NS
		Joints smoked‖	2	IG1	3	89	9.4 (9.8)	6.9 (8.2)	95	8.3 (8.8)	8.5 (9.8)	RR=0.76 (0.0.60 to 0.96)§	<0.05
					6	90	9.4 (9.8)	7.3 (8.4)	87	8.3 (8.8)	7.5 (10.7)	RR=1.46 (0.73 to 1.46)§	NR, NS
	Palfai, 2014[101]	Cannabis use days	3	IG1	3	54	30.3 (28.4)	30.3 (30.3)	49	39.6 (28.4)	38.3 (32.0)	NR	NR, NS
					6		30.3 (28.4)	29.3 (29.7)		39.6 (28.4)	37.1 (32.4)	NR	NR, NS
	Stein, 2011[105]	Any cannabis use‡	3	IG1	3	163	163 (100.0)	NR	169	169 (100.0)	NR	OR=0.53 (0.33 to 0.86)	<0.01
					6	163	163 (100.0)	NR	169	169 (100.0)	NR	OR=0.74 (0.47 to 1.17)	0.202
Adults	Bernstein, 2005[81¶]	Cocaine and opiates abstinence‡#	1	IG1	6	403**	0 (0.0)	70 (17.4)	375**	0 (0.0)	48 (12.8)	OR=1.51 (0.98 to 2.26)	0.052
		Cocaine abstinence‡#	1	IG1	6	376	0 (0.0)	84 (22.3)	344	0 (0.0)	58 (16.9)	OR=1.51 (1.01 to 2.24)	0.045
		Opiates abstinence‡#	1	IG1	6	189	0 (0.0)	76 (40.2)	160	0 (0.0)	49 (30.6)	OR=1.57 (1.00 to 2.47)	0.05
Adults	Bernstein, 2005[81¶]	Cocaine levels††	1	IG1	6	376	616 (NR)	436 (NR)	344	485 (NR)	464 (NR)	NR	0.058

Table 14. Results for drug use (KQ 4a) for trials among young adults and adults

Target pop	Author, year	Outcome	Recall (mo)	Arm	FU (mo)	IG n	IG BL mean (sd)*	IG FU mean (sd)†	CG n	CG BL mean (sd)*	CG FU mean (sd)†	Study-reported between group difference	Study-reported p-value
		Opiate levels††	1	IG1	6	189	26.4 (NR)	18.8 (NR)	160	30.7 (NR)	22.9 (NR)	NR	0.186
		Severity of disorder (ASI - Drug)‡‡	1	IG1	6	490	0.3 (0.1)	NR	472	0.2 (0.1)	NR	NR	0.06
		Severity of disorder (ASI - Medical)‡‡	1	IG1	6	490	0.6 (0.3)	NR	472	0.5 (0.4)	NR	NR	0.055
	Blow, 2017[82]	Drug use days	3	IG1	3	104	41.9 (33.5)	39.7 (35.8)	106	56.0 (34.6)	51.1 (37.1)	NR	NR
				IG2	3	95	47.9 (34.8)	46.8 (35.7)	106	56.0 (34.6)	51.1 (37.1)	NR	NR
				IG1	6	110	41.9 (33.5)	34.5 (35.8)	114	56.0 (34.6)	48.2 (39.0)	NR	NR
				IG2	6	105	47.9 (34.8)	43.5 (37.7)	114	56.0 (34.6)	48.2 (39.0)	NR	NR
				IG1	12	112	41.9 (33.5)	30.7 (34.7)	110	56.0 (34.6)	44.3 (38.1)	ES=-0.24 (-0.41 to -0.07)	<0.05
				IG2	12	108	47.9 (34.8)	42.7 (37.0)	110	56.0 (34.6)	44.3 (38.1)	ES=-0.13 (-0.28 to 0.03)	NR, NS
		Cannabis use days	3	IG1	3	104	35.6 (34.6)	34.5 (35.7)	130	50.3 (36.3)	45.1 (38.2)	NR	NR
				IG2	3	95	43.3 (36.2)	43.4 (36.2)	130	50.3 (36.3)	45.1 (38.2)	NR	NR
				IG1	6	110	35.6 (34.6)	31.0 (35.1)	130	50.3 (36.3)	43.2 (39.5)	NR	NR
				IG2	6	105	43.3 (36.2)	40.2 (37.6)	130	50.3 (36.3)	43.2 (39.5)	NR	NR
		Cannabis use days	3	IG1	12	112	35.6 (34.6)	28.3 (35.0)	130	50.3 (36.3)	41.4 (38.3)	ES=-0.24 (-0.42 to -0.06)	<0.05
				IG2	12	108	43.3 (36.2)	41.5 (37.8)	130	50.3 (36.3)	41.4 (38.3)	ES=-0.17 (-0.34 to -0.01)	<0.05
Adults	Bogenschutz, 2014[83]	Drug use days§§	1	IG1	3	375	14.8 (11.2)	9.4 (11.7)	382	16.3 (11.4)	10.9 (12.1)	MD=0.70 (-0.83 to 2.23)	0.57

Table 14. Results for drug use (KQ 4a) for trials among young adults and adults

Target pop	Author, year	Outcome	Recall (mo)	Arm	FU (mo)	IG n	IG BL mean (sd)*	IG FU mean (sd)†	CG n	CG BL mean (sd)*	CG FU mean (sd)†	Study-reported between group difference	Study-reported p-value
Adult					6		14.8 (11.2)	8.2 (11.2)		16.3 (11.4)	9.7 (11.6)	NR	NR, NS
					12		14.8 (11.2)	8.6 (11.2)		16.3 (11.4)	7.9 (11.1)	NR	NR, NS
		Drug use days	1	IG1	3	375	16.4 (11.0)	11.9 (12.0)	382	18.5 (10.9)	13.7 (12.4)	NR	NR, NS
					6		16.4 (11.0)	10.8 (12.1)		18.5 (10.9)	12.5 (12.2)	NR	NR, NS
					12		16.4 (11.0)	10.7 (11.8)		18.5 (10.9)	10.9 (12.1)	NR	NR, NS
		Drug use abstinence‡ ††§§	3	IG1	3	275	20 (5.7)	31 (11.3)	280	25 (7.4)	15 (5.4)	NR	0.02
					6	282	20 (5.7)	38 (13.5)	282	25 (7.4)	27 (9.6)	NR	NR, NS
					12	265	20 (5.7)	45 (17.0)	268	25 (7.4)	46 (17.2)	NR	NR, NS
		Drug use abstinence‡ ††	3	IG1	3	274	9 (2.4)	11 (4.0)	285	9 (2.6)	7 (2.4)	NR	NR, NS
					6	275	9 (2.4)	8 (2.9)	282	9 (2.6)	6 (2.1)	NR	NR, NS
					12	260	9 (2.4)	19 (7.3)	264	9 (2.6)	13 (4.9)	NR	NR, NS
	Gelberg, 2015[87]	Drug use days§§	1	IG1	3	129	10.6 (NR)	7.1 (5.8 to 8.5)	132	10.7 (NR)	9.9 (8.5 to 11.2)	MD=2.68 (0.76 to 4.60)	<0.01
	Gelberg, 2017[88]	Drug use days§§	1	IG1	3	23	11.4 (11.2)	6.6 (NR)	28	12.4 (10.6)	12.9 (NR)	MD=5.28 (-0.06 to 10.6)	0.053
		Any drug use‡‖	1	IG1	3	21	21 (100)	5 (25)	26	26 (100)	15 (56)	OR=0.10 (0.01 to 0.99)	<0.05
	Gryczynski, 2016[112]	ASSIST, total score	3	IG1	3	36	26.4 (9.5)	24.4 (4.2) ¶¶¶	35	34.2 (13.8)	27.8 (4.3) ¶¶¶	β=-2.0 (2.7)	0.46
	Humenuik, 2011[89]	ASSIST, total score	3	IG1§§§	3	103	34.9 (22.3)	31.1 (19.7)	115	39.0 (24.6)	31.3 (18.7)	NR	0.11

Table 14. Results for drug use (KQ 4a) for trials among young adults and adults

Target pop	Author, year	Outcome	Recall (mo)	Arm	FU (mo)	IG n	IG BL mean (sd)*	IG FU mean (sd)†	CG n	CG BL mean (sd)*	CG FU mean (sd)†	Study-reported between group difference	Study-reported p-value
		ASSIST, cannabis score				74	16.8 (7.7)	15.1 (9.5)	72	16.2 (6.7)	12.3 (7.0)	NR	0.08
		ASSIST, stimulant score‖‖				23	20.9 (7.9)	16.2 (11.8)	33	18.5 (7.6)	13.2 (10.5)	NR	0.8
	Martino, 2018[95]	Substance use days###	1	IG1	3	145	22.8 (21.4 to 24.3)	16.6 (14.8 to 18.6)	151	23.5 (22.2 to 24.9)	19.5 (18.1 to 21.1)	NR	NR
				IG2		143	23.9 (22.4 to 25.5)	16.9 (15.0 to 19.0)	151	23.5 (22.2 to 24.9)	19.5 (18.1 to 21.1)	NR	NR
				IG1	6	145	22.8 (21.4 to 24.3)	16.3 (14.4 to 18.5)	151	23.5 (22.2 to 24.9)	17.9 (16.1 to 19.9)	β=-0.032 (-0.115 to 0.052)	0.461
				IG2		143	23.9 (22.4 to 25.5)	16.3 (14.3 to 18.7)	151	23.5 (22.2 to 24.9)	17.9 (16.1 to 19.9)	β=-0.016 (-0.068 to 0.100)	0.706
	Poblete, 2017[102]	ASSIST, total score	3	IG1	3	400	27.1 (9.2)	28.1 (14.4)	406	26.6 (9.7)	27.9 (15.0)	MD=-0.13 (-1.47 to 1.74)	NR, NS
		ASSIST, cannabis score				143	9.6 (4.6)	10.4 (6.4)	144	10.0 (4.3)	9.8 (6.7)	MD=-.021 (-1.25 to 1.66)	NR, NS
		ASSIST, cocaine score				41	11.1 (5.1)	11.1 (9.2)	53	10.4 (5.1)	10.3 (8.5)	MD=-0.11 (-3.69 to 3.48)	NR, NS
	Roy-Byrne, 2014[103]	Drug use days§§	1	IG1	3	378	14.4 (11.3)	12.0 (12.1)	389	13.3 (10.7)	9.8 (10.6)	β=0.89 (-0.49 to 2.26)	NR, NS
					6	381	14.4 (11.3)	11.8 (10.6 to 13.0)	389	13.3 (10.7)	10.5 (9.5 to 11.7)	NR	NR, NS
					9	377	14.4 (11.3)	11.4 (10.3 to 12.7)	384	13.3 (10.7)	10.4 (9.4 to 11.6)	NR	NR, NS
					12	435	14.4 (11.3)	11.5 (10.3 to 12.7)	433	13.3 (10.7)	10.0 (9.0 to 11.3)	OR=1.20 (0.96 to 1.50)¶¶	NR, NS
Adults	Roy-Byrne, 2014[103]	Severity of disorder (ASI - Drug)§§	1	IG1	3	370	0.11 (0.1)	0.1 (0.09)	379	0.1 (0.1)	0.09 (0.09)	β=0.008 (-0.006 to 0.021)	NR, NS

Table 14. Results for drug use (KQ 4a) for trials among young adults and adults

Target pop	Author, year	Outcome	Recall (mo)	Arm	FU (mo)	IG n	IG BL mean (sd)*	IG FU mean (sd)†	CG n	CG BL mean (sd)*	CG FU mean (sd)†	Study-reported between group difference	Study-reported p-value
					6	374	0.11 (0.1)	0.1 (0.1 to 0.1)	373	0.1 (0.1)	0.1 (0.1 to 0.1)	NR	NR, NS
					9	372	0.11 (0.1)	0.1 (0.1 to 0.1)	375	0.1 (0.1)	0.1 (0.1 to 0.1)	NR	NR, NS
					12	435	0.11 (0.1)	0.1 (0.1 to 0.1)	433	0.1 (0.1)	0.1 (0.1 to 0.1)	β=0.005 (-0.005 to 0.016)	NR, NS
	Saitz, 2014[104]	Drug use days	1	IG1	6	169	15.1 (11.7)	14.2 (12.5)	175	14.3 (11.4)	13.8 (12.1)	IRR=0.97 (0.77 to 1.22)##	0.81
			1	IG2	6	173	13.8 (11.2)	14.1 (12.1)	175	14.3 (11.4)	13.8 (12.1)	IRR=1.05 (0.84 to 1.32)##	0.81
		Drug use days >1 time	1	IG1	6	169	10.5 (11.1)	10.8 (12.0)	175	9.6 (11.1)	9.1 (11.3)	IRR=1.20 (0.86 to 1.66)##	0.31
			1	IG2	6	173	9.4 (11.1)	11.1 (12.2)	175	9.6 (11.1)	9.1 (11.3)	IRR=1.19 (0.86 to 1.65)##	0.31
		Any drug use‡**	3	IG1	6	169	160 (97.0)	150 (94.9)	175	157 (95.7)	150 (91.5)	OR=1.65 (0.65 to 4.21)	0.57
			3	IG2	6	173	157 (95.7)	152 (93.2)	175	157 (95.7)	150 (91.5)	OR=1.29 (0.54 to 3.06)	0.57
		Severity of disorder (ASSIST score)***	3	IG1	6	169	21.8 (18.4)	24.8 (17.1)	175	22.9 (19.5)	25.8 (19.4)	β=-1.00 (-3.62 to 1.62)	0.50
			3	IG2	6	173	22.0 (18.6)	25.9 (19.9)	175	22.9 (19.5)	25.8 (19.4)	β=0.73 (-1.41 to 2.87)	0.50
	Watkins, 2017[108]	Opioid or any alcohol abstinence‡	1	IG1	6	138	NA	45 (32.8)	123	NA	27 (22.3)	ES=0.10 (0.01 to 0.23)	0.03
		Opioid, any alcohol, cocaine, methamphetamine, and marijuana abstinence‡	1	IG1	6	138	NA	36 (26.3)	123	NA	19 (15.6)	ES=0.13 (0.03 to 0.23)	0.01
Adults	Watkins, 2017[108]	Opioid abstinence‡	1	IG1	6	138	135 (72.0)	122 (8.7)	123	129 (67.9)	98 (79.9)	ES=0.07 (-0.07 to 0.22)	0.33
		Heroin abstinence‡	1	IG1	6	138	156 (83.4)	129 (93.5)	123	152 (80.0)	110 (89.4)	NR	NR

Table 14. Results for drug use (KQ 4a) for trials among young adults and adults

Target pop	Author, year	Outcome	Recall (mo)	Arm	FU (mo)	IG n	IG BL mean (sd)*	IG FU mean (sd)†	CG n	CG BL mean (sd)*	CG FU mean (sd)†	Study-reported between group difference	Study-reported p-value
		Prescription opioid abstinence‡	1	IG1	6	138	145 (77.5)	124 (89.9)	123	144 (75.8)	115 (93.5)	NR	NR
		Cocaine abstinence‡	1	IG1	6	138	152 (81.3)	120 (87.0)	123	163 (85.8)	109 (88.6)	NR	NR
		Methamphetamine abstinence‡	1	IG1	6	138	141 (75.4)	125 (90.6)	123	140 (73.7)	100 (81.3)	NR	NR
		Heroin abuse or depend‡††	1	IG1	6	138	51 (27.0)	34 (24.6)	123	64 (34.0)	36 (29.3)	NR	NR
		Prescription opioid abuse or depend‡††	1	IG1	6	138	32 (17.1)	25 (18.1)	123	27 (14.2)	17 (13.8)	NR	NR
	Woolard, 2013[109]	Alcohol and cannabis conjoint use days	1	IG1	3	211	6.5 (5.7 to 7.3)	2.0 (1.3 to 3.0)	224	6.2 (5.4 to 7.0)	2.7 (1.9 to 3.6)	NR	NR
			1	IG1	12	206	6.5 (5.7 to 7.3)	1.3 (0.8 to 1.5)	220	6.2 (5.4 to 7.0)	2.2 (1.6 to 2.9)	NR	0.02
		Cannabis use days	1	IG1	3	211	12.8 (11.4 to 14.3)	10.7 (9.1 to 12.3)	224	12.4 (11.0 to 13.8)	10.6 (9.0 to 12.2)	NR	NR
			1	IG1	12	206	12.8 (11.4 to 14.3)	9.4 (7.8 to 11.0)	220	12.4 (11.0 to 13.8)	10.0 (8.4 to 11.6)	NR	0.83
		Heavy cannabis use days‡‡‡	1	IG1	3	211	5.3 (4.5 to 6.2)	4.8 (3.4 to 6.3)	224	4.9 (4.2 to 5.6)	3.5 (2.3 to 4.8)	NR	NR
			1	IG1	12	206	5.3 (4.5 to 6.2)	3.2 (2.2 to 4.5)	220	4.9 (4.2 to 5.6)	3.6 (2.5 to 5.0)	NR	0.30
	Zahradnik, 2009[111]	Prescription drug abstinence‡	1 day	IG1	3	56	NA	10 (17.9)	70	NA	6 (8.6)	ES: 0.28	0.17
					12	56	NA	14 (25.0)	70	NA	14 (20.0)	OR=1.42 (0.57 to 3.52)	0.45

* Baseline n may differ from n analyzed
† Or 95% CI as reported
‡ n (%)
§ Rate ratio calculated using negative binomial regression models
‖ Number of joints smoked during a typical week
¶ Analysis of outcomes was limited to 778/1175 participants who had biologically confirmed cocaine or heroin use at baseline
# n analyzed = n positive at baseline
** Cocaine or opiates
†† Based on hair sample (units = ng/10 mg)
‡‡ Scale range 0-1, where lower scores indicate better outcomes

Table 14. Results for drug use (KQ 4a) for trials among young adults and adults

§§ For the most frequently used drug
‖ Among those eligible for a cocaine or amphetamine-type stimulant brief intervention
¶¶ Odds ratio calculated using negative binomial regression models
Incidence rate ratio calculated using negative binomial regression models
*** Scale range 0-273, where lower scores indicate better outcomes
††† With or without cooccurring alcohol or prescription opioid/heroin abuse or dependence
‡‡‡ Defined as being "somewhat high" or "very high" on days used cannabis
§§§ Results for US sample only
‖‖ Based on urine samples
¶¶¶ Standard error
Any substance use (including nicotine, cannabis, alcohol, and other drugs)

Abbreviations: ASI = Addiction Severity Index; ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; BL = baseline; CG = control group; CI = confidence interval; ES = effect size; FU = followup; IG = intervention group; IRR = incidence rate ratio; MD = mean difference; mo. = months; NR = not reported; NS = not statistically significant; OR = odds ratio; pop = population; recall = period of time respondents are asked to recall their substance use; RR = rate ratio; sd = standard deviation

Table 15. Results for health, social, and legal outcomes (KQ 4b) for trials among young adults and adults

Target pop	Author, year	Outcome	Scale range	Recall (mo)	Arm	FU	IG n	IG BL mean (sd)	IG FU mean (sd)	CG n	CG BL mean (sd)	CG FU mean (sd)	Study-reported between group difference	Study-reported p-value
Young adults	Bernstein, 2009[80]	Drove after cannabis use‖	NA	1	IG1	3	42	8 (14.5)	6 (14.3)	55	9 (14.1)	10 (18.2)	OR=0.82 (0.24 to 2.76)	0.745
						12	47	8 (14.5)	8 (17.0)	55	9 (14.1)	13 (23.6)	OR=0.60 (0.12 to 1.75)	0.352
		Rode in car with person high after cannabis use‖				3	42	12 (21.8)	11 (26.2)	55	11 (17.2)	13 (23.6)	OR=1.01 (0.39 to 2.62)	0.985
						12	47	12 (21.8)	10 (21.3)	55	11 (17.2)	13 (23.6)	OR=0.81 (0.31 to 2.10)	0.668
	Lee, 2010[93]	Cannabis-related consequences	0-90*	2	IG1	3	171	2.11 (2.69)	2.47 (3.77)	170	1.86 (2.23)	1.99 (2.76)	NR	NR, NS
						6		2.11 (2.69)	2.59 (3.96)		1.86 (2.23)	2.19 (2.95)	NR	NR, NS
	Lee, 2013[94]	Cannabis-related consequences	0-100†	2	IG1	3	87	10.45 (4.9)	7.84 (4.9)	90	10.38 (5.9)	8.67 (6.0)	RR=0.90 (0.76 to 1.07)	<0.10
						6	82	10.45 (4.9)	6.54 (5.3)	83	10.38 (5.9)	6.75 (6.5)	RR=1.15 (0.9 to 1.47)	NR, NS
	Palfai, 2014[101]	Cannabis-related consequences	0-19‡	3	IG1	3	54	3.74 (3.89)	2.19 (3.00)	49	4.51 (3.72)	3.43 (3.74)	NR	NR
						6	54	3.74 (3.89)	2.12 (2.51)	49	4.51 (3.72)	2.97 (1.72)	β=0.66 (0.53)	>0.05
	Stein, 2011[105]	Cannabis-related consequences	0-38§	3	IG1	3	163	4.82 (4.66)	NR	169	4.99 (4.71)	NR	β=-0.40	0.353
						6	163	4.82 (4.66)	NR	169	4.99 (4.71)	NR	β=-0.10	0.89
Adults	Gelberg, 2015[87]	QOL, mental health component§§	0-100	NA	IG1	3	129	42.69 (12.57)	43.71 (11.78)	132	42.94 (12.28)	44.39 (12.21)	MD=0.25 (NR)	0.848
		QOL, physical health component§§	0-100	NA	IG1	3	129	42.97 (12.11)	45.07 (12.18)	132	43.1 (12.01)	44.47 (12.21)	MD=1.59 (NR)	0.115
	Martino, 2018[95]	Entered substance use treatment or self-help program	NA	6	IG1	6	145	NA	NR	151	NA	NR	OR=0.391 (0.559 to 1.551)	0.810
					IG2		143	NA	NR	151	NA	NR	OR=0.968 (0.579 to 1.617)	0.990

Table 15. Results for health, social, and legal outcomes (KQ 4b) for trials among young adults and adults

Target pop	Author, year	Outcome	Scale range	Recall (mo)	Arm	FU	IG n	IG BL mean (sd)	IG FU mean (sd)	CG n	CG BL mean (sd)	CG FU mean (sd)	Study-reported between group difference	Study-reported p-value
Adults	Roy-Byrne, 2014[103]	All-cause mortality‖	NA	NA	IG1	12	426	NA	10 (2.0)	422	NA	7 (2.0)	OR=1.42 (0.54 to 3.78)	0.48
		Consequences - Employment	0-1	1	IG1	12	426	0.79 (0.23)	0.78 (0.24)	422	0.79 (0.23)	0.78 (0.24)	β=0.006 (-0.016 to 0.028)	0.58
		Consequences - Family/social	0-1	1	IG1	12	426	0.17 (0.22)	0.11 (0.18)	422	0.17 (0.22)	0.13 (0.20)	β=-0.020 (-0.046 to 0.006)	0.14
		Consequences - Legal	0-1	1	IG1	12	426	0.06 (0.12)	0.04 (0.10)	422	0.07 (0.15)	0.04 (0.12)	β=0.000 (-0.014 to 0.014)	0.95
		Consequences - Medical	0-1	1	IG1	12	426	0.65 (0.32)	0.54 (0.35)	422	0.66 (0.35)	0.56 (0.36)	β=-0.004 (-0.050 to 0.042)	0.86
		Consequences - Psychiatric	0-1	1	IG1	12	426	0.37 (0.24)	0.31 (0.26)	422	0.39 (0.24)	0.32 (0.26)	β=0.004 (-0.026 to 0.034)	0.79
		Drug treatment admissions‖¶	NA	12	IG1	12	426	37 (8.7)	60 (14.1)	422	53 (12.6)	57 (13.5)	OR=1.16 (0.77 to 1.73)	0.48
		Inpatient hospitalizations‖	NA	12	IG1	12	426	113 (26.5)	106 (24.9)	422	108 (25.6)	98 (23.2)	OR=1.09 (0.78 to 1.51)	0.62
		Emergency department visits‖	NA	12	IG1	12	426	215 (50.5)	204 (47.8)	422	213 (50.5)	198 (46.9)	OR=1.04 (0.76 to 2.06)	0.77
		Outpatient visits‖	NA	12	IG1	12	426	381 (89.4)	402 (94.4)	422	380 (90.0)	399 (94.5)	OR=1.00 (0.53 to 1.88)	0.99
		Felony or gross misdemeanor arrests‖	NA	12	IG1	12	426	36 (8.5)	41 (9.6)	426	43 (10.2)	37 (8.8)	OR=1.21 (0.74 to 1.98)	0.45
	Saitz, 2014[91, 104]	Consequences	0-45#	1	IG1	6	169	9.3 (11.8)	12.1 (13.8)	175	11.3 (13.3)	9.4 (12.1)	IRR=0.95 (0.71 to 1.26)	0.71
					IG2	6	173	9.2 (11.3)	12.7 (13.7)	175	11.3 (13.3)	9.4 (12.1)	IRR=1.11 (0.83 to 1.47)	0.71
		Anxiety‖**	NA	NA	IG1	6	169	59 (33.9)	49 (29.0)	175	57 (32.2)	59 (33.7)	NR	NR
					IG2	6	173	60 (33.9)	55 (31.8)	175	57 (32.2)	59 (33.7)	NR	NR
		Depression‖††	NA	NA	IG1	6	169	63 (36.2)	43 (25.4)	175	60 (33.9)	57 (32.6)	NR	NR
					IG2	6	173	66 (37.3)	53 (30.8)	175	60 (33.9)	57 (32.6)	NR	NR

Table 15. Results for health, social, and legal outcomes (KQ 4b) for trials among young adults and adults

Target pop	Author, year	Outcome	Scale range	Recall (mo)	Arm	FU	IG n	IG BL mean (sd)	IG FU mean (sd)	CG n	CG BL mean (sd)	CG FU mean (sd)	Study-reported between group difference	Study-reported p-value
Adults	Saitz, 2014[91, 104]	Health-related QOL	0-100‡‡	NA	IG1	6	169	70.8 (18.8)	71.5 (19.4)	175	71.5 (19.6)	72.1 (20.6)	NR	NR
					IG2	6	173	68.5 (22.4)	68.5 (20.7)	175	71.5 (19.6)	72.1 (20.6)	NR	NR
		ED visit‖ for addiction or mental health	NA	3	IG1	6	169	12 (6.9)	13 (7.7)	175	18 (10.2)	17 (9.7)	OR=0.79 (0.36 to 1.76)	0.57
					IG2	6	173	17 (9.6)	11 (6.4)	175	18 (10.2)	17 (9.7)	OR=0.63 (0.27 to 1.44)	0.54
		Hospitalization for addiction or mental health‖	NA	3	IG1	6	169	12 (6.9)	10 (5.9)	175	7 (4.0)	8 (4.6)	OR=0.95 (0.29 to 3.09)	1.00
					IG2	6	173	10 (5.7)	12 (7.0)	175	7 (4.0)	8 (4.6)	OR=1.44 (0.49 to 4.42)	1.00
		Specialty treatment for addiction or mental health‖	NA	3	IG1	6	169	NR	53 (31.4)	175	NR	44 (25.1)	OR=1.41 (0.83 to 2.39)	0.41
					IG2	6	173	NR	51 (29.5)	175	NR	44 (25.1)	OR=0.98 (0.57 to 1.68)	0.93
		Receipt of any addiction treatment‖	NA	6	IG1	6	174	NR	31 (17.8)	177	NR	30 (16.9)	OR=1.11 (0.57 to 2.15)	0.76
					IG2	6	177	NR	17 (9.6)	177	NR	30 (16.9)	OR=0.36 (0.17 to 0.78)	0.02
	Watkins, 2017[108]	Consequences	0-15#	1	IG1	6	138	9.1 (4.9)	7.0 (5.9)	123	9.6 (4.8)	6.2 (5.5)	ES=1.55 (-0.21 to 3.31)	0.08
		ED visit or hospital stay‖	NA	3				72 (38.5)	27 (19.6)		67 (35.3)	28 (22.8)	NR	NR
		QOL, mental health component§§	0-100	NA				40.1 (10.8)	41.0 (12.4)		39.5 (10.9)	40.8 (12.2)	ES=-1.61 (-5.61 to 2.39)	0.43
		QOL, physical health component§§	0-100	NA				47.6 (9.9)	48.1 (11.5)		47.2 (10.2)	46.7 (10.8)	ES=1.49 (-2.05 to 5.03)	0.41
	Woolard, 2013[109]	Cannabis-related injuries	NA	12	IG1	12	206	2.8	1.7	220	2.5	1.5	NR	NR, NS

* 18 items from Rutger's Marijuana Problem Index with categorical responses from 0 (never) to 4 (more than 10 times)
† 18 items from Rutger's Marijuana Problem Index with categorical responses from 1 (never) to 5 (more than 10 times) plus 10 study-developed items unique to the physical and motivational effects of marijuana use with binary coding of 0 (not experienced) and 1 (experienced)
‡ 19 items from Marijuana Problem Scale with binary coding of 0 (not experienced) and 1 (experienced)
§ 19 items from Marijuana Problem Scale with categorical responses of 0 (experiencing none), 1 (minor), or 2 (major)
‖ n (%)

Table 15. Results for health, social, and legal outcomes (KQ 4b) for trials among young adults and adults

¶ Excluded detoxification services
# As measured with the Short Inventory of Problems; higher score indicates worse outcome.
** Number with anxiety symptoms where OASIS score ≥8
†† Number with depression symptoms where PHQ-9 score ≥10
‡‡ High value indicates better outcome
§§ As measured by SF-12 Health Survey

Abbreviations: BL = baseline; CG = control group; ES = effect size; FU = followup; IG = intervention group; IRR = incidence rate ratio; mo = months; NA = not applicable; NR = not reported; NS = not statistically significant; OR = odds ratio; pop = population; recall = period of time respondents are asked to recall their substance use; RR = rate ratio; sd = standard deviation

Table 16. Results for drug use (KQ 4a) for trials among pregnant and postpartum women

Target pop	Author, year	Outcome	Recall (mo)	FU (mo)	IG n	IG BL	IG FU	CG n	CG BL	CG FU	Study-reported between group difference	Study-reported p-value
Postpartum women	Ondersma, 2007[99]	Any drug use, n (%)	3	4	39	NR	26 (67.6)	37	NR	31 (83.7)	OR=2.48 (0.59 to 10.42)	NR, NS
		Any cannabis use, n (%)	3	4	39	NR	26 (66.1)	37	NR	29 (78.0)	OR=2.13 (0.58 to 7.78)	NR, NS
		Any other (non-cannabis) drug use, n (%)	3	4	39	NR	4 (9.9)	37	NR	8 (21.3)	OR=2.41 (0.66 to 8.83)	NR, NS
		Any drug use frequency*	3	4	55	NR	NR	52	NR	NR	ES=0.46 (0.15 to 1.53)	0.042
		Cannabis use frequency*	3	4	55	2.81 (NR)	1.91 (NR)	52	2.47 (NR)	2.08 (NR)	ES=0.39 (0.01 to 0.97)	0.202
		Other (non-cannabis) drug use frequency*	3	4	55	0.28 (NR)	0.11 (NR)	52	0.11 (NR)	0.34 (NR)	ES= 0.40 (0.02 to 0.78)	0.032
	Ondersma, 2014[98]	Abstinence from drugs (self-report and urine), n (%)	7 days	3	72	0 (0.0)	19 (26.4)	71	0 (0.0)	7 (9.9)	OR=3.28 (1.3 to 8.39)	0.010
				6	72	0 (0.0)	10 (13.9)	71	0 (0.0)	7 (9.9)	OR=1.47 (0.53 to 4.12)	0.456
		Drug use days, median	3	3	53	NR	25.6	52	NR	51.4	Effect size=0.60	0.058
				6	53	NR	31.6	52	NR	77.2	Effect size=0.57	0.207
	Ondersma, 2018[100]	Any drug use (self-report), n (%)	3	3	252	NR	134 (53)	248	NR	129 (52)	RR=1.02 (0.84 to 1.23)	NR, NS
			3	6	252	NR	121 (48)	248	NR	122 (49)	RR=0.97 (0.79 to 1.20)	NR, NS
		Any drug use (urine), n (%)	3	3	252	NR	131 (52)	248	NR	129 (52)	RR=1.01 (0.84 to 1.22)	NR, NS
			3	6	252	NR	118 (47)	248	NR	117 (47)	RR=0.99 (0.79 to 1.24)	NR, NS
		Any cannabis use (self-report), n (%)	3	3	252	NR	113 (45)	248	NR	117 (47)	RR=0.95 (0.74 to 1.20)	NR, NS
			3	6	252	NR	113 (45)	248	NR	117 (47)	RR=0.97 (0.77 to 1.21)	NR, NS
		Any cannabis use (urine), n (%)	3	3	252	NR	103 (41)	248	NR	109 (44)	RR=0.93 (0.73 to 1.18)	NR, NS
			3	6	252	NR	103 (103)	248	NR	107 (43)	RR=0.95 (0.75 to 1.21)	NR, NS
Postpartum	Ondersma, 2018[100]	Drug use days, median (IQR)	3	3	252	NR	1.0 (0 to 14.9)	248	NR	1.0 (0 to 13.7)	OR=0.98 (0.68 to 1.4)	NR, NS

Table 16. Results for drug use (KQ 4a) for trials among pregnant and postpartum women

Target pop	Author, year	Outcome	Recall (mo)	FU (mo)	IG n	IG BL	IG FU	CG n	CG BL	CG FU	Study-reported between group difference	Study-reported p-value
			3	6	252	NR	0.8 (0 to 22.7)	248	NR	1.4 (0 to 23.1)	OR=0.97 (0.71 to 1.34)	NR, NS
Pregnant women	Tzilos Wernette, 2017[106]	Any alcohol or cannabis use, n (%)	3	4	31	24 (77)	7 (23)	19	11 (58)	8 (42)	OR=0.16 (0.04 to 0.74)	0.02
	Yonkers, 2012[110]	% of days using drugs, mean (sd)	1	Delivery	80	21 (34)	7 (22)	83	18 (27)	6 (17)	β=0.08 (-0.76 to 0.92)	NR, NS
				3 mo. post-delivery	71	21 (34)	13 (24)	72	18 (27)	14 (25)	β=-0.21 (-1.11 to 0.69)†	NR, NS
		Abstinence from alcohol and drugs (self-report and urine), n (%)	1	Delivery	55	35 (43.2)‡	41 (74.5)	51	26 (32.5)§	39 (76.5)	OR=0.77 (0.32 to 1.84)	0.5
				3 mo. post-delivery	64	35 (43.2)‡	21 (32.8)	64	26 (32.5)§	22 (34.4)	OR=0.76 (0.27 to 2.11)†	NR, NS
		Abstinence from drugs (urine), n (%)	1	Delivery	55	45 (55.6)‖	46 (83.6)	51	43 (53.8)¶	43 (84.3)	OR=0.96 (0.34 to 2.72)	NR, NS
				3 mo. post-delivery	64	45 (55.6)‖	38 (59.4)	64	43 (53.8)¶	33 (51.6)	OR=1.21 (0.57 to 2.57)†	NR, NS
		Abstinence from alcohol and drugs (self-report), n (%)	1	Delivery	80	40 (48.8)#	61 (76.3)	83	35 (40.7)**	62 (74.6)	OR=0.77 (0.36 to 1.67)	0.79
				3 mo. post-delivery	71	40 (48.8)#	29 (40.8)	72	35 (40.7)**	27 (37.5)	OR=1.05 (0.42 to 2.62)†	NR, NS

* Categorical responses where 0 = never, 1 = once or twice, 2 = monthly, 3 = weekly, and 4 = daily or almost daily
† From delivery to 3 months post-delivery
‡ 35/81=43.2% at baseline
§ 26/80=32.5% at baseline
‖ 45/81=55.6%
¶ 43/80=53.8%
# 40/82=48.8%
** 35/86=40.7% at baseline

Abbreviations: BL = baseline; CG = control group; FU = followup; IG = intervention group; IQR = interquartile range; mo = months; NA = not applicable; NR = not reported; NS = not statistically significant; OR = odds ratio; pop = population; recall = period of time respondents are asked to recall their substance use; RR = relative risk; sd = standard deviation

Table 17. Summary of evidence, by Key Question

Key Question	No. of Studies (k), no. of Observations (n)	Summary of Findings	Consistency/ Precision Reporting Bias	Overall Study Quality	Body of Evidence Limitations	EPC Assessment of Overall Strength of Evidence	Applicability
KQ 1. Benefits of screening	k=0	NA	NA	NA	NA	Insufficient	NA
KQ 2. Screening accuracy	k=28 cross-sectional studies n=65,720*	Thirty different screening tools were evaluated including brief frequency-based tools, risk assessment tools, and indirect screeners. Among adolescents, sensitivity of frequency-based and risk assessment tools for detecting any cannabis use or unhealthy cannabis use ranged from 0.68 to 0.98 (95% CI range, 0.64 to 0.99) and specificity ranged from 0.82 to 1.00 (95% CI range, 0.80 to 1.00). Among adults, sensitivity of frequency-based and risk assessment tools for detecting unhealthy use of "any drug" ranged from 0.71 to 1.00 (95% CI range, 0.62 to 1.00) and specificity ranged from 0.87 to 0.97 (95% CI range, 0.83 to 0.98). Tests were less accurate in detecting unhealthy use of prescription opioids or sedatives then other specific drugs, especially cannabis. Sensitivity and specificity of frequency-based and risk assessment tools for detecting any prenatal drug use (not including alcohol) was lower than the estimates found for non-pregnant adults and ranged from 0.37 to 0.76 (95% CI range, 0.24 to 0.86) and 0.68 to 0.83 (95% CI range, 0.55 to 0.91).	Reasonably consistent/ Imprecise None suspected	Good: 11 Fair: 17	Each instrument was not evaluated in more than 1 or 2 studies. No studies restricted inclusion to young adults specifically (the age group with the highest prevalence of use). Low prevalence of some drugs makes it difficult to determine if the screening tools are accurate for those substances. Few studies included biologic confirmation of drug use. Few studies among pregnant women using brief screeners.	Low	Most studies conducted in U.S.-based primary care population; although included studies represented samples with generally higher prevalence of drug use and drug use disorders than U.S. national estimates. Higher representation of nonwhite and low SES participants.
KQ 3. Harms of screening	k=0	NA	NA	NA	NA	Insufficient	NA
KQ 4a. Benefits of interventions: Drug use and	k=26 RCTs n=9542	No consistent effect of the interventions on rates of self-reported or biologically confirmed drug use or other risky behaviors such as alcohol use or risky sexual behaviors at 3 to 12 months	Reasonably consistent/ Imprecise	Good: 4 Fair: 22	Modest sample sizes in most trials with inadequate power for important subgroup analyses.	Low	Applicable to U.S.-based screen-detected drug-using persons.

Table 17. Summary of evidence, by Key Question

Key Question	No. of Studies (k), no. of Observations (n)	Summary of Findings	Consistency/ Precision Reporting Bias	Overall Study Quality	Body of Evidence Limitations	EPC Assessment of Overall Strength of Evidence	Applicability
other risky behavior		followup. Frequency and quantity of drug use generally decreased, and rates of abstinence increased in both intervention and control groups with no statistically significant between-group differences detected.			Most drug use measures based on self-report with heterogeneous measures. Small effect sizes may reflect research structure. Control groups may have been influenced to alter behavior based on assessment schedules alone.		Evidence for adolescents and young adults primarily focused on cannabis use only. Trials among adults represented black adults with lower SES and high rates of comorbid mental health illnesses. Drug use spanned casual cannabis use to severe opiate and stimulant use.
KQ 4b. Benefits of interventions: Health, social, and legal outcomes	k=13 RCTs n=4739	None of the trials found a statistically significant difference between intervention and control groups on health, social or legal outcomes (including global measures of drug-related consequences) at 6- to 12-month followup.	Reasonably consistent/ Imprecise None suspected	Good: 3 Fair: 10		Low	
KQ 5. Harms of interventions	k=4 n=1491	There were no harms or unintended effects of the interventions.	Reasonably consistent/ Reasonably precise None suspected	Good: 0 Fair: 4	Few trials reported potential harms of interventions; findings limited to two trials among college students and one trial among postpartum women.	Low†	Applicable to college-aged cannabis users in the US and postpartum women.

* N includes one U.S.-based community sample (n=42,923) that only evaluated a single-item alcohol question for predicting problematic drug use. Without this study, total n = 22,797.

† No *a priori* serious harms hypothesized related to primary care relevant counseling interventions.

Abbreviations: EPC = Evidence-based Practice Center

Table 18. Estimated positive and negative predictive values based on US prevalence of current drug use and study reported sensitivity and specificity for drug use screening instruments*

Population	Substance	Prevalence of current drug use[12]	PPV 70/80†	PPV 80/90†	PPV 90/90†	NPV 70/80†	NPV 80/90†	NPV 90/90†
Adolescents	Any illicit drug	7.9	23.1	40.7	43.6	96.9	98.1	99.1
	Marijuana	6.5	19.6	35.7	38.5	97.5	98.5	99.2
	Prescription drug (misuse)	1.6	5.4	11.5	12.8	99.4	99.6	99.8
	Cocaine	0.1	0.3	0.8	0.9	100.0	100.0	100.0
	Hallucinogens	0.5	1.7	3.9	4.3	99.8	99.9	99.9
	Inhalants	0.6	2.1	4.6	5.2	99.8	99.9	99.9
	Heroin	0	NA	NA	NA	NA	NA	NA
Young adults	Any illicit drug	23.2	51.4	70.7	73.1	89.8	93.7	96.8
	Marijuana	20.8	47.9	67.8	70.3	91.0	94.5	97.2
	Prescription drug (misuse)	4.6	14.4	27.8	30.3	98.2	98.9	99.5
	Cocaine	1.6	5.4	11.5	12.8	99.4	99.6	99.8
	Hallucinogens	1.9	6.3	13.4	14.8	99.3	99.6	99.8
	Inhalants	0.4	1.4	3.1	3.5	99.8	99.9	100.0
	Heroin	0.3	1.0	2.4	2.6	99.9	99.9	100.0
Adults (excluding young adults)	Any illicit drug	8.9	25.5	43.9	46.8	96.5	97.9	98.9
	Marijuana	7.2	21.4	38.3	41.1	97.2	98.3	99.1
	Prescription drug (misuse)	2.0	6.7	14.0	15.5	99.2	99.5	99.8
	Cocaine	0.6	2.1	4.6	5.2	99.8	99.9	99.9
	Hallucinogens	0.3	1.0	2.4	2.6	99.9	99.9	100.0
	Inhalants	0.2	0.7	1.6	1.8	99.9	100.0	100.0
	Heroin	0.2	0.7	1.6	1.8	99.9	100.0	100.0
Pregnant women	Any illicit drug	6.3	19.0	35.0	37.7	97.5	98.5	99.3

* All prevalence, PPV, NPV, sensitivity, and specificity values are percentages

† Sensitivity/specificity

Abbreviations: PPV = positive predictive value; NA = not applicable; NPV = negative predictive value

Appendix A. Comparison of DSM-IV and DSM-5 Substance Use Disorders

DSM-IV	DSM-5
Substance abuse: One or more symptoms	**Substance Use Disorder: Two out of 11 criteria clustering in a 12-month period are needed to meet disorder threshold**
Recurrent substance-related legal problems	DROPPED
Recurrent substance use in situations where it is physically hazardous	SAME
Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home	SAME
Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance	SAME
	ADDED Craving or a strong desire or urge to use the substance
Substance dependence: Three or more symptoms in the same 12-month period (or one symptom if dependence criteria have been met previously in the lifetime)	
Substance is taken in larger amounts or over a longer period than was intended	SAME
There is a persistent desire or unsuccessful efforts to cut down or control substance use	SAME
A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects	SAME
Important social, occupational, or recreational activities are given up or reduced because of substance use	SAME
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 substance use	SAME
Tolerance, as defined by either: (1) a need for markedly increased amounts of substance to achieve intoxication or desired effect or (2) a markedly diminished effect with continued use of the same amount of the substance	SAME
Withdrawal, as manifested by either: (1) the characteristic withdrawal syndrome for the substance (excludes Cannabis, Hallucinogens, and Inhalants) (2) the substance (or a similar substance) is taken to relieve or avoid withdrawal symptoms	Withdrawal, as manifested by either: (1) the characteristic withdrawal syndrome for the substance (excludes Phencyclidine, Other Hallucinogens, and Inhalants (2) the substance (or a closely related substance) is taken to relieve or avoid withdrawal symptoms

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
Cannabinoids	Marijuana† (Cannabis)	Blunt, Bud, Dope, Ganja, Grass, Green, Herb, Joint, Mary Jane, Pot, Reefer, Sinsemilla, Skunk, Smoke, Trees, Weed; Hashish: Boom, Gangster, Hash, Hemp	Various brand names in states where the sale of marijuana is legal‡	Greenish-gray mixture of dried, shredded leaves, stems, seeds, and/or flowers; resin (hashish) or sticky, black liquid (hash oil)	Smoked, eaten (mixed in food or brewed as tea)	I	Short-term: Enhanced sensory perception and euphoria followed by drowsiness/relaxation; slowed reaction time; problems with balance and coordination; increased heart rate and appetite; problems with learning and memory; hallucinations; anxiety; panic attacks; psychosis. Long-term: Mental health problems, chronic cough, frequent respiratory infections. Youth: possible loss of IQ points when repeated use begins in adolescence. Pregnancy: babies born with problems with attention, memory, and problem solving.
Club drugs	MDMA (3,4-methylenedioxy-methamphetamine)	Ecstasy, Molly, Adam, clarity, Eve, lover's speed, peace, uppers	No commercial uses	Colorful tablets with imprinted logos, capsules, powder, liquid	Swallowed, snorted	I	Short-term: Lowered inhibition; enhanced sensory perception; confusion; depression; sleep problems; anxiety; increased heart rate and blood pressure; muscle tension; teeth clenching; nausea; blurred vision; faintness; chills or sweating; sharp rise in body temperature leading to liver, kidney, or heart failure and death. Long-term: Long-lasting confusion, depression, problems with attention, memory, and sleep; increased anxiety, impulsiveness, aggression; loss of appetite; less interest in sex. Youth: Unknown

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
							Pregnancy: Unknown
	Rohypnol (Flunitrazapam)	Circles, Date Rape Drug, Forget Pill, Forget-Me Pill, La Rocha, Lunch Money, Mexican Valium, Mind Eraser, Pingus, R2, Reynolds, Rib, Roach, Roach 2, Roaches, Roachies, Roapies, Rochas Dos, Roofies, Rope, Rophies, Row-Shay, Ruffies, Trip-*and-Fall, Wolfies*	Flunitrazepam, Rohypnol®	Tablet	Swallowed (as a pill or as dissolved in a drink), snorted	IV§	Short-term: Drowsiness, sedation, sleep; amnesia, blackout; decreased anxiety; muscle relaxation, impaired reaction time and motor coordination; impaired mental functioning and judgment; confusion; aggression; excitability; slurred speech; headache; slowed breathing and heart rate. Long-term: Unknown Youth: Unknown Pregnancy: Unknown
	GHB (*gamma-hydroxybutyrate*)	G, Georgia home boy, grievous bodily harm, liquid ecstasy, soap, scoop, good, liquid X	Gamma-hydroxybutyrate or sodium oxybate (Xyrem®)	Colorless liquid, white powder	Swallowed	I	Short-term: Euphoria, drowsiness, decreased anxiety, confusion, memory loss, hallucinations, excited and aggressive behavior, nausea, vomiting, unconsciousness, seizures, slowed heart rate and breathing, lower body temperature, coma, death. Long-term: Unknown Youth: Unknown Pregnancy: Unknown

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
							Other health-related issues: Sometimes used as a date-rape drug
Dissociative drugs	Ketamine	Cat Valium, K, Special K, vitamin K	Ketalar®	Liquid, white powder	Injected, snorted, or smoked (powder added to tobacco or marijuana cigarettes), swallowed	III	Short-term: Problems with attention, learning, and memory; dreamlike states, hallucinations; sedation; confusion and problems speaking; loss of memory; problems moving, to the point of being immobile; raised blood pressure; unconsciousness; slowed breathing that can lead to death. Long-term: Ulcers and pain in the bladder; kidney problems; stomach pain; depression; poor memory. Youth: Unknown Pregnancy: Unknown Other health-related issues: Sometimes used as a date-rape drug; Risk of HIV, hepatitis, and other infectious diseases from shared needles
	PCP (*phencyclidine*)	Angel dust, boat, hog, love boat, peace pill	No commercial uses	White or colored powder, tablet, or capsule; clear liquid	Injected, snorted, swallowed, smoked (powder added to mint, parsley, oregano, or marijuana)	I/II	Short-term: Delusions, hallucinations, paranoia, problems thinking, a sense of distance from one's environment, anxiety. Low doses: slight increase in breathing rate; increased blood pressure and heart rate; shallow breathing; face redness and sweating; numbness of the hands or feet; problems with movement. High doses: lowered blood pressure, pulse rate, breathing rate; nausea; vomiting; blurred vision; flicking up and down of the

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
							eyes; drooling; loss of balance; dizziness; violence; suicidal thoughts; seizures, coma, and death. Long-term: Memory loss, problems with speech and thinking, depression, weight loss, anxiety. Youth: Unknown Pregnancy: Unknown Other health-related issues: PCP has been linked to self-injury; Risk of HIV, hepatitis, and other infectious diseases from shared needles.
	Salvia† (*salvia divinorum*)	Magic mint, Maria Pastora, Sally-D, Shepherdess' s Herb, Diviner's Sage	Sold legally in most states as *Salvia divinorum*	Smoked, chewed, or brewed as tea	Smoked, chewed, or brewed as tea	Not scheduled‖	Short-term: Short-lived but intense hallucinations; altered visual perception, mood, body sensations; mood swings, feelings of detachment from one's body; sweating. Long-term: Unknown Youth: Unknown Pregnancy: Unknown
Hallucinogens	Ayahuasca†	Aya, Yagé, Hoasca	No commercial uses	Brewed as tea	Swallowed as tea	I¶	Short-term: Strong hallucinations including perceptions of otherworldly imagery, altered visual and auditory perceptions; increased blood pressure; vomiting. Long-term: Unknown Youth: Unknown

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
							Pregnancy: Unknown
	DMT†	DMT, Dimitri	No commercial uses	White or yellow crystalline powder	Smoked, injected	I	Short-term: Intense visual hallucinations, depersonalization, auditory distortions, and an altered perception of time and body image, usually resolving in 30-45 minutes or less. Physical effects include hypertension, increased heart rate, agitation, seizures, dilated pupils, involuntary rapid eye movements, dizziness, and incoordination. Long-term: Unknown Youth: Unknown Pregnancy: Unknown Other health-related issues: At high doses, coma and respiratory arrest have occurred.
	LSD (*lysergic acid diethylamide*)	Acid, blotter, cubes, microdot, yellow sunshine, blue heaven	No commercial uses	Tablet; capsule; clear liquid; small, decorated squares of absorbent paper that liquid has been added to	Swallowed or absorbed through mouth tissues	I	Short-term: Rapid emotional swings; distortion of a person's ability to recognize reality, think rationally, or communicate with others; raised blood pressure, heart rate, body temperature; dizziness and insomnia; loss of appetite; dry mouth; sweating; numbness; weakness; tremors; enlarged pupils. Long-term: Frightening flashbacks (called Hallucinogen Persisting Perception Disorder [HPPD]); ongoing visual disturbances, disorganized thinking, paranoia, and mood swings. Youth: Unknown

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
							Pregnancy: Unknown
	Mescaline (Peyote)	Buttons, cactus, mesc	No commercial uses	Fresh or dried buttons, capsule	Swallowed (chewed or soaked in water and drunk)	I	Short-term: Enhanced perception and feeling; hallucinations; euphoria; anxiety; increased body temperature, heart rate, blood pressure; sweating; problems with movement. Long-term: Unknown Youth: Unknown Pregnancy: Unknown
	Psilocybin†	Little Smoke, Magic Mushrooms, Purple Passion, Shrooms	No commercial uses	Fresh or dried mushrooms with long, slender stems topped by caps with dark gills	Swallowed (eaten, brewed as tea, or added to other foods)	I	Short-term: Hallucinations, altered perception of time, inability to tell fantasy from reality, panic, muscle relaxation or weakness, problems with movement, enlarged pupils, nausea, vomiting, drowsiness. Long-term: Risk of flashbacks and memory problems. Youth: Unknown Pregnancy: Unknown Other health-related issues: Risk of poisoning if a poisonous mushroom is accidentally used.
Opioids	Heroin	Smack, horse, brown sugar, dope, H, junk, skag, skunk, white horse, China white, cheese (with OTC cold medicine and	No commercial uses	White or brownish powder, or black sticky substance known as “black tar heroin”	Injected, smoked, or snorted	I	Short-term: Euphoria; warm flushing of skin; dry mouth; heavy feeling in the hands and feet; clouded thinking; alternate wakeful and drowsy states; itching; nausea; vomiting; slowed breathing and heart rate. Long-term: Collapsed veins; abscesses (swollen tissue with

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
		antihistamine)					pus); infection of the lining and valves in the heart; constipation and stomach cramps; liver or kidney disease; pneumonia. Youth: Unknown Pregnancy: miscarriage, low birth weight, neonatal abstinence syndrome. Other health-related issues: Risk of HIV, hepatitis, and other infectious diseases from shared needles.
	Kratom (*Mitragyna speciosa*)	Herbal Speedball, Biak-biak, Ketum, Kahuam, Ithang, Thom	None	Fresh or dried leaves, powder, liquid, gum	Chewed (whole leaves); eaten (mixed in food or brewed as tea); occasionally smoked	Not scheduled	Short-term: Sensitivity to sunburn, nausea, itching, sweating, dry mouth, constipation, increased urination, loss of appetite. Low doses: increased energy, sociability, alertness. High doses: sedation, euphoria, decreased pain. Long-term: Anorexia, weight loss, insomnia, skin darkening, dry mouth, frequent urination, constipation. Hallucination and paranoia with long-term use at high doses. Youth: Unknown Pregnancy: Unknown
Other Compounds	Inhalants	Solvents (paint thinners, gasoline, glues); gases (butane, propane, aerosol	Various	Various forms[#]	Inhaled through nose or mouth	Not scheduled	Short-term: Confusion; nausea; slurred speech; lack of coordination; euphoria; dizziness; drowsiness; disinhibition, lightheadedness, hallucinations/delusions; headaches; sudden sniffing death due to heart failure (from butane,

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
		propellants, nitrous oxide); nitrates (isoamyl, isobutyl, cyclohexyl): laughing gas, poppers, snappers, whippets					propane, and other chemicals in aerosols); death from asphyxiation, suffocation, convulsions or seizures, coma, or choking. Nitrites: enlarged blood vessels, enhanced sexual pleasure, increased heart rate, brief sensation of heat and excitement, dizziness, headache. Long-term: Liver and kidney damage; bone marrow damage; limb spasms due to nerve damage; brain damage from lack of oxygen that can cause problems with thinking, movement, vision, and hearing. Nitrites: increased risk of pneumonia. Youth: Unknown Pregnancy: low birth weight, bone problems, delayed behavioral development due to brain problems, altered metabolism and body composition.
Over-the-counter Cough/Cold medicines	Dextromethorphan or DXM	Robotripping, Robo, Triple C	Various (many brand names include “DM”)	Syrup, capsule	Swallowed	Not scheduled	Short-term: Euphoria; slurred speech; increased heart rate, blood pressure, temperature; numbness; dizziness; nausea; vomiting; confusion; paranoia; altered visual perceptions; problems with movement; buildup of excess acid in body fluids. Long-term: Unknown Youth: Unknown Pregnancy: Unknown

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
							Other health-related issues: Breathing problems, seizures, and increased heart rate may occur from other ingredients in cough/cold medicines.
Prescription Opioids	Codeine	Captain Cody, Cody, Lean, Schoolboy, Sizzurp, Purple Drank With *glutethimide:* Doors & Fours, Loads, Pancakes and Syrup	Codeine (various brand names)	Tablet, capsule, liquid	Injected, swallowed (often mixed with soda and flavorings)	II/III/V	Short-term: Pain relief, drowsiness, nausea, constipation, euphoria, confusion, slowed breathing, death. Long-term: Unknown Youth: Unknown Pregnancy: Miscarriage, low birth weight, neonatal abstinence syndrome. Older adults: higher risk of accidental misuse or abuse because many older adults have multiple prescriptions, increasing the risk of drug-drug interactions, and breakdown of drugs slows with age; also, many older adults are treated with prescription medications for pain. Other health-related issues: Risk of HIV, hepatitis, and other infectious diseases from shared needles.
	Fentanyl	Apache, China Girl, China White, Dance Fever, Friend, Goodfella, Jackpot, Murder 8, Tango and Cash, TNT	Fentanyl (Actiq®, Duragesic®, Sublimaze®)	Lozenge, sublingual tablet, film, buccal tablet	Injected, smoked, or snorted	II	
	Hydrocodone or Dihydrocodeine	Vike, Watson-387	Hydrocodone or dihydrocodeinone (Vicodin®, Lortab®, Lorcet®, and others)	Capsule, liquid, tablet	Swallowed, snorted, injected	II	
	Hydromorphone	D, Dillies, Footballs, Juice, Smack	Hydromorphone (Dilaudid®)	Liquid, suppository	Injected, rectal	II	
	Meperidine	Demmies, Pain Killer	Meperidine (Demerol®)	Tablet, liquid	Swallowed, snorted, injected	II	

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
	Methadone	Amidone, Fizzies *With MDMA:* chocolate chip cookies	Methadone (Dolophine®, Methadose®)	Tablet, dispersible tablet, liquid	Swallowed, injected	II	
	Morphine	M, Miss Emma, monkey, white stuff	Morphine (Duramorph®, Roxanol®)	Tablet, liquid, capsule, suppository	Injected, swallowed, or smoked	II/III	
	Oxycodone	O.C., Oxycet, Oxycotton, Oxy, Hillbilly Heroin, Percs	Oxycodone (OxyContin®, Percodan®, Percocet®, and others)	Capsule, liquid, tablet	Swallowed, snorted, injected	II	
	Oxymorphone	Biscuits, Blue Heaven, Blues, Mrs. O, O Bomb, Octagons, Stop Signs	Oxymorphone (Opana®)	Tablet	Swallowed, snorted, injected	II	
Prescription Sedatives (Tranquilizers, Depressants)	Barbiturates	Barbs, Phennies, Red Birds, Reds, Tooies, Yellow Jackets, Yellows	pentobarbital (Nembutal®), phenobarbital (Luminal®)	Pill, capsule, liquid	Swallowed, injected	II/III/IV	Short-term: Drowsiness, slurred speech, poor concentration, confusion, dizziness, problems with movement and memory, lowered blood pressure, slowed breathing. Long-term: Unknown Youth: Unknown Pregnancy: Unknown Other health-related issues: Sleep medications are sometimes used as date rape drugs. Risk of HIV, hepatitis, and other infectious diseases from shared needles.
	Benzodiazepines	Candy, Downers, Sleeping Pills, Tranks	alprazolam (Xanax®), chlorodiazepoxide (Limbitrol®), diazepam (Valium®), lorazepam (Ativan®), triazolam (Halicon®)	Pill, capsule, liquid	Swallowed, injected	IV	
	Sleep Medications	Forget-me Pill, Mexican Valium, R2,	eszopiclone (Lunesta®), zaleplon	Pill, capsule, liquid	Swallowed, injected	IV	

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
		Roche, Roofies, Roofinol, Rope, Rophies	(Sonata®), zolpidem (Ambien®)				
Prescription Stimulants	Amphetamines	Bennies, Black Beauties, Crosses, Hearts, LA Turnaround, Speed, Truck Drivers, Uppers	Amphetamine (Adderall®, Benzedrine®)	Tablet, capsule	Swallowed, snorted, smoked, injected	II	Short-term: Increased alertness, attention, energy; increased blood pressure and heart rate; narrowed blood vessels; increased blood sugar; opened-up breathing passages. High doses: dangerously high body temperature and irregular heartbeat; heart failure; seizures. Long-term: Heart problems, psychosis, anger, paranoia. Youth: Unknown Pregnancy: Unknown Other health-related issues: Risk of HIV, hepatitis, and other infectious diseases from shared needles.
	Methylphenidate	JIF, MPH, R-ball, Skippy, The Smart Drug, Vitamin R	Methylphenidate (Concerta®, Ritalin®)	Liquid, tablet, chewable tablet, capsule	Swallowed, snorted, smoked, injected, chewed	II	
Steroids	Steroids (Anabolic)	Juice, Gym Candy, Pumpers, Roids	Nandrolone (Oxandrin®), oxandrolone (Anadrol®), oxymetholone (Winstrol®), stanozolol (Durabolin®), testosterone cypionate (Depo-testosterone®)	Tablet, capsule, liquid drops, gel, cream, patch, injectable solution	Injected, swallowed, applied to skin	III	Short-term: Headache, acne, fluid retention (especially in the hands and feet), oily skin, yellowing of the skin and whites of the eyes, infection at the injection site. Long-term: Kidney damage or failure; liver damage; high blood pressure, enlarged heart, or changes in cholesterol leading to increased risk of stroke or heart attack, even in young people; aggression; extreme mood swings; anger (“roid rage”); paranoid jealousy; extreme irritability; delusions; impaired judgment.

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
							Youth: Unknown Adolescents: stunted growth Pregnancy: Unknown Males: Shrunken testicles, lowered sperm count, infertility, baldness, development of breasts, increased risk for prostate cancer. Females: Facial hair, male-pattern baldness, menstrual cycle changes, enlargement of the clitoris, deepened voice. Other health-related issues: Risk of HIV, hepatitis, and other infectious diseases from shared needles.
Stimulants	Cocaine	Blow, bump, C, candy, Charlie, coke, crack, flake, rock, snow, toot	Cocaine hydrochloride topical solution (anesthetic rarely used in medical procedures)	White powder, whitish rock crystal	Snorted, smoked, or injected	II	Short-term: Narrowed blood vessels; enlarged pupils; increased body temperature, heart rate, and blood pressure; headache; abdominal pain and nausea; euphoria; increased energy, alertness; insomnia, restlessness; anxiety; erratic and violent behavior, panic attacks, paranoia, psychosis; heart rhythm problems, heart attack; stroke, seizure, coma. Long-term: Loss of sense of smell, nosebleeds, nasal damage and trouble swallowing from snorting; infection and death of bowel tissue from decreased blood flow; poor nutrition and weight loss from decreased appetite. Youth: Unknown

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
							Pregnancy: Premature delivery, low birth weight, neonatal abstinence syndrome. Other health-related issues: Risk of HIV, hepatitis, and other infectious diseases from shared needles.
	Khat† (*Catha edulis*)	Abyssinian Tea, African Salad, Catha, Chat, Kat, Oat	No commercial uses	Fresh or dried leaves	Chewed brewed as tea	I**	Short-term: Euphoria, increased alertness and arousal, increased blood pressure and heart rate, depression, inability to concentrate, irritability, loss of appetite, insomnia. Long-term: Tooth decay and gum disease; gastrointestinal disorders such as constipation, ulcers, stomach inflammation, and increased risk of upper gastrointestinal tumors; cardiovascular disorders such as irregular heartbeat, decreased blood flow, and heart attack. Youth: Unknown Pregnancy: Unknown Other health-related issues: In rare cases associated with heavy use: psychotic reactions such as fear, anxiety, grandiose delusions (fantastical beliefs that one has superior qualities such as fame, power, and wealth), hallucinations, and paranoia.
	Methamphetamine	Crank, Chalk, Crystal, Fire, Glass, Go Fast, Ice, Meth, Speed	Desoxyn®	White powder or pill; crystal meth looks like pieces of	Swallowed, snorted, smoked, or injected	II	Short-term: Increased wakefulness and physical activity; decreased appetite; increased breathing, heart rate, blood pressure, temperature; irregular heartbeat.

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
				glass or shiny blue-white “rocks” of different sizes			Long-term: Anxiety, confusion, insomnia, mood problems, violent behavior, paranoia, hallucinations, delusions, weight loss, severe dental problems (“meth mouth”), intense itching leading to skin sores from scratching. Youth: Unknown Pregnancy: Premature delivery; separation of the placenta from the uterus; low birth weight; lethargy; heart and brain problems. Other health-related issues: Risk of HIV, hepatitis, and other infectious diseases from shared needles.
Synthetics (Other)	Synthetic Cannabinoids	K2, Spice, Black Mamba, Bliss, Bombay Blue, Fake Weed, Fire, Genie, Moon Rocks, Skunk, Smacked, Yucatan, Zohai	No commercial uses	Dried, shredded plant material that looks like potpourri and is sometimes sold as “incense”	Smoked, swallowed (brewed as tea)	I	Short-term: Increased heart rate; vomiting; agitation; confusion; hallucinations, anxiety, paranoia; increased blood pressure and reduced blood supply to the heart; heart attack. Long-term: Unknown Youth: Unknown Pregnancy: Unknown Other health-related issues: Use of synthetic cannabinoids has led to an increase in emergency room visits in certain areas.
	Synthetic Cathinones (Bath salts)	Bloom, Cloud Nine, Cosmic Blast, Flakka, Ivory Wave, Lunar Wave,	No commercial uses for ingested "bath salts"	White or brown crystalline powder sold in small	Swallowed, snorted, injected	I††	Short-term: Increased heart rate and blood pressure; euphoria; increased sociability and sex drive; paranoia, agitation, and hallucinations; psychotic and

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Substance category	Substance name	Street name(s)	Commercial name(s)	Common form(s)	Common ways taken	DEA schedule*	Possible health effects
		Scarface, Vanilla Sky, White Lightning		plastic or foil packages labeled "not for human consumption " and sometimes sold as jewelry cleaner; tablet, capsule, liquid			violent behavior; nosebleeds; sweating; nausea, vomiting; insomnia; irritability; dizziness; depression; suicidal thoughts; panic attacks; reduced motor control; cloudy thinking. Long-term: Breakdown of skeletal muscle tissue; kidney failure; death. Youth: Unknown Pregnancy: Unknown Other health-related issues: Risk of HIV, hepatitis, and other infectious diseases from shared needles.

* DEA Drug Schedules: Drugs, substances, and certain chemicals used to make drugs are classified into five (5) distinct categories or schedules depending upon the drug's acceptable medical use and the drug's abuse or dependency potential. The abuse rate is a determinate factor in the scheduling of the drug.
Schedule I: defined as drugs with no currently accepted medical use and a high potential for abuse. These are considered the most dangerous drugs of all the drug schedules with potentially severe psychological and/or physical dependence.
Schedule II: defined as drugs with a high potential for abuse, with use potentially leading to severe psychological or physical dependence. These drugs are also considered dangerous.
Schedule III: defined as drugs with a moderate to low potential for physical and psychological dependence.
Schedule IV: defined as drugs with a low potential for abuse and low risk of dependence.
Schedule V: defined as drugs with lower potential for abuse than Schedule IV and consist of preparations containing limited quantities of certain narcotics. Schedule V drugs are generally used for antidiarrheal, antitussive, and analgesic purposes.
† It is not known whether substance is addictive.
‡ Marijuana for recreational use is legal in Alaska, California, Colorado, Maine, Massachusetts, Michigan, Nevada, Oregon, Vermont, Washington and the District of Columbia. Marijuana for medical use is legal in Arizona, Arkansas, Connecticut, Delaware, Florida, Hawaii, Illinois, Louisiana, Maryland, Minnesota, Missouri, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Ohio, Oklahoma, Pennsylvania, Rhode Island, Utah, and West Virginia.
§ Rohypnol® is not approved for medical use in the United States; it is available as a prescription sleep aid in other countries
‖ Labeled drug of concern by DEA and illegal in some states
¶ DMT is Schedule I, but plants containing it are not controlled.
# Various forms may include: Paint thinners or removers, degreasers, dry-cleaning fluids, gasoline, lighter fluids, correction fluids, permanent markers, electronics cleaners and freeze sprays, glue, spray paint, hair or deodorant sprays, fabric protector sprays, aerosol computer cleaning products, vegetable oil sprays, butane lighters, propane tanks, whipped cream aerosol containers, refrigerant gases, ether, chloroform, halothane, nitrous oxide.
** Cathinone is Schedule I, making khat use illegal, but the khat plant is not controlled.
†† Some formulations have been banned by the DEA.

Appendix B. Commonly Abused Illicit, Prescription and Over-the-Counter Drugs

Abbreviations: DEA = Drug Enforcement Agency; HIV = human immunodeficiency virus; IQ = intelligence quotient; Motivational Enhancement Therapy (MET); OCT = over the counter

Appendix C. Literature Search Strategies

Key:
/ = subject heading
$ = truncation
*=truncation
ab = word in abstract
adj# = adjacent within x number of words
hw = subject heading word
id = key phrase identifier
kw = keyword
md = methodology
pt = publication type
ti = word in title

Cochrane Central Register of Controlled Trials (CENTRAL)

#1	(drug or drugs or substance* or opioid* or opiate* or amphetamine* or amfetamine* or benzodiazepine* or morphine* or methadone* or prescription* or phencyclidine* or solvent* or inhalant* or barbiturate* or depressant* or sedative* or stimulant* or psychotherapeutic or psycho-therapeutic or ritalin or adderall or methylphenidate or oxycodone or hydrocodone or pain relief or pain reliever* or pain medication*):ti,ab,kw near/3 (addict* or abuse* or abusing or abusive or misuse* or mis-use* or misusing or mis-using or non medical or extramedical or extra medical or illicit* or illegal* or unlawful* or unsanction* or habit* or dependen* or disorder or disorders or consumption or diversion*):ti,ab,kw
#2	("drug use" or "substance use"):ti
#3	marijuana:ti,ab,kw
#4	Cannabinoid*:ti,ab,kw
#5	cocaine:ti,ab,kw
#6	methamphetamine:ti,ab,kw
#7	(mdma or ecstasy):ti,ab,kw
#8	(hallucinogen$ or lsd):ti,ab,kw
#9	[or #1-#8]
#10	screen*:ti,ab,kw
#11	assessment:ti,ab,kw next (tool* or instrument*):ti,ab,kw
#12	((drug or substance) next (use or misuse or mis-use or abuse)):ti,ab,kw near/5 (scale* or inventor* or questionnaire* or survey* or index* or checklist* or interview*):ti,ab,kw
#13	"Addiction Severity Index":ti,ab,kw
#14	"Antenatal Psychosocial Health Assessment":ti,ab,kw
#15	"NIDA-Modified ASSIST":ti,ab,kw
#16	"Cut down Annoyed Guilty Eye-opener":ti,ab,kw
#17	"Chemical Use Abuse and Dependence Scale":ti,ab,kw
#18	"Drug Abuse Problem Assessment for Primary Care":ti,ab,kw
#19	DUDIT:ti,ab,kw
#20	"Relax Alone Forget Friends Trouble":ti,ab,kw
#21	"Reduce Annoyed Guilty Start":ti,ab,kw
#22	SMAST-AID:ti,ab,kw
#23	"4Ps Plus":ti,ab,kw
#24	"Substance Use Risk Profile-Pregnancy":ti,ab,kw
#25	[#10-`#24]

#26 #9 and #25

#27 (advice or advise*):ti,ab,kw

#28 counsel*:ti,ab,kw

#29 behavio*:ti,ab,kw and chang*:ti,ab,kw

#30 behavio*:ti,ab,kw and intervention*:ti,ab,kw

#31 behavio*:ti,ab,kw and modification*:ti,ab,kw

#32 (motivational next interview*):ti,ab,kw

#33 (cognitive next behavio*):ti,ab,kw or cbt:ti,ab,kw

#34 behavio*:ti,ab,kw and therapy:ti,ab,kw

#35 (brief next intervention*):ti,ab,kw

#36 "self help":ti,ab,kw

#37 computer:ti,ab,kw next (based or mediated or assisted):ti,ab,kw

#38 email*:ti,ab,kw or internet:ti,ab,kw or (text next messag*):ti,ab,kw or web:ti,ab,kw or website:ti,ab,kw

#39 "patient education":ti,ab,kw or "health education":ti,ab,kw or "health promotion":ti,ab,kw

#40 "12 step":ti,ab,kw or "twelve step":ti,ab,kw or "narcotics anonymous":ti,ab,kw

#41 intervention*:ti or psychosocial:ti

#42 [or #27-#41]

#43 #9 and #42

#44 #26 or #43 Publication Year from 2006 to 2016, in Trials

Ovid Medline, Ovid MEDLINE In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily Update

1 substance-related disorders/

2 amphetamine-related disorders/

3 cocaine-related disorders/

4 inhalant abuse/

5 marijuana abuse/

6 opioid-related disorders/

7 heroin dependence/

8 morphine dependence/

9 phencyclidine abuse/

10 substance abuse, intravenous/

11 street drugs/

12 hallucinogens/

13 ((drug or drugs or substance$ or opioid$ or opiate$ or amphetamine$ or amfetamine$ or benzodiazepine$ or morphine$ or methadone$ or prescription$ or phencyclidine$ or solvent$ or inhalant$ or barbiturate$ or depressant$ or sedative$ or stimulant$ or psychotherap$ or psycho-therap$ or ritalin or adderall or methylphenidate or oxycodone or hydrocodone or pain relief or pain reliever$ or pain medication$) adj3 (addict$ or abuse$ or abusing or abusive or misuse$ or mis-use$ or misusing or mis-using or non medical or extramedical or extra medical or illicit$ or illegal$ or unlawful$ or unsanction$ or habit$ or dependen$ or disorder or disorders or consumption or diversion$)).ti,ab.

14 (drug use$ or substance use$).ti.

15 marijuana.ti,ab.

16 (cannabis or cannabinoid$).ti,ab.

17 cocaine.ti,ab.

18 methamphetamine$.ti,ab.

19 (mdma or ecstasy).ti,ab.

20 (hallucinogen$ or lsd).ti,ab.

21 or/1-20

22 Mass screening/

23 screen$.ti,ab.

24 (assessment adj (tool$ or instrument$)).ti,ab.

25 ((drug use$ or drug misuse$ or drug abuse$ or substance use$ or substance misuse$ or substance abuse$) adj5 (scale$ or inventor$ or questionnaire$ or survey$ or index$ or checklist$ or interview$)).ti,ab.

26 Substance Abuse Detection/

27 or/22-26

28 Addiction Severity Index.ti,ab.

29 Antenatal Psychosocial Health Assessment.ti,ab.

30 "Alcohol Smoking and Substance Involvement Screening Test ".ti,ab.

31 NIDA Quick Screen.ti,ab.

32 NIDA-Modified ASSIST.ti,ab.

33 Cut down Annoyed Guilty Eye-opener.ti,ab.

34 "Chemical Use Abuse and Dependence Scale".ti,ab.

35 Drug Abuse Problem Assessment for Primary Care.ti,ab.

36 "Drug and Alcohol Problem Screen".ti,ab.

37 DUDIT.ti,ab.

38 drug abuse screening test$.ti,ab.

39 Relax Alone Forget Friends Trouble.ti,ab.

40 Reduce Annoyed Guilty Start.ti,ab.

41 Rapid Drug Problems Screen$.ti,ab.

42 Substance Abuse Subtle Screening Inventory.ti,ab.

43 ("Short Michigan Alcoholism Screening Test" and drugs).ti,ab.

44 SMAST-AID.ti,ab.

45 Simple Screening Instrument for Substance Abuse.ti,ab.

46 Single-Question screening test$.ti,ab.

47 Texas Christian University Drug Screen.ti,ab.

48 4Ps Plus.ti,ab.

49 "Substance Use Risk Profile-Pregnancy".ti,ab.

50 Cannabis Abuse Screening Test.ti,ab.

51 Substance Abuse Detection/is

52 or/28-51

53 clinical trials as topic/ or controlled clinical trials as topic/ or randomized controlled trials as topic/

54 (clinical trial or controlled clinical trial or randomized controlled trial).pt.
55 Random$.ti,ab.
56 control groups/ or double-blind method/ or single-blind method/
57 clinical trial$.ti,ab.
58 controlled trial$.ti,ab.
59 or/53-58
60 21 and (27 or 52) and 59
61 "Sensitivity and Specificity"/
62 "Predictive Value of Tests"/
63 ROC Curve/
64 False Negative Reactions/
65 False Positive Reactions/
66 Diagnostic Errors/
67 "Reproducibility of Results"/
68 Reference Values/
69 Reference Standards/
70 Observer Variation/
71 Receiver operat$.ti,ab.
72 ROC curve$.ti,ab.
73 sensitivit$.ti,ab.
74 specificit$.ti,ab.
75 predictive value.ti,ab.
76 accuracy.ti,ab.
77 false positive$.ti,ab.
78 false negative$.ti,ab.
79 miss rate$.ti,ab.
80 error rate$.ti,ab.
81 or/61-80
82 (21 and 27) or 52
83 81 and 82
84 60 or 83
85 limit 84 to (english language and yr="2006 -Current")
86 remove duplicates from 85
87 Behavior Therapy/
88 Cognitive Therapy/
89 Counseling/
90 Directive Counseling/
91 Patient Education as Topic/
92 Risk Reduction Behavior/
93 Feedback, psychological/

94 Health education/
95 Health promotion/
96 Motivation/
97 Internet/
98 Motivational interviewing/
99 Persuasive communication/
100 Self-help groups/
101 Text messaging/
102 Therapy, computer-assisted/
103 (advice or advise$).ti,ab.
104 counsel$.ti,ab.
105 behavio?r$ chang$.ti,ab.
106 behavio?r$ intervention$.ti,ab.
107 behavio?r$ modification$.ti,ab.
108 motivational interview$.ti,ab.
109 (cognitive behavio$ or behavio$ therapy or cbt).ti,ab.
110 brief intervention$.ti,ab.
111 self help.ti,ab.
112 text messag$.ti,ab.
113 (web or website).ti,ab.
114 (computer adj (based or mediated or assisted)).ti,ab.
115 12 step.ti,ab.
116 twelve step.ti,ab.
117 Narcotics anonymous.ti,ab.
118 (intervention$ or psychosocial).ti.
119 or/87-118
120 21 and 119
121 *Substance-Related Disorders/dt, pc, rh, th [Drug Therapy, Prevention & Control, Rehabilitation, Therapy]
122 *Amphetamine-Related Disorders/dt, pc, rh, th
123 *Cocaine-Related Disorders/dt, pc, rh, th
124 *Inhalant Abuse/dt, pc, rh, th
125 *Marijuana Abuse/dt, pc, rh, th
126 *Opioid-Related Disorders/dt, pc, rh, th
127 *Heroin Dependence/dt, pc, rh, th
128 *Phencyclidine Abuse/dt, pc, rh, th
129 *Substance Abuse, Intravenous/dt, pc, rh, th
130 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129
131 clinical trials as topic/ or controlled clinical trials as topic/ or randomized controlled trials as topic/
132 (clinical trial or controlled clinical trial or randomized controlled trial).pt.
133 Random$.ti,ab.

134 control groups/ or double-blind method/ or single-blind method/

135 clinical trial$.ti,ab.

136 controlled trial$.ti,ab.

137 131 or 132 or 133 or 134 or 135 or 136

138 130 and 137

139 limit 138 to (english language and yr="2006 -Current")

140 remove duplicates from 139

141 86 or 140

142 Animals/ not (Humans/ and Animals/)

143 141 not 142

PsycInfo

1 Drug Abuse/

2 Drug Usage/

3 Drug Dependency/

4 Drug Addiction/

5 Inhalant Abuse/

6 Glue Sniffing/

7 Polydrug Abuse/

8 Drug Abstinence/

9 Intravenous Drug Usage/

10 Marijuana Usage/

11 Cocaine/

12 Opiates/

13 Hallucinogenic Drugs/

14 Phencyclidine/

15 Methamphetamine/

16 Methylenedioxymethamphetamine/

17 Lysergic Acid Diethylamide/

18 ((drug or drugs or substance$ or opioid$ or opiate$ or amphetamine$ or amfetamine$ or benzodiazepine$ or morphine$ or methadone$ or prescription$ or phencyclidine$ or solvent$ or inhalant$ or barbiturate$ or depressant$ or sedative$ or stimulant$ or psychotherap$ or psycho-therap$ or ritalin or adderall or methylphenidate or oxycodone or hydrocodone or pain relief or pain reliever$ or pain medication$) adj3 (addict$ or abuse$ or abusing or abusive or misuse$ or mis-use$ or misusing or mis-using or non medical or extramedical or extra medical or illicit$ or illegal$ or unlawful$ or unsanction$ or habit$ or dependen$ or disorder or disorders or consumption or diversion$)).ti,ab,id.

19 (drug use$ or substance use$).ti.

20 marijuana.ti,ab,id.

21 (cannabis or cannabinoid$).ti,ab,id.

22 cocaine.ti,ab,id.

23 methamphetamine$.ti,ab,id.

24 (mdma or ecstasy).ti,ab,id.

25 (hallucinogen$ or lsd).ti,ab,id.

26 or/1-25

27 Screening/

28 Health Screening/

29 Screening Tests/

30 Intake Interview/

31 Symptom Checklists/

32 Interviews/

33 Questionnaires/

34 Rating Scales/

35 Self Report/

36 General Health Questionnaire/

37 Computer Assisted Diagnosis/

38 screen$.ti,ab,id.

39 (assessment adj (tool$ or instrument$)).ti,ab,id.

40 ((drug use$ or drug misuse$ or substance use$ or substance misuse$) adj5 (scale$ or inventor$ or questionnaire$ or survey$ or index$ or checklist$ or interview$)).ti,ab,id.

41 self report$.ti,ab,id.

42 identif$.ti.

43 or/27-42

44 Addiction Severity Index.ti,ab,tm.

45 Antenatal Psychosocial Health Assessment.ti,ab,tm.

46 "Alcohol Smoking and Substance Involvement Screening Test ".ti,ab,tm.

47 NIDA Quick Screen.ti,ab,tm.

48 NIDA-Modified ASSIST.ti,ab,tm.

49 Cut down Annoyed Guilty Eye-opener.ti,ab,tm.

50 "Chemical Use Abuse and Dependence Scale".ti,ab,tm.

51 Drug Abuse Problem Assessment for Primary Care.ti,ab,tm.

52 "Drug and Alcohol Problem Screen".ti,ab,tm.

53 DUDIT.ti,ab,tm.

54 drug abuse screening test$.ti,ab,tm.

55 Relax Alone Forget Friends Trouble.ti,ab,tm.

56 Reduce Annoyed Guilty Start.ti,ab,tm.

57 Rapid Drug Problems Screen$.ti,ab,tm.

58 Substance Abuse Subtle Screening Inventory.ti,ab,tm.

59 ("Short Michigan Alcoholism Screening Test" and drugs).ti,ab,tm.

60 SMAST-AID.ti,ab,tm.

61 Simple Screening Instrument for Substance Abuse.ti,ab,tm.

62 Single-Question screening test$.ti,ab,tm.

63 Texas Christian University Drug Screen.ti,ab,tm.

64 4Ps Plus.ti,ab,tm.
65 "Substance Use Risk Profile-Pregnancy".ti,ab,tm.
66 Cannabis Abuse Screening Test.ti,ab,tm.
67 or/44-66
68 random$.ti,ab,id,hw.
69 placebo$.ti,ab,id,hw.
70 controlled trial$.ti,ab,id,hw.
71 clinical trial$.ti,ab,id,hw.
72 Clinical Trial.md.
73 Experiment Controls/
74 or/68-73
75 26 and (43 or 67) and 74
76 Test Validity/
77 Test Reliability/
78 Interrater Reliability/
79 validity.ti,ab,id.
80 reliability.ti,ab,id.
81 Receiver operat$.ti,ab,id.
82 ROC curve$.ti,ab,id.
83 sensitivit$.ti,ab,id.
84 specificit$.ti,ab,id.
85 predictive value.ti,ab,id.
86 accuracy.ti,ab,id.
87 false positive$.ti,ab,id.
88 false negative$.ti,ab,id.
89 miss rate$.ti,ab,id.
90 error rate$.ti,ab,id.
91 or/76-90
92 (26 and 43) or 67
93 91 and 92
94 75 or 93
95 limit 94 to (english language and yr="2006 -Current")
96 Health Promotion/
97 Motivation/
98 Behavior Modification/
99 Behavior Change/
100 behavio?r$ chang$.ti,ab,id.
101 behavio?r$ intervention$.ti,ab,id.
102 behavio?r$ modification$.ti,ab,id.
103 behavior therapy/

104 cognitive behavior therapy/
105 cognitive therapy/
106 Cognitive Techniques/
107 (cognitive behavio$ or behavio$ therapy or cbt).ti,ab,id.
108 brief intervention$.ti,ab,id.
109 Persuasive Communication/
110 Motivational Interviewing/
111 motivational interview$.ti,ab,id.
112 Health Knowledge/
113 Health Behavior/
114 Health Education/
115 Client Education/
116 Feedback/
117 Online Therapy/
118 Computer Assisted Therapy/
119 Computer Mediated Communication/
120 Computer Assisted Testing/
121 Internet/
122 (computer adj (based or mediated or assisted)).ti,ab,id.
123 text messag$.ti,ab,id.
124 email$.ti,ab,id.
125 internet.ti,ab,id.
126 (web or website).ti,ab,id.
127 Self Help Techniques/
128 self help.ti,ab,id.
129 counseling/
130 Group Counseling/
131 counseling.ti,ab,id.
132 counselling.ti,ab,id.
133 advice.ti,ab,id.
134 advise$.ti,ab,id.
135 (intervention$ or psychosocial).ti.
136 or/96-135
137 26 and 136
138 68 or 69 or 70 or 71 or 72 or 73
139 137 and 138
140 limit 139 to (english language and yr="2006 -Current")
141 95 or 140

Appendix C. Literature Search Strategies

PubMed, publisher-supplied records

#27	Search #26 AND publisher[sb] AND ("2006/01/01"[Date - Publication] : "3000"[Date - Publication]) AND English[Language]
#26	Search (#11 OR #24) AND #25
#25	Search random*[tiab] OR clinical trial*[tiab] OR controlled trial*[tiab]
#24	Search #6 AND #23
#23	Search #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
#22	Search intervention*[ti] OR psychosocial[ti]
#21	Search “12 step”[tiab] OR “twelve step”[tiab] OR “narcotics anonymous”[tiab]
#20	Search "patient education"[tiab] OR "health education"[tiab] OR "health promotion"[tiab]
#19	Search email*[tiab] OR internet[tiab] OR text messag*[tiab] OR web[tiab] OR website[tiab]
#18	Search cbt[tiab] OR brief intervention*[tiab] OR computer based[tiab] OR computer mediated[tiab] OR computer assisted[tiab] OR self help[tiab]
#17	Search behavio*[tiab] AND therapy[tiab]
#16	Search motivational interview*[tiab] OR cognitive behavio*[tiab]
#15	Search behavio*[tiab] AND modification*[tiab]
#14	Search behavio*[tiab] AND intervention*[tiab]
#13	Search behavio*[tiab] AND chang*[tiab]
#12	Search counsel*[tiab] OR advice[tiab] OR advise*[tiab]
#11	Search #6 AND #10
#10	Search #7 OR #8 OR #9
#9	Search (drug use*[tiab] OR drug misuse*[tiab] OR drug abuse*[tiab] OR substance use*[tiab] OR substance misuse*[tiab] OR substance abuse*[tiab]) AND (scale*[tiab] OR inventor*[tiab] OR questionnaire*[tiab] OR survey*[tiab] OR index*[tiab] OR checklist*[tiab] OR interview*[tiab])
#8	Search (assessment tool*[tiab] OR assessment instrument*[tiab])
#7	Search screen*[tiab]
#6	Search #3 OR #4 OR #5
#5	Search marijuana[tiab] OR cannabis[tiab] OR cannabinoid*[tiab] OR cocaine[tiab] OR methamphetamine[tiab] OR mdma[tiab] OR ecstasy[tiab] OR hallucinogen*[tiab] OR lsd[tiab]
#4	Search drug use*[tiab] OR substance use*[tiab]
#3	Search #1 AND #2
#2	Search addict*[tiab] OR abuse*[tiab] OR abusing[tiab] OR misus*[tiab] OR mis us*[tiab] nonmedical[tiab] OR "non medical"[tiab] OR extramedical[tiab] OR "extra medical"[tiab] OR illicit*[tiab] OR illegal*[tiab] OR unlawful*[tiab] OR unsanction*[tiab]
#1	Search drug[tiab] OR drugs[tiab] OR substance*[tiab] OR opioid*[tiab] OR opiate*[tiab] OR amphetamine*[tiab] OR amfetamine*[tiab] OR benzodiazepine*[tiab] OR morphine*[tiab] OR methadone*[tiab] OR prescription*[tiab] OR phencyclidine*[tiab] OR solvent*[tiab] OR inhalant*[tiab]

OR barbiturate*[tiab] OR depressant*[tiab] OR sedative*[tiab] OR stimulant*[tiab] OR psychotherapeutic*[tiab] OR Ritalin[tiab] OR Adderall[tiab] OR methylphenidate[tiab] OR oxycodone[tiab] OR hydrocodone[tiab] OR pain relief[tiab] OR pain reliever*[tiab] OR pain medication*[tiab]

Appendix C Table 1. Inclusion and Exclusion Criteria

	Included	Excluded
Aim	Screening for illicit drug use and/or nonmedical pharmaceutical drug use and interventions for nondependent drug use, with or without addressing other substances or behaviors	Studies in which the only aim is targeting another behavior (e.g., unhealthy alcohol use, tobacco use) (i.e., change in drug use is not a stated aim but is a reported outcome)
Condition	Use of the following drugs, defined as *any* drug use that can result in poor health consequences, including meeting criteria for a drug use disorder: • Cannabinoids (marijuana, hashish, synthetic cannabinoids) • Club drugs (3,4-methylenedioxymethamphetamine [MDMA or ecstasy], flunitrazepam [Rohypnol], gamma-hydroxybutyrate [GHB], synthetic cathinones [bath salts]) • Dissociative drugs (ketamine, phencyclidine [PCP] and analogs, *Salvia divinorum* [salvia], dextromethorphan [DXM]) • Hallucinogens (lysergic acid diethylamide [LSD or acid], N,N-dimethyltryptamine [DMT], mescaline, psilocybin) • Inhalants (also known as volatile substances) • Illicit opioids (heroin, opium, *Mitragyna speciosa* [kratom], illicitly manufactured fentanyl [IMF]) • Stimulants (cocaine, amphetamine, *Catha edulis* [khat], methamphetamine) • Prescription opioid pain relievers • Prescription sedatives (barbiturates, benzodiazepines, sleep medications) • Prescription stimulants • Over-the-counter drugs (e.g., DXM) • Combination of any of the above	• Medical use of drugs as prescribed • Nonpsychoactive drugs (e.g., anabolic steroids, laxatives, aspirin)
Population	**All KQs:** Adolescents and adults age 12 years and older **KQs 1–3:** Studies whose participants are not selected on the basis of drug use or a related behavior or condition **KQs 4, 5:** Studies in which at least 50% of the enrolled sample is recruited via population-based screening A priori subpopulations at greater risk for drug use or its consequences will be examined based on the following factors: age (particularly young adults ages 18 to 25 years and adolescents ages 12 to 17 years), sex, race/ethnicity, socioeconomic status, pregnancy status, concurrent substance use (tobacco or alcohol), severity of the disorder, and presence of comorbid mental health conditions	Studies limited to: • Treatment-seeking individuals (including those responding to recruitment advertising) • Persons with psychotic disorders (e.g., schizophrenia) • Persons presenting in an emergency setting for drug-related issues (e.g., motor vehicle injury) • Persons receiving chronic opioid therapy • Other groups not generalizable to primary care (e.g., psychiatric inpatients, persons who are court-mandated to receive treatment, persons who are incarcerated) • **KQs 4, 5:** Persons with dependent drug use (or studies in which >50% of the enrolled sample is persons with dependent drug use)
Screening	**KQs 1, 3:** Screening for drug use using a brief standardized instrument or set of questions that is conducted in person or via telephone, mail, or electronically **KQ 2:** Accuracy of screening instruments, such as the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST); Cut down, Annoyed, Guilty, Eye-opener–Adapted to Include Drug Use (CAGE-AID); Car, Relax, Alone, Forget, Friends,	• Studies without any screening instruments or questions • Laboratory tests • Newborn screening tests for drug exposure (e.g., testing of meconium, infant hair, or umbilical cord specimens)

Appendix C Table 1. Inclusion and Exclusion Criteria

	Included	Excluded
	Trouble (CRAFFT); Drug Abuse Screening Test (DAST), including the DAST-10; Global Appraisal of Individual Needs-Short Screener (GAIN-SS); 4P's Plus (Past use, Pregnancy, use by Parents and Partners); National Institute on Drug Abuse Quick Screen; and single screening questions (SSQs)	
Interventions	• Counseling designed to reduce drug use, with or without referral • Counseling interventions can vary in their approach (e.g., 12-step, cognitive behavioral therapy, motivational enhancement therapy), specific strategies (e.g., action plans, diaries), delivery method (e.g., face-to-face, electronic, individual, group-based), length of contact (e.g., brief, extended), and the number of contacts (e.g., single, multiple)	• Interventions to prevent drug use initiation • Contingency management • Vocational rehabilitation • Community-based media or policy interventions • Interventions to prevent initiation of use among nonusers • Pharmacotherapy
Comparisons	**KQs 1, 3:** • No screening • Usual care **KQ 2:** Reference standard (i.e., structured or semistructured clinical interview) **KQs 4, 5:** • No intervention • Usual care • Waitlist • Attention control (e.g., intervention is similar in format and intensity but on a different content area) • Minimal intervention (e.g., no more than one single brief contact per year, brief written materials such as pamphlets)	Active intervention
Settings	**KQs 1–3:** Population-based screening that takes place in a setting that is applicable to primary care, including: primary care clinics; prenatal clinics; obstetrics/gynecology clinics; emergency departments; specialty medical treatment settings (e.g., diabetes management); school health clinics; and research clinic/office, home, or other community settings, including electronic or computer-based screening **KQs 4, 5:** Interventions in a screen-detected population that take place in a traditional primary care setting or one that is applicable to or referable from primary care, including: primary care clinics; prenatal clinics; obstetrics/gynecology clinics; behavioral/mental health clinics; emergency departments; substance abuse treatment centers; school health clinics; and research clinic/office, home, or other community settings, including electronic or computer-based interventions. Screening to identify eligible participants must take place in broad-based, general setting comparable to primary care with a defined population (e.g., primary care clinic, WIC program, orientation for incoming college freshman).	Screening that takes place in: • Behavioral/mental health clinic • Substance abuse treatment center • Worksites, including occupational screening • Inpatient/residential facility • Other institutions (e.g., correctional facility)

Appendix C Table 1. Inclusion and Exclusion Criteria

	Included	Excluded

Outcomes	**KQs 1a, 4a:**
	• Drug use (**required**) (self-report and/or biologic measures):
	  ○ Abstinence (use/no use)
	  ○ Frequency and/or quantity of drug use
	  ○ Severity of drug use disorder (reported as an index measured by a standardized questionnaire, such as the Short Inventory of Problems, Addiction Severity Index, or Severity of Dependence Scale)
	• Composite substance use
	• Other risky behaviors (e.g., alcohol, tobacco, or other drug use; risky sexual behaviors)
	
	KQs 1b, 4b:
	• All-cause mortality
	• Drug-related mortality (intentional and unintentional)
	• Drug-related morbidity (e.g., mental health symptoms/disorders, STI/HIV transmission, hepatitis B or C virus transmission, respiratory infection, cardiovascular complications, stroke, seizure, nonfatal overdose, injuries and accidents, cognitive impairment, visit to emergency department, hospital inpatient stay)
	• Obstetrical/perinatal/neonatal outcomes (e.g., perinatal mortality, preterm labor/delivery, low birth weight, placental abruption, intrauterine growth restriction, preeclampsia, antepartum or postpartum hemorrhage, gestational hypertension, decreased neonate length/head circumference, neonate neurobehavioral effects, congenital anomalies, neonatal abstinence syndrome, neonatal intensive care unit admission, decreased length of neonate hospitalization)
	• Quality of life
	• Drug-related problems, such as legal problems, social and family relations, employment, and school/educational outcomes
	
	KQ 2: Sensitivity and specificity or data to calculate one or both
	
	KQs 3, 5:
	• Serious harms at any time point after the screening or intervention began (e.g., death, seizure, cardiovascular event, other medical issue requiring urgent medical treatment, serious obstetrical/perinatal/neonatal complication attributable to included medications)
	• Demoralization due to failed quit attempt
	• Stigma, labeling, and/or discrimination
	• Privacy issues (e.g., insurability status)
	• Job loss
	• Interference with the doctor-patient relationship
		• Attitudes, knowledge, and beliefs related to drug use
		• Intention to change behavior
		• Intervention participation/compliance

Outcome assessment timing	At least 3 months after baseline measurement (except for studies in pregnant women, for which shorter lengths of followup will be included)	

Appendix C Table 1. Inclusion and Exclusion Criteria

	Included	Excluded
Study design	**KQs 1, 3:** Studies that compare individuals who receive screening with those receiving no screening or usual care, including randomized controlled trials and nonrandomized controlled trials **KQ 2:** Studies of screening accuracy reporting sensitivity and specificity compared with a structured or semistructured clinical interview **KQ 4, 5:** Randomized, controlled trials and nonrandomized controlled trials	Prospective and retrospective cohort studies, case control studies, time series studies, before-after studies with no comparison group, cross-sectional studies, case studies, case series, editorials/commentaries
Country	Studies conducted in countries categorized as "Very High" on the 2014 Human Development Index (as defined by the United Nations Development Programme)	Studies conducted in countries that are not categorized as "Very High" on the 2014 Human Development Index
Publication date	Studies whose primary results were published from 1992 to present	Studies whose primary results were published prior to 1992
Language	English	Non-English
Quality	Fair or good quality	Poor quality (according to design-specific USPSTF criteria)

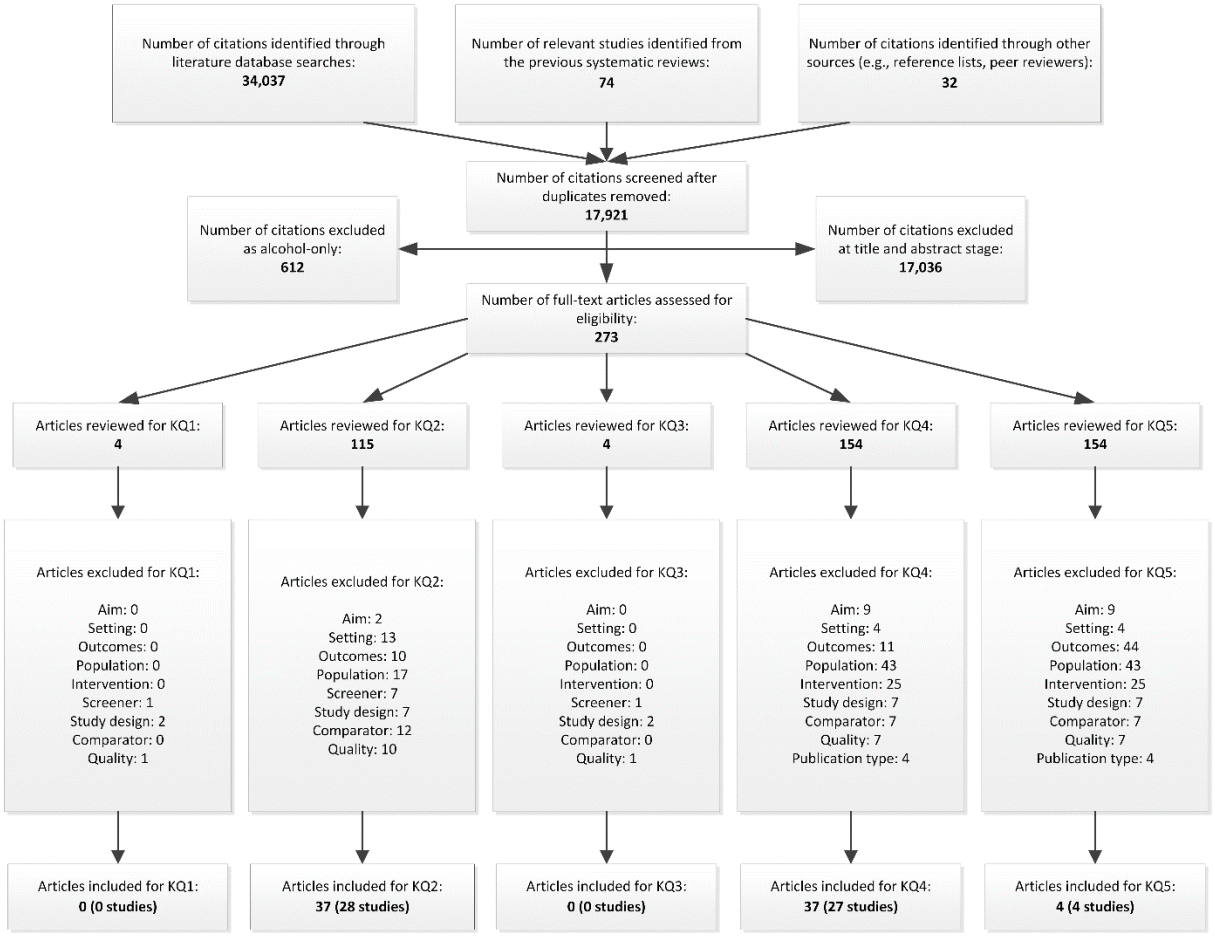
Appendix C. Table 2. Study Design-Specific Quality Rating Criteria*

Study Design	Adapted Quality Criteria
Diagnostic accuracy studies, adapted from the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) I[144] and II[145] instrument	**Patient Selection** • Was a consecutive or random sample of patients enrolled? • Did the study avoid inappropriate exclusions? **Index Test** • Were the index test results interpreted without knowledge of the reference standard results? • If a threshold was used, was it prespecified or was a range of values presented? **Reference Standard** • Is the reference standard likely to correctly classify the target condition? • Were the reference standard results interpreted without knowledge of the index test? • Were staff trained in the use of the reference standard? • Was fidelity of the reference standard monitored or reported? **Flow and Timing** • Was there an appropriate interval between the index test and reference standard? • Did all patients receive a reference standard? • Did all patients receive the same reference standard? o Were all patients included in the analysis?
RCT[37]	**Bias arising in the randomization process or due to confounding** • Valid random assignment/random sequence generation method used • Allocation concealed • Balance in baseline characteristics **Bias in selecting participants into the study** • CCT only: No evidence of biased selection of sample **Bias due to departures from intended interventions** • Fidelity to the intervention protocol • Low risk of contamination between groups • Participants were analyzed as originally allocated **Bias from missing data** • No, or minimal, post-randomization exclusions • Outcome data are reasonably complete and comparable between groups • Reasons for missing data are similar across groups • Missing data are unlikely to bias results **Bias in measurement of outcomes** • Blinding of outcome assessors • Outcomes are measured using consistent and appropriate procedures and instruments across treatment groups • No evidence of biased use of inferential statistics **Bias in reporting results selectively** • No evidence that the measures, analyses, or subgroup analyses are selectively reported

* All studies were classified as good, fair, or poor according to the USPSTF Procedure Manual.[37]

Abbreviations: RCT = randomized controlled trial

Appendix D. Literature Flow Diagram



Appendix E. List of Included Studies

Below is a list of included studies and their ancillary publications (indented below main results publication):

KQ1 and KQ3:

No included studies

KQ2:

Bastiani L, Siciliano V, Curzio O, et al. Optimal scaling of the CAST and of SDS Scale in a national sample of adolescents. Addict Behav. 2013;38(4):2060-7. PMID: 23396173. http://dx.doi.org/10.1016/j.addbeh.2012.12.016

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Appendix F. List of Excluded Studies

Reason for Exclusion*	
E1	**Study Aim:** Not applicable/relevant to key question
E2a	**Setting:** Not in very high human development index country*
E2b	**Setting:** Screening and/or intervention is not conducted in, recruited from, or feasible for primary care
E2c	**Setting:** Conducted in emergency department or urgent care setting
E3a	**Population:** • For screening, participants selected on the basis of alcohol or drug use or a related behavior or condition • For interventions: Not among a screen-detected population (i.e., <50% of enrolled sample is recruited via population-based screening) or among those with addiction or dependence
E3b	**Population:** Otherwise out-of-scope (e.g., psychotic disorder, persons on chronic opioid therapy, court-mandated, incarcerated)
E3c	**Population:** Children <12 years
E4	**Outcome**: No measure of drug use (only a composite substance use index) or no measure related to sensitivity and specificity for screening accuracy
E5a	**Screening tool (KQ1, 2, 3):** Assessment for drug or alcohol use does NOT include a brief standardized instrument or set of questions that is conducted in person or via telephone, mail, or electronically
E5b	**Screening tool accuracy (KQ2):** Not an included instrument (NIAAA one- or two-item screener or comparable, BSTAD, AUDIT and AUDIT-C, ASSIST, CARET, TWEAK, and T-ACE).
E5c	**Intervention:** Not an included intervention (e.g., medication, *only* contingency management, vocational rehabilitation, financial incentive)
E5e	**Intervention:** Prevention
E6	**Comparator:** Not an included comparator (e.g., screening results given to control providers [KQ1,3], no reference standard [KQ2], active intervention [KQ4,5])
E7	**Condition:** Nonpsychoactive drug (e.g., laxative, anabolic steroid)
E8	**Follow-up: KQ1, 4:** Less than 3 months postbaseline (except among pregnant women)
E9	**Study design:** KQ1, 3, 4, 5=RCTs and CCTs, KQ2=screening accuracy, KQ5=large cohort or case control studies for medication trials
E10	**Study Quality:** Poor

* Assigned at full-text phase

Abbreviations: E = exclude

Appendix F. List of Excluded Studies

1. Aalborg A, Miller B, Husson G, et al. Implementation of adolescent family-based substance use prevention programmes in health care settings: Comparisons across conditions and programmes. Health education journal. 2012;71(1):53-61. PMID: 22984294. **KQ4E5e, KQ5E5e.**
2. Abrams TE. Capsule commentary on McNeely et al., Validation of self-administered single item screening questions (SISQs) for unhealthy alcohol and drug use in primary care patients. J Gen Intern Med. 2015;30(12):1845. **KQ2E9.**
3. Adamson SJ, Kay-Lambkin FJ, Baker AL, et al. An improved brief measure of cannabis misuse: The Cannabis Use Disorders Identification Test-Revised (CUDIT-R). Drug Alcohol Depend. 2010;110(1-2):137-43. **KQ2E3a.**
4. Alexander TL. Substance abuse screening with deaf clients: Development of a culturally sensitive scale. Dissertation Abstracts International Section A: Humanities and Social Sciences. 2005;66(2-A):756. **KQ2E4.**
5. Ali R, Meena S, Eastwood B, et al. Ultra-rapid screening for substance-use disorders: the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST-Lite). Drug Alcohol Depend. 2013;132(1-2):352-61. PMID: 23561823. **KQ2E2a.**
6. Altieri KM. Validating the Alcohol and Drug Use Survey and determining the relationships of familial and age-related variables with substance abuse of adolescents in a correctional facility. Dissertation Abstracts International Section A: Humanities and Social Sciences. 2002;63(2-A):506. **KQ2E2b.**
7. Araujo M, Golpe S, Brana T, et al. Psychometric validation of the POSIT for screening alcohol and other drugs risk consumption among adolescents. Adicciones. 2017;0(0):958. PMID: 28492958. **KQ2E10.**
8. Ashman TA, Schwartz ME, Cantor JB, et al. Screening for substance abuse in individuals with traumatic brain injury. Brain Inj. 2004;18(2):191-202. PMID: 14660230. **KQ2E3b.**
9. Assadi SM, Radgoodarzi R, Ahmadi-Abhari SA. Baclofen for maintenance treatment of opioid dependence: a randomized double-blind placebo-controlled clinical trial [ISRCTN32121581]. BMC psychiatry. 2003;3:16. PMID: 14624703. **KQ4E5c, KQ5E5c.**
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11. Bagley SM, Anderson BJ, Stein MD. Usefulness of the CRAFFT to diagnose alcohol or cannabis use disorders in a sample of emerging adults with past-month alcohol or cannabis use. Journal of child & adolescent substance abuse. 2017;26(1):18-23. **KQ2E3a.**
12. Baldus C, Miranda A, Weymann N, et al. "CAN Stop"--implementation and evaluation of a secondary group prevention for adolescent and young adult cannabis users in various contexts--study protocol. BMC Health Serv Res. 2011;11:80. PMID: 21501479. **KQ4E3a, KQ5E3a.**
13. Bannink R, Broeren S, Joosten-van Zwanenburg E, et al. Effectiveness of a Web-based tailored intervention (E-health4Uth) and consultation to promote adolescents' health: randomized controlled trial. J Med Internet Res. 2014;16(5):e143. PMID: 24878521. **KQ4E5e, KQ5E5e.**
14. Bashford J, Flett R, Copeland J. The Cannabis Use Problems Identification Test (CUPIT): development, reliability, concurrent and predictive validity among adolescents and adults. Addiction. 2010;105(4):615-25. PMID: 20403014. **KQ2E2b.**
15. Batki SL, Washburn AM, Delucchi K, et al. A controlled trial of fluoxetine in crack cocaine dependence. Drug

Alcohol Depend. 1996;41(2):137-42. PMID: 8809502. **KQ4E5c, KQ5E5c.**

16. Becker J, Haug S, Kraemer T, et al. Feasibility of a group cessation program for co-smokers of cannabis and tobacco. Drug & Alcohol Review. 2015;34(4):418-26. PMID: 25676414. **KQ4E9, KQ5E9.**

17. Bedregal LE, Sobell LC, Sobell MB, et al. Psychometric characteristics of a Spanish version of the DAST-10 and the RAGS.[Erratum appears in Addict Behav. 2006 Sep;31(9):1730]. Addict Behav. 2006;31(2):309-19. PMID: 15979248. **KQ2E3a.**

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19. Berman AH, Wennberg P, Sinadinovic K. Changes in mental and physical well-being among problematic alcohol and drug users in 12-month Internet-based intervention trials. Psychol Addict Behav. 2015;29(1):97-105. PMID: 25664387. **KQ4E3a, KQ5E3a.**

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Appendix G. List of Abbreviations for Screening Tests and Reference Standards

Abbreviation	Instrument
4P's Plus	Parents Partner Past Pregnancy
ADI	Adolescent Diagnostic Interview
ASSIST	Alcohol, Smoking and Substance Involvement Screening Test
AUDIT	Alcohol Use Disorders Identification Test
AUDIT-C	Alcohol Use Disorders Identification Test - Consumption
BSTAD	Brief Screener for Tobacco, Alcohol, and Other Drugs
CAST	Cannabis Abuse Screening Test
CIDI	Composite International Diagnostic Interview
CPQ-A-S	Cannabis Problems Questionnaire for Adolescents Shortened
CRAFFT	Car Relax Alone Forget Family/Friends Trouble
DAST-2	2-Item Drug-Abuse Screening Test
DAST-10	10-Item Drug-Abuse Screening Test
DAST-28	28-Item Drug-Abuse Screening Test
DISC-IV	Diagnostic Interview for Children Version IV
DSM	Diagnostic and Statistical Manual of Mental Disorders
InDUC	Inventory of Drug Use Con-sequences
M-CIDI	Munich-Composite International Diagnostic Interview
MINI	Multi International Neuropsychiatric Interview
NESARC	National Epidemiologic Survey on Alcohol and Related Conditions
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NSDUH	National Survey on Drug Use and Health
PDUQp	Prescription Drug Use Questionnaire Patient Version
PESQ-PS	Personal Experience Screening Questionnaire
POSIT	Problem Oriented Screening Instrument for Teenagers
PRO	Prenatal Risk Overview
PSQ	Parent Screening Questionnaire
SCID	Structured Clinical Interview for the DSM
SDS	Severity of Dependence Scale
SIP	The Short Inventory of Problems
SIP-DU	The Short Inventory of Problems—Modified for Drug Use
SoDU	Screen of Drug Use
SUBS	Substance Use Brief Screen
TAPS	Tobacco, Alcohol, Prescription Medication, and Other Substance Use
TICS	Two-Item Conjoint Screen
TLFB	Timeline Follow Back
WIDUS	Wayne Indirect Drug Use Screener

Appendix H. List of Ongoing Studies (as of November 2018)

Study Reference Trial Identifier	Principal Investigator/Study Contact (if different)	Study name	Location	N	Description	2019 Status
NCT01501318	Matthew G Hile, PhD matthew.hile@mimh.edu	Impact of Personalized Feedback Alone on Substance Use Behaviors	US	40	The investigators seek to develop a more efficient and effective approach to providing brief behavioral health interventions for risky substance use behaviors by comparing a brief coach directed intervention to a tailored report only group.	Completed Nov 2012. No published records.
NCT02191605	Steven J Ondersma, PhD s.ondersma@wayne.edu	Computer-delivered Screening & Brief Intervention for Marijuana Use in Pregnancy	US	80	The investigators will test two technology-based, highly practical interventions that could reduce the number of children who are prenatally exposed to marijuana.	Completed Oct 2017. No published records.
NCT03165175	Suzanne L Hurtado, MPH NR	Mobile Application for Prescription Drug-Abuse Education (MAPDE)	US	60	The aims of this pilot study are: (1) to assess the feasibility and acceptability of a mobile application to educate military members about the risks of prescription drug misuse; (2) to determine if there is evidence that the mobile application plus treatment as usual reduces the risk of prescription drug misuse and shows differences in related measures compared to treatment as usual among military medical clinic patients currently taking prescription medication; and (3) if evidence of reduced risk is found, to estimate effect sizes for a future effectiveness trial.	Ongoing: Est. Completion Date Sep 2018
NCT03037476	Irene M Geisner, PhD geisner@uw.edu	Personalized Health Assessment Related to Medications (Project PHARM)	US	1050	This project proposes to evaluate the efficacy of Screening and Brief Interventions (SBIs) for reducing college students' PSM misuse through two different routes of screening and intervention across 9 colleges and universities spanning the United States.	Ongoing: Est. Completion Date Jun 2019

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Study Reference Trial Identifier	Principal Investigator/Study Contact (if different)	Study name	Location	N	Description	2019 Status
NCT02408952	Stacy A Sterling, DrPH stacy.a.sterling@kp.org	Screening for Youth Alcohol and Drug Use: A Study of Primary Care Providers	US	9084	This study evaluates the implementation and effectiveness of two modalities of Screening, Brief Intervention and Referral to Treatment (SBIRT) to reduce adolescent alcohol and other drug (AOD) use in a large pediatrics clinic.	Ongoing: Est. Completion Date Jun 2018. No published records.
NCT02744118	V. Fan Tait, MD/ Kristen Kaseeska, MPH kkaseeska@aap.org	Helping Eliminate Marijuana Use Through Pediatric Practice (HEMPP)	US	1020	This study adapts the Public Health Service (PHS) 5As model for use with adolescent marijuana users and pilot the intervention to test feasibility and acceptability in pediatric primary care settings.	Ongoing: Est. Completion Date Mar 2019
NCT03074877	Ty Ridenour, PhD tridenour@rti.org	Substance Use Screening and Prevention for Adolescents in Pediatric Primary Care (SKY)	US	1000	This study is to test the effectiveness of integrating and adapting two National Institute on Drug Abuse (NIDA)-funded procedures for use in primary care pediatric clinics serving low-income youth.	Ongoing: Est. Completion Date May 2019
NCT02893514	Donna Shelley, MD shelld01@nyumc.org	Leveraging Technology to Address Unhealthy Drug Use in Primary Care Settings	US	250	This study will develop a clinical decision support tool that assists primary care providers in carrying out substance use interventions, and then compare (in Phase 2) two clinical scenarios, screening only (SO) vs. SUSIT, (on dose of substance use brief intervention received) and changes in drug use at 3 and 6 months, among primary care patients.	Ongoing: Est. Completion Date June 2019
NCT03069118	Meghan Moynihan, PhD meghan@workithealth.com	90-Day Online Substance Use Program	US	200	To test the effectiveness of a remote behavioral intervention and coaching support for risky substance users in a randomized control trial.	Ongoing: Est. Completion Date Dec 2017. No published records.

Appendix H. List of Ongoing Studies (as of November 2018)

Study Reference Trial Identifier	Principal Investigator/Study Contact (if different)	Study name	Location	N	Description	2019 Status
5R01DA041328 (NIH RePORTER)	Victoria H. Coleman-Cowger, PhD colemancowger@battelle.org	Comparison of Substance Use Screeners in Assessing Prescription Drug Abuse and Other Illicit Drug Use Among Pregnant Women	US	500	To compare and validate three existing substance use screeners – 4 P's, NIDA Quick Screen/ASSIST, and the Substance Use Risk Profile-Pregnancy scale	Ongoing: Est. Completion Date Aug 2019
5R21DP006082-02 (NIH RePORTER)	Kimberly Yonkers, MD kimberly.yonkers@yale.edu	Prenatal Substance Use Screening: Validation and Comparison of Promising Measures	US	NR	To validate and compare screening tools for maternal substance use.	Ongoing: Est. Completion Date Aug 2018. No published records.