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Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults: Updated Systematic Evidence Review for the U.S. Preventive Services Task Force

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Structured Abstract

Importance: Illicit and nonmedical drug use is common in adolescents and young adults, and increases the risk of injury, death, and other harmful outcomes.

Objective: To systematically review the benefits and harms of primary care-relevant interventions to prevent illicit and nonmedical drug use in children, adolescents, and young adults to inform the United States Preventive Services Task Force.

Data Sources: MEDLINE, PubMED, PsycINFO, and the Cochrane Central Register of Controlled Trials; references of relevant publications, government Web sites.

Study Selection: English-language randomized and nonrandomized clinical trials of behavioral counseling interventions to prevent illicit and nonmedical drug use among young people with no history of regular or problematic illicit drug use.

Data Extraction and Synthesis: Two investigators independently reviewed abstracts and full-text articles, then we extracted data from studies rated as fair- and good-quality, based on predetermined criteria. We extracted illicit drug use outcomes as well as health, social, legal, other behavioral (e.g., use of other substances, other risky behaviors), and harms-related outcomes. Random-effects meta-analysis was used to estimate the benefits of the interventions. Strength-of-evidence ratings were made based on consistency, precision, study quality, and evidence of reporting bias, taking into account the size of the evidence base and other noted limitations.

Results: We identified 29 trials (N=18,353) that met our inclusion criteria. Twenty-six of the trials focused on nonpregnant youth covering ages 10 through 24 years, collectively, and are referred to as "general prevention" trials. Health outcomes were reported in 16 of the general prevention trials, but no single outcome was widely reported and most showed no group differences. Some of the general prevention interventions reduced illicit and nonmedical drug use; however, results were inconsistent across the body of literature and the pooled effect did not show a statistically significant association with illicit drug use (pooled SMD=-0.08 [95% CI, -0.16 to 0.001], k=24 [from 23 studies], n=12,801, I^2=57.0%), pooling a wide range of outcomes (e.g., any use, frequency of use, score on a continuous use scale). Among 26 general prevention trials reporting any use of either cannabis or all drugs, the absolute percent of participants using illicit drugs ranged from 2.3 to 38.6 percent in the control groups and 2.4 to 33.7 percent in the intervention groups at followup ranging from 3 to 32 months, and the median absolute risk difference between groups was -2.8 percent, favoring the intervention group (range, -11.5% to +14.8%). When examining the change in total number of times illicit drugs were used in the previous 3 months, the pooled mean difference between groups was -0.21 times (95% CI, -0.44 to 0.02, k=11, n=3651, I^2=51.0%). The remaining three trials provided an intensive, multitarget, perinatal home-visiting intervention to pregnant Native American youth (Family Spirit intervention). Only one of the Family Spirit trials (the largest, best-quality of the three) found a reduction in depression, externalizing behaviors, and illicit drug use, only at the last (38-month) followup for most outcomes. Across all 29 trials, only one trial reported on harms, a Family Spirit trial, and found no group differences, after controlling for contact time. Two general

prevention trials reported statistically significantly higher illicit drug use in the intervention group at followup.

Limitations: Health outcomes were sparsely reported, and drug-related outcomes were very heterogeneous, including any illicit use, frequency of use, and use scores for either cannabis only or all illicit drugs combined. We did not include general prevention interventions that did not appear to have drug-specific content and that did not report illicit drug use outcomes. This led to the exclusion of programs including children younger than the age of 10, since trials in young children did not target drug use specifically and typically reported behavioral and academic outcomes rather than illicit drug use outcomes.

Conclusions: We found low strength of evidence on the benefits of behavioral counseling interventions to prevent illicit and nonmedical substance use in young people due to inconsistency and imprecision of findings. Health, social, and legal outcomes were sparsely reported and few showed improvement. Some interventions were associated with reductions in illicit and nonmedical drug use; however, others showed no benefit and two found paradoxical increases in use.

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Chapter 1. Introduction

Condition Background

Condition Definition

This review focuses on illicit and nonmedical drug use in young people.[1, 2] Illicit drugs are those that are illegal, including cannabis under federal law (even though recreational use is legal in some states), and prescription medications that are not taken as directed by the person for whom they were prescribed. Nonmedical use refers to use of a prescription and over-the-counter drugs in ways other than instructed.[3] For brevity, we will use the term "illicit" to encompass illicit and nonmedical use. This review does not cover interventions addressing the prevention of alcohol or tobacco use (unless they are part of an intervention that also addresses drug use); tobacco use prevention is covered by a separate USPSTF review,[4, 5] as is counseling to reduce alcohol use among youth with a history of alcohol use.[6]

Illicit Drug use occurs along a continuum that ranges from abstinence to a severe use disorder (**Table 1**), and youth generally move progressively to higher levels of use, however they may also move backward from problematic use and above to lower use levels. In this report, we include interventions related to preventing illicit drug use among children, adolescents, and young adults in the abstinence, sporadic, and limited use stages. General preventive counseling may be offered broadly to all young people without knowing their history or illicit drug use, or may be delivered after establishing that they do not already regularly use illicit drugs. In this review, we do not address the complementary literature on counseling to reduce of illicit drug use among young persons with problematic use or a substance use disorder; this literature is examined in another USPSTF review on screening for illicit drug use and interventions to be delivered to those who screen positive for problematic use.[7] For the current review, we considered regular use (on at least a weekly basis) to be problematic use.

Prevalence of Illicit and Nonmedical Drug Use

The 2018 Monitoring the Future report on adolescent drug use indicates that 47.8 percent of 12th graders in the United States have ever used an illicit drug (cannabis/hashish, cocaine [including crack], heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used nonmedically), with cannabis being the most frequently used drug (lifetime prevalence was 13.9%, 32.6%, and 43.6% among 8th, 10th, and 12th graders, respectively).[8] The National Survey on Drug Use and Health (NSDUH), administered by the Substance Abuse and Mental Health Services Administration (SAMHSA), reports previous-month illicit drug use among 7.9 percent of adolescents ages 12 to 17 years in 2016, or approximately 2.0 million adolescents (**Table 2**).[9] Among adolescents ages 12 to 17 years, previous-month use of cannabis was 6.5 percent, while an estimated 1.6 percent used prescription psychotherapeutic drugs nonmedically, including pain relievers (1.0%), tranquilizers (0.5%), stimulants (0.4%), and sedatives (0.1%). Other illicit drugs were used by a smaller percentage: cocaine (0.1%), hallucinogens (0.5%), and inhalants (0.6%). To put the rates of illicit drug use in context with the use of other substances, in 2016 the

rate of any previous-month alcohol use was 9.2 percent and tobacco use was 3.4 percent in persons ages 12 to 17 years.[9]

Young adults ages 18 to 25 years have the highest rate of illicit and nonmedical drug use, with 23.2 percent (as compared with 7.9% of adolescents) using illicit drugs in the past month, according to the 2016 NSDUH results.[9] Similar to adolescents, the drugs most commonly used were cannabis (20.8%) and prescription psychotherapeutic drugs (4.6%).[9] For comparison, 23.5% of young adults used tobacco in the past month and 57.1% had used alcohol.

While there has been a long-term declining trend in the use of illicit drugs in adolescents in the US since the late-1990s, the use of cannabis has increased in each of the past 2 years for both 8th and 10th graders; from 2016 to 2018 annual prevalence increased from 9.4% to 10.5% in 8th graders and 23.9% to 27.5% in 10th graders, while holding relatively steady in 12th graders (35.6% in 2016, 35.9% in 2018).[8]

Initiation of illicit drug use during college is relatively common. A 2012 survey found that 25 percent of cannabis users started using after starting college.[10] Similarly, a survey during a 5-year period from 2004 to 2009 found 61.8 percent of college students had been offered prescription stimulants, mostly by friends with a prescription, and 31.0 percent had used prescriptions illicitly by their fourth year of college.[11] In one 2015 study, the risk of cannabis initiation among high school graduates who had never used cannabis was found to be 51 percent higher among those who went on to college than among peers who did not go onto college.[12]

The prevalence of illicit drug use is not equally distributed across the U.S. population. Specific populations of adolescents that experience a higher prevalence of substance use include males of any race/ethnicity and nonwhite Hispanic adolescents.[13-15] Illicit drug use, including nonmedical use of prescription drugs, is more common in sexual minority adolescents than their heterosexual peers.[16 17]

Burden of Illicit and Nonmedical Drug Use

Illicit drug use is associated with multiple negative health, social, and economic consequences. In 2015, drug overdose (both intentional and unintentional) accounted for 9.7 per 100,000 deaths in those ages 15 to 24 years.[18] National tracking systems of fatal poisonings, which capture deaths due to drug use, report that the majority of poisoning deaths are due to illicit and legal drugs (9 of 10 poisoning deaths for all ages are caused by drugs).[19] Between 1999 and 2016, drug overdose death rates among 15 to 24-year-olds increased from 3.2 (CI NR) to 12.4 (CI NR) per 100,000. Over the same time period, opioid-related deaths among 15 to 19-year-olds increased from 0.78 (95% CI 0.68 to 0.88) to 2.75 (95% CI 2.55 to 2.96) per 100,000,[20] and the rate associated with synthetic opioids other than methadone continued to rise in 2017.[21] Eight-five percent of these deaths were unintentional.[20]

Illicit drug use is associated with an increased risk of motor vehicle accidents,[22, 23] violence,[24, 25] and suicidal behavior[26, 27] in young people. In 2016, 73.6% percent of all deaths in young people ages 10 to 24 years in the United States resulted from three causes: unintentional injuries, including motor vehicle accidents (41.4%); suicide (17.3%); and homicide (14.9%).[28]

In 2011, the Drug Abuse Warning Network (DAWN) estimated that approximately 1.1 million emergency department (ED) visits by individuals ages 0 to 21 years involved illicit drugs.[29, 30] Cannabis, cocaine, ecstasy, and stimulants were the most commonly reported illicit drugs that led to an ED visit by children and adolescents.[29] DAWN also estimated that in 2011 there were over 79,000 ED visits related to nonmedical use of prescription opioids of those ages 12 to 25 years.[31] Visits to EDs of adolescents ages 12 to 20 years involving alcohol and illicit drugs were more likely to result in a serious outcome than visits involving alcohol alone (33% vs. 12%).[32]

Illicit drug use can also have deleterious effects on educational achievement and attainment. Cross-sectional and longitudinal studies show that students who dropped out of school or were at risk for dropping out of school had higher rates of cannabis use than students who remained in school or graduated.[33] A long-term cohort study of black urban youth that matched participants who had used cannabis at least 20 times by age 16 with those who had not on a wide range of demographic, psychosocial, academic, and family characteristics found increased odds of becoming a high school dropout (OR=3.11, 95% CI 1.31 to 7.38) and reduced odds of obtaining a college degree (OR=0.32, 95% CI 0.14 to 0.76) among the heavier users.[34] Analysis of the 1997 National Longitudinal Survey of Youth, representing those between the ages of 12 and 16 living in the United States, found that African Americans were 247% and Hispanics 60% more likely than Whites to be arrested for a drug distribution offense in the period of observation. African Americans' greater likelihood of arrest was not explained by differences in youth's rate of offending or the community context, but represents disparities in arrests and sentencing.[35] Juvenile arrests have been shown to be related to poor rates of high school graduation and college enrollment.[36] Studies that examined the relationship between other noncannabis drug use and dropping out of school report mixed results, with some showing that illicit drug use and dropping out of high school are related, while others indicate that the association varies by race/ethnicity and is confounded by other factors.[33] A recent review including studies among nationally representative samples of high school students found a significant relationship between poorer academic performance (including dropping out of school), and nonmedical use of prescription drugs.[37] In addition, problematic illicit drug use decreases the risk of both continuous college enrollment[38] and college graduation.[39]

Some long-term negative psychosocial and neurocognitive effects have been associated specifically with adolescent cannabis use. For example, a prospective cohort study found an increased risk of anxiety in midlife (up to age 42) in those who had used cannabis 20 or more times by age 16 compared with those who had not (OR 2.12, 95% CI 1.00 to 4.48), even after controlling for anxiety, depression, suicidality, and a wide range of other factors during adolescence and for cannabis use in adulthood.[34] In addition, a longitudinal study with annual substance use assessment and measures of emotional functioning at 3-year intervals starting at age 11 found that, among youth who had used cannabis 100 or more times, emotional resiliency and negative emotionality changed little between cannabis initiation (mean age 13) and long-term followup (mean age 23), but for matched controls who had used cannabis fewer than 10 times, emotional resiliency increased and negative emotionality decreased over time.[40] In other words, emotional development was hindered in those who had used cannabis 100 or more times. Finally, evidence is also mounting that heavy cannabis use increases the risk of psychosis.[41-43]

Similarly, meta-analyses of nonacute neurocognitive effects show associations between cannabis consumption and lower performance on abstract thinking, attention, learning, and psychomotor functioning.[44, 45] These effects may be reversible in adults; however, other studies show that impairments in psychomotor velocity, attention, memory, and planning are more likely to linger after 4 weeks' abstinence in those who began using cannabis in adolescents.[46] A long-term prospective birth cohort found that persistent cannabis use was associated with neuropsychological decline across multiple domains (even after controlling for years of education), impairment was more severe and more persistent among adolescent-onset users, and functioning was less likely to be restored up to one year after cessation in adolescent-onset users.[47]

Perception of Risk Among Youth

Despite growing evidence of the potential harms of heavy cannabis use, there has been a steep decline in recent years in the proportion of 12th graders who see "great risk" in regularly using cannabis, dropping from 77.8 percent in 1990 to 31.1 percent in 2016.[48] Interestingly, ratings of other substances as having "great risk" have held steady or increased among young people, including heroin use (76.6% in 1990, 78.7% in 2016 for occasional use), alcohol (47.1% in 1990, 48.4% in 2016 for weekly binge use), and smoking (68.2% in 1990, 76.5% in 2016 for smoking 1 pack per day or more).[48] Evidence of the effect of legalization of recreational marijuana is mixed. Data from the Monitoring the Future survey found steep declines in ratings of harmfulness after legalization of recreational use in Washington state, but not Colorado; in Washington, the prevalence of perceived harmfulness of marijuana use declined among 8th and 10th graders from 74.9 to 60.7 percent, and from 62.8 to 46.6 percent, respectively.[49]

Risk and Protective Factors

Research has identified multiple risk and protective factors that influence adolescent substance use. Risk factors include: substance use by immediate family members,[50] poor parental supervision[51] and household disruption, low academic performance or aspirations, decreased participation in school activities, poor relationships with teachers,[52] untreated attention-deficit disorder and attention-deficit/hyperactivity disorder, perceived peer acceptance of substance use and actual use among peers,[51] experience of violence or trauma including childhood sexual abuse,[53] victimization of lesbian, gay, or bisexual identities,[54] delinquent behavior,[37] gambling,[55] poor mental health, [54, 56] use of alcohol or tobacco,[37] sensation seeking, [37] low school connectedness,[57] and poor parental monitoring.[37]Protective factors include: parents who set clear rules and enforce them, parents who regularly talk with their children about the dangers of substance use,[51] having a parent in recovery, having a positive school climate [51, 52] and a positive sense of community, involvement in religious or other community programs, and having adequate opportunities in the community for prosocial involvement.[51, 52, 58, 59]

Evidence to date is mixed on the effect of legalization of recreational cannabis on the risk of cannabis use in adolescents. Based on the Monitoring the Future survey, use increased in Washington 2.0 percentage points among eighth graders and 4.1 percentage points among 10th graders following legalization, however prevalence did not increase in Colorado, and did not

increase in 12th graders in either state.[49] However, a survey that recruited U.S. teenagers ages 14 to 18 years via social media found that lifetime prevalence of vaping and/or edible use was approximately 15 percent greater among those in states with any legal cannabis status (medical and/or recreational). Adolescents started using edibles approximately 5 months earlier in states where legalization had been in place for 10 years or longer compared with those in states with less than 5 years or no legalization.[60]

Behavioral Interventions to Prevent Illicit and Nonmedical Drug Use

A wide range of approaches have been explored to prevent initiation of illicit drug use, including a number of family-based interventions that could potentially be feasible for implementation in healthcare settings (e.g., in primary care, or offered broadly by a health system).[61] Most of these programs target substance use broadly, including alcohol and often tobacco use as well as illicit drug use. The programs may target the parent only, the youth only, or both, and commonly address many of the following topics: substance use knowledge, attitudes, and values; parental monitoring and behavior management; fostering school success; positive family relationships; self-regulation and stress management; problem-solving; resisting peer pressure; promoting a future orientation; supporting positive ethnic identity.[61] These programs may be delivered individually or in groups, in-person or via computer or DVD. Most of these interventions have been tested in the context of schools, with recruitment from schools and the interventions typically taking place after school, on school grounds. In addition, some computer-based interventions have been developed, covering similar content areas, which have been designed for implementation in school, home, and health care settings.[62]

Current Clinical Practice in the United States and Recent Recommendations

We found no information on the use of behavioral counseling in primary care to prevent initiation of illicit drug use among young people who have not used drugs, or escalation of use among those who do not use them regularly. Preventing and reducing illicit drug use among adolescents is explicitly prioritized as an objective of Healthy People 2020. These objectives include increasing the proportion of high school seniors who have never used illicit drugs, decreasing the proportion of young people who use cannabis for the first time, and decreasing the proportion of adolescents who report using cannabis and nonmedical use of prescription drugs or inhalants.[63] Looking more broadly than prevention of use among those who do not use, SAMHSA recommends that universal screening for substance use, brief intervention, and/or referral to treatment (SBIRT) become a part of routine health care to reduce the health burden related to substance use and substance use disorders.[64] SBIRT is an early intervention approach that targets individuals with nondependent substance use and provides strategies for intervention before the need for more extensive or specialized treatment. In child and adolescent populations, the term “brief intervention” includes a wide spectrum of clinical actions intended to prevent, delay, or reduce substance use among individuals with a variety of experience with substances. According to SAMHSA, a brief intervention usually involves one to five sessions of 5 minutes to 1 hour in duration.[65] These interventions can be delivered via face-to-face sessions, written self-help materials, a computer intervention, or telephone counseling.

The American Academy of Pediatrics (AAP) has developed guidelines through Bright Futures for counseling about illicit substance use.[66] The AAP specifically recommends that pediatricians provide substance abuse education to adolescents during routine clinical care, incorporating the SBIRT guidelines designed by SAMHSA.[66, 67] For patient reporting no substance use, the AAP recommends providing "positive reinforcement for making this smart decision", and further suggest the use of normative correction statements such as "I am glad to hear that you, just like most others your age, have never used illicit drugs." For patients who use substances, it advises that brief counseling and in-office followup may be sufficient if substances are not used regularly and there have been no adverse consequences of substance use. More intensive intervention and referral for treatment are indicated when children or adolescents are identified as having experienced adverse events related to their substance use (e.g., injuries associated with acute intoxication, trouble with the law, decline in school performance), are regularly using illicit drugs, or are using illicit drugs to "feel normal."[67]

Additionally, the National Institute for Health and Care Excellence in the United Kingdom recommends that clinicians consider providing preventive skills training to young people who are assessed as vulnerable to illicit and nonmedical drug use as well as to their parents or caregivers. See **Table 3** for a brief description of these and other relevant guidelines.

Previous USPSTF Recommendation

In 2014, the USPSTF concluded that current evidence was insufficient to assess the balance of benefits and harms of primary care-based behavioral interventions to prevent or reduce illicit drug or nonmedical pharmaceutical use in children and adolescents (**I statement**). Evidence was judged as insufficient due to inadequate evidence of the benefits of these interventions on health outcomes and illicit drug initiation or use, with only 6 included studies, several covering narrow populations. The recommendation applies to children and adolescents younger than age 18 years who have not been diagnosed with a substance use disorder.[68] There are additional USPSTF recommendations on substance-related services for young people: **I statements** for screening and brief behavioral counseling interventions to reduce both illicit drug use[69]and unhealthy alcohol use[70], and a **B recommendation** for education or brief counseling to prevent initiation of tobacco use among school-aged children and adolescents.[71]

Chapter 2. Methods

Scope and Purpose

This systematic review examined the evidence on benefits and harms of interventions to prevent illicit and nonmedical drug use in children, adolescents, and young adults. It will be used by the USPSTF to update its 2014 recommendation on this topic. Because of the paucity of evidence in the previous review, we expanded this update to include trials with shorter minimum followup time, additional settings, and included trials of young adults. On the other hand, the scope was narrowed from the previous review to no longer include trials among adolescents with regular or problematic drug use because interventions to reduce illicit and nonmedical drug use in these populations are addressed in another USPSTF review.[7]

Key Questions and Analytic Framework

Using the USPSTF's methods (detailed in **Appendix A**), we developed an analytic framework (**Figure 1**) and three Key Questions (KQs):

1. Do primary care–feasible or referable interventions to prevent drug use in children, adolescents, and young adults improve health outcomes or other related outcomes?
2. Do primary care–feasible or referable interventions to prevent drug use in children, adolescents, and young adults improve drug use outcomes?
3. What are the harms of primary care–feasible or referable interventions to prevent drug use in children, adolescents, and adults?

Data Sources and Searches

We developed a search strategy designed to capture relevant literature published from 6 months prior to the search date in the previous USPSTF review to identify newly published studies of behavioral counseling interventions to prevent illicit drug use in children, adolescents, and young adults, as well as previously published studies targeting young adults that were not included in the previous review's searches (**Appendix A**). We searched MEDLINE, PubMed (for publisher-supplied records only), PsycINFO, and the Cochrane Central Register of Controlled Trials for relevant English-language literature published between January 1, 2013 (for children and adolescents), or January 1, 1992 (for young adults), and January 30, 2019. A research librarian developed and executed the search, which was peer-reviewed by a second research librarian. Surveillance searches were continued through March 20, 2020 to identify newly published studies that may affect the findings of the review. This was accomplished through review of publications in high-impact-factor journals and article alerts. One relevant RCT was identified during the surveillance window and was included in this review.[72]

We evaluated all studies included in the previous review for inclusion in the current review. In addition, since the current review reduced the minimum followup required and expanded the list

of allowable settings, we reviewed studies from the "excluded studies" appendix of the previous review that had been excluded due to the setting or insufficient followup. We also examined the reference lists of other reviews, meta-analyses, and primary studies to identify additional potential studies for inclusion. 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/) for ongoing trials. We imported the literature from these sources directly into EndNote® X9 (Thomson Reuters, New York, NY).

Study Selection

Detailed inclusion and exclusion criteria were developed to guide study selection (**Appendix A Table 1**). This review comprised studies that targeted children, adolescents, and young adults (age ≤25 years), including pregnant females, who did not regularly use illicit drugs or medications for nonmedical psychoactive effects. This included interventions targeting parents or caregivers to prevent or reduce illicit drug use in young persons.

We included randomized controlled trials (including cluster randomized trials), and nonrandomized controlled trials assessing behavioral counseling interventions designed to prevent or reduce illicit and nonmedical drug use. Interventions to assist or support young people in avoiding the use of illicit drugs are considered, and may include educational and/or motivational messages and may be delivered through a variety of means, including in person, over the phone, via computer, through print materials. The interventions could target other risk behaviors in addition to illicit drug use (e.g., alcohol use, tobacco use, risky sexual behavior) but were required to have some intervention content that directly addressed illicit drug use. Consistent with other USPSTF reviews on substance-related topics, we also required that studies report a drug use outcome for inclusion in the review.[6] A minimum of 3 months' followup was required. Interventions were excluded that included components that could not be replicated in a health care setting, such as broad public health, media, or policy interventions.

We included trials conducted in health care settings or judged to be generalizable to primary care, including research settings, community settings, school health clinics, and virtual settings. Interventions in community or research settings were included if all components of the intervention were judged feasible for implementation in a healthcare setting, i.e., clinicians and/or related staff in the primary care setting should have [or could have] the skills necessary to deliver the intervention, or could refer to others in the health system with the necessary skills. We excluded trials in inpatient, residential, or other institutional settings and those conducted in substance abuse treatment centers. In addition, we excluded studies conducted in classroom and most other school settings based on the logic that effects of school-based interventions may not generalize to primary care because of the pre-existing relationships among participants and between participants and school staff, the limited capability for confidentiality in school settings, and the potential for disciplinary consequences when illicit drug use is revealed. However, we included studies if they used schools only for recruitment purposes, as long as they recruited from multiple schools and met at locations other than schools, or if they studied entirely online interventions that did not involve interactions among students at the same school or between students and teachers.

Comparative effectiveness studies were excluded, and allowable control groups included no intervention (e.g., usual care, wait list), a minimal intervention (e.g., pamphlets, links to pre-existing internet resources, or no more than a single brief contact per year), and attention controls (with similar format and intensity but a different content area). We limited inclusion to English language studies in countries rated as "Very High" human development according to the United Nations, based on 2015 indicators. [73]

Two reviewers independently reviewed titles and abstracts for potential inclusion, then two reviewers reviewed the full-text articles. Discrepancies were resolved via discussion and consultation with the larger review team as needed. Title, abstract, and full-text review were conducted in DistillerSR (Evidence Partners, Ottawa, Canada).

Quality Assessment and Data Abstraction

Two reviewers applied USPSTF design-specific criteria (**Appendix A Table 2**)[74] to assess the methodological quality of all eligible studies. We assigned each study a quality rating of "good," "fair," or "poor." Discordant quality ratings were reviewed and discussed, with consultation from the full review team as needed. Studies rated as poor quality were excluded from the review. Good-quality studies were those that met all or nearly all of the specified quality criteria (e.g., comparable groups were assembled initially and maintained throughout the study, and followup was 90% or higher), whereas fair-quality studies did not meet all of these criteria but did not have serious threats to their internal validity related to the design, execution, or reporting of the study. Intervention studies rated as poor quality generally had several important limitations, including at least one of the following risks of bias: very high attrition (generally >40%), differential attrition between intervention arms (generally >20%); substantial lack of baseline comparability between groups without adjustment; or issues in trial conduct, analysis, or reporting of results that put the validity of the findings in doubt (e.g., possible selective reporting, inappropriate exclusion of participants from analyses, questionable validity of randomization and allocation concealment procedures).

For all of the included studies, one reviewer extracted key elements into standardized abstraction forms in DistillerSR. A second reviewer checked the data for accuracy. For each study, we abstracted its general characteristics (e.g., author, year, study design, recruitment methods), clinical and demographic characteristics of the sample and setting (e.g., age, race/ethnicity, baseline clinical characteristics, setting, country), and results. Outcomes of interest included health outcomes (e.g., drug-related morbidity, injuries or accidents, quality of life, consequences of illicit drug use, mortality, pain); social, educational, and related outcomes (e.g., global functioning, educational attainment and school performance, incarceration and criminal activity); behavioral outcomes (illicit drug use, other substance use, other risky behaviors); and harms (e.g., treatment-related harms, demoralization due to failed quit attempt, harms of parents discovering child's illicit drug use, discontinuation of effective treatment due to fears of addiction).

Data Synthesis and Analysis

We created summary tables for all KQs showing study, population, intervention characteristics, and outcomes for qualitative evidence synthesis. Three trials provided very intensive pre- and post-natal home visits to pregnant American Indian youth. Because these trials (the Family Spirit trials) were substantially different from the other included trials, both due to the population of interest and the nature of the intervention, results will be discussed separately for Family Spirit trials and the remaining trials, which we will refer to as the "general prevention" trials. However, summary tables encompass all included studies unless specified otherwise.

We assigned prevention type according to the SAMHSA definitions[75] for universal direct prevention (interventions that target the general public and/or the whole population that has not been identified on the basis of individual risk, referred to as "universal" [since indirect universal interventions were out of scope for this review]) or selective prevention (interventions that target individuals or a specific population whose risk of developing mental or substance abuse disorders is significantly higher than average). Indicated prevention programs (i.e., those that target individuals at high risk who have minimal but detectable signs or symptoms of mental illness or substance abuse problems) were out of scope for this review but were included in a separate review of covering screening and treatment for unhealthy substance use.[7]

Since an illicit drug use outcome was required for inclusion in the review, we selected this as our primary outcome for meta-analysis. Trials were almost evenly divided between reporting a continuous measure, most commonly the number of times illicit drugs were used over a specified period, and the dichotomous outcomes of any illicit drug use or any cannabis use. Continuous measures were converted to Hedges g, which is a standardized mean difference (SMD), based on either change from baseline or mean post-test scores, after converting all "times used" variables to the same time window of the previous 3 months. For dichotomous outcomes, log-ORs were converted to Cohen's d and then converted to Hedges g using standard formulae.[76] Odds ratios were either extracted from the studies directly or calculated based on the study-reported numbers of persons with and without the event for each group.

We conducted pooled analyses of the general prevention trials (i.e., all trials except the Family Spirit intervention trials). We ran random effects meta-analyses on SMDs for three categories of substances: illicit and nonmedical drug use (preferentially choosing outcomes covering any illicit or nonmedical use of drugs over cannabis-specific measures if they were both provided), alcohol use (preferentially selecting any use over risky or unhealthy use), and tobacco. Across all of these categories, dichotomous outcomes were preferentially included if both continuous and dichotomous outcomes were reported, due to the ease of interpretation. Where multiple intervention groups or followup timepoints were provided, we selected the intervention group with the most intensive or comprehensive drug prevention component, reported at 6 to 12 months if available or the closest to that time frame. In addition, we conducted separate analyses pooling ORs and between-group mean differences to better understand effects in the native units. We also provided analyses of cannabis-specific results in native units.

We used the DerSimonian and Laird (DL) model for pooling. In addition, because the DL method is prone to insufficient coverage of the full 95 percent confidence intervals when the

number of studies is small or statistical heterogeneity is high (and I^2 were typically near or above 50% in this review), we also ran restricted maximum likelihood (REML) models with the Knapp-Hartung correction for small samples when pooling fewer than 10 trials. We generated a funnel plot and ran Egger's test to explore small-study effects, which can be an related to publication bias.[77]Additionally, we conducted meta-regression and subgroup analyses to explore factors that were associated with effect size for the primary drug use outcome, pooling SMDs. We examined the following as potential effect modifiers: study quality (good vs. fair), publication year, majority nonwhite sample (yes vs. no or race and ethnicity not reported), country (United States vs. other), setting (health care vs. other), type of prevention (universal vs. selective), intervention duration, planned number of intervention sessions, estimated hours of contact with the intervention, group (vs. individual) sessions, mode of intervention (computer only vs. others), whether the intervention focused only on illicit drug use (vs. targeting additional substances or other behaviors), whether then intervention focused only on substance use (vs. also targeting other behaviors), specific additional intervention targets (separate regressions for presence of family functioning, risky sexual behavior, mental health, and other social or legal outcomes as intervention targets), age group (middle school age only [approximately 10 to 14] vs. others), and type of control group (usual care, waitlist, or no intervention vs. attention control or minimal intervention). We used Stata version 15.1 (StataCorp LP, College Station, TX) for all analyses. All significance testing was 2-sided, and results were considered statistically significant if the p-value was 0.05 or less.

Grading the Strength of the Body of Evidence

We graded the strength of the overall body of evidence for each key question. We adapted the Evidence-based Practice Center approach,[78] which is based on a system developed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group.[79] 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 key questions (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). Study quality reflects the quality ratings of the individual trials 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 key question (e.g., evidence of reporting bias, lack of replication of interventions, nonreporting of outcomes important to patients).

We graded the overall strength of evidence as high, moderate, low, or insufficient. "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 to change the estimate. A grade of "insufficient" indicates that evidence is either unavailable or does not permit an estimate of an effect. At least two independent reviewers rated the overall strength of evidence for each intervention type. We resolved discrepancies through consensus discussion with the full review team, consulting with outside reviewers as needed.

Expert Review and Public Comment

A draft Research Plan for this review was available for public comment from May 10 to June 7, 2018. Comments from five individuals, organizations, and groups of organizations were received and resulted in updates to the proposed scope of the review that included clarification and improved consistency of wording and the addition of some pertinent outcomes. The draft version of this report was reviewed by experts and USPSTF Federal Partners and posted for public comment on the USPSTF Web site from October 1 to October 28, 2019.

USPSTF Involvement

We worked with USPSTF members at key points throughout this review, particularly when determining the scope and methods for this review and developing the Analytic Framework and KQs. After revisions reflecting the public comment period, the USPSTF members approved the final analytic framework, KQs, and inclusion and exclusion criteria. The Agency for Healthcare Research and Quality (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

Literature Search

We reviewed 4452abstracts and 351 full-text articles for all KQs (**Appendix A Figure 1**) and included 29 trials (28 RCTs, 1 CCT[80]), reported in 38 publications.[72, 80-115] The list of included and excluded studies (with reasons for exclusion) are available in **Appendix B** and **Appendix C**, respectively. We included all six trials that were included in the previous review.[80, 92, 105, 107, 108, 114]In addition, we included six trials that had been excluded by the previous review due to setting and population[83, 85, 98, 100, 110, 113] as well as 17 newly published studies. The most common reasons for exclusion were due to the intervention (included elements that are not feasible for a health care setting, such as school- and community-level components, or lacked drug-specific content), the setting (e.g., in schools or residential settings), condition (targeted youth with regular use, hazardous use, or a drug use disorder), and population (e.g., conducted in general adult populations, or among youth with psychotic disorders or who were mandated to an intervention). Six studies were excluded due to poor quality.

Description of Included Studies

Population and Setting

Most of the 29 included trials (N=18,353) addressed broad audiences for universal prevention, but some focused on selected populations at increased risk of substance use or harms from substance use, including three that were limited to pregnant American Indian youth ages 12 to 19 or 22 years, [83, 85, 113] as well as trials limited to girls in foster care,[98] sexual minority teens (self-identifying as lesbian, gay, bisexual, transgender, or questioning),[112] youth with asthma,[105] youth who were truant[88] or had school-related behavior problems[90],or showed early signs of at-risk illicit drug use[103] See **Table 4** for a list of all included studies, and **Tables 5** and **6** for summaries of the study and population characteristics.

In addition to the trials conducted exclusively with pregnant females, several others were limited to females,[92, 98, 107, 108, 110, 111] and one was limited to Swiss male conscripts.[94] Collectively, the trials included young people ages 10 through 24 years. Ten trials (35%) recruited only pre-adolescents and young adolescents (approximately 10-14 years),[81, 90, 92, 93, 98, 102, 107, 108, 110, 111] two (7%) recruited young adults (17 or 19 years and older),[94, 100] and the remaining either focused on high school-aged youth or covered a wide age range inclusive of high school age. Twenty-two (76%) of the included trials were conducted in the United States, and the remaining were in Germany,[81] the Netherlands,[82, 102] Poland,[93] Czech Republic,[94] Sweden,[95] and Australia.[106] One trial had sites in both the United States and the Czech Republic.[80] Reporting of race and ethnic background of participants was incomplete, but among the 21 trials conducted in the United States, three were limited to Native American females,[83, 85, 113] one was limited to females of Asian descent,[92] and ten included a majority of black and Hispanic youth.[88, 90, 96, 97, 103, 107, 108, 114-116] Detailed information on race and other population characteristics is provided in **Appendix D**

Table 1. Participants in twelve of the trials were recruited from health care settings: primary care clinics,[72, 80, 96, 103, 106, 114-116] rural outpatient clinics,[105] or the Indian Health Service.[83, 85, 113]

Baseline substance use was variably reported (see **Appendix D Table 1**). Two trials were limited to youth who had used cannabis in the previous 3 months[100] or one year,[114] and one trial was limited to youth with no cannabis use in the previous year.[115] Of all 11 trials reporting the proportion or participants with cannabis use at baseline, the median was 24.0 percent with previous use (interquartile range [IQR], 12.2% to 18.5%, with recall periods ranging from lifetime to the previous month). The median proportion with previous alcohol use at baseline was 37.7 percent (IQR 32.3% to 53.1%), among the 11 trials reporting the proportion with previous alcohol use.

Intervention Characteristics

Table 7 shows a summary of the intervention characteristics for all 34 intervention groups in the 29 included trials, and detailed information is available in **Appendix D Tables 2 and 3**. The aims of almost all interventions included other outcomes in addition to illicit drug use. Only four appeared to focus on illicit drugs without explicit discussion of other substances or behaviors.[100, 110-112] Nine trials focused broadly on substance use, including alcohol and/or tobacco, in their intervention messages.[72, 80, 94, 102, 103, 105, 114-116] The remaining were broad prevention trials that addressed additional behaviors such as family functioning,[81, 90, 92, 93, 95, 98, 107, 108] risky sexual behavior,[82, 90, 96, 98, 106] broader mental health and emotional well-being (including social skills training),[82, 92, 98, 106-108] truancy and delinquent behaviors,[88] and breastfeeding and infant care.[83, 85, 113]

Across all trials, planned intervention dose was variable, with a median of three sessions (IQR 1-10 session), but a range of 1 10-minute session to 46 sessions. Duration ranged from 1 day to over 3 years, with a median of 6 weeks (IQR, 1 day–26 weeks). The intervention with the greatest number of sessions was a 46-session intervention among girls in foster care and their caregivers, initiated the summer before the girls entered eighth grade.[98] The intervention involved six 2-hour group sessions for caregivers and the girls separately, followed by up to 40 individual coaching sessions for the girls that focused on establishing and maintaining positive peer relations, increasing knowledge of accurate norms for problem behaviors, and increasing self-competence in academic and social areas. Coaches also emphasized the risks of substance use and discussed issues around dating and partner relations. On average, participants completed 5.6 of the 6 group sessions and 20 of the 40 individual coaching sessions.

Interventions for 12 of the trials were delivered exclusively through a computer;[82, 90, 92, 100, 102, 107, 108, 110-112, 114, 115] two of these were delivered within school classroom settings but were included in this review because they had no interactive components involving the teachers or other students.[82, 102] Another computer-based intervention was an online version of Familias Unidas and involved eight online, prerecorded simulated parent group sessions that were accessed via a website and four interactive parent-adolescent family sessions that were delivered by a trained facilitator.[90] This was a computer-based adaptation of a widely-studied intervention usually delivered to groups in an after-school setting. Like the after-school versions, the online version included in this review covered family communication, supportive parenting, and parental

monitoring, with specific content addressing substance use and risky sexual behavior. Participants viewed and attended an average of 8.9 of the 12 sessions (combining the group videos and the interactive family sessions), and 72 percent completed all four of the family sessions.

Three computer-based interventions targeted mothers and daughters, with separate and joint activities.[92, 107, 108] These interventions involved nine to 12 sessions that typically required 45 minutes per session. The program helped mothers learn to better communicate with their daughters, monitor their daughters' behavior and activities, build their daughters' self-image and self-esteem, establish rules about and consequences for substance use, create family rituals, and refrain from communicating unrealistic expectations. The girls acquired skills for managing stress, conflict, and mood; for resisting peer pressure; and for enhancing body esteem and self-efficacy. Only one of these studies reported adherence, finding that 97 percent of participants completed all available sessions.[107]

Interventions for seven trials (with 9 intervention arms) took place in primary care settings.[72, 80, 96, 106, 114-116] One of the primary care-based interventions centered on clinician training, providing education and personal coaching (based on role plays with adolescent actors) for screening and counseling during primary care visits to reduce risky behaviors (tobacco use, alcohol use, illicit drug use, risky sex, unsafe driving/passenger safety) and increase protective behaviors.[106] This intervention also included print materials for patients and clinicians and a supported plan-do-study-act cycle of continuous quality improvement (QI). Two of the primary care-based interventions were parallel studies, recruiting from the same larger population but limiting one study to youth with no cannabis use in the prior year[115] and one to youth with cannabis use in the prior year.[114] These trials had both in-person and online-only versions of the motivational interview intervention, but somewhat different intervention content. One of these reported that 93 percent of participants completed the interventions immediately or within 2 weeks of their appointment.[115] Other similar primary care-based trials involved a single in-person motivational interviews.[72, 80, 116] Four of these primary care-based trials had majority black and Hispanic or majority non-white samples.[72, 114-116]

Three trials examined a home-visiting intervention for pregnant American Indian adolescents and young adults recruited through the Indian Health Service.[83, 85, 113] The intervention (Family Spirit) involved 25 to 43 highly structured, culturally tailored, pre- and post-natal home visits by Native paraprofessionals that covered three target domains: parenting skills across early childhood, maternal life skills and psychosocial development, and maternal drug abuse prevention. The largest and best quality of these trials reported that 74 percent of participants completed at least 50 percent of the Family Spirit lessons by 12 months postpartum[83]; adherence rates were higher in the other two, which were characterized as pilot studies.[85, 113]

Quality Assessment

Six trials were rated as good-quality and the remaining 23 were fair-quality; six were excluded due to poor quality.[117-122]Among those excluded, very high attrition was the most common concern, but two had other concerns, including lack of assurance of baseline comparability along with either missing important information or additional more minor concerns about other

methods issues. Several had generally good methods but were graded down for high attrition.[82, 96, 102, 106, 115, 116] The remaining trials that were rated as fair-quality typically had more than one area where methodologic standards were not clearly met. The most common concerns were high attrition (>10%); differential attrition between groups (by >10%); lack of information on comparability between groups at baseline; and minor concerns or lack of reporting on randomization methods, allocation concealment, and blinding of outcomes assessment.

KQ1. Do Primary Care-Feasible or Referable Interventions to Prevent Drug Use in Children, Adolescents, and Young Adults Improve Health Outcomes or Other Related Outcomes?

Summary of Results

Health, social, or legal outcomes were reported in 16 of the general prevention trials[81, 82, 88, 90, 92, 93, 95, 98, 100, 106-108, 111, 114-116] and all three Family Spirit trials.[83, 85, 113] No single outcome was widely reported. Mental health outcomes were the most commonly-reported health outcomes, and were reported by 9 of the general prevention trials [81, 82, 92, 93, 95, 98, 107, 108, 111] and all three Family Spirit trials.[83, 85, 113] Most general prevention trials found no group differences on mental health symptom scales after 3 to 24 months, and results were mixed in the Family Spirit trials. There were beneficial findings for family functioning outcomes (family communication, parental monitoring, and maternal closeness) in three general prevention trials examining computer-based interventions among middle school-aged females and their mothers[92, 107, 108] (**Figure 2**) at up to 24 months' followup. Other outcomes examined in the general prevention trials included consequences of illicit drug use (3 trials),[100, 114, 116] health-related quality of life (1 trial),[82] arrests (1 trial).[88] No studies reported mortality or morbidity outcomes.

Detailed Results

All health, social, or legal outcomes are shown in **Appendix D Table 4**, which were reported in 16 of the general prevention trials[81, 82, 88, 90, 92, 93, 95, 100, 106, 111, 115, 116 98, 107, 108, 114] None of the general prevention trials reported mortality, nor did any report on the onset of medical conditions. The most commonly reported health, social or legal outcomes were measures of mental health symptoms or functioning, reported in 9 general prevention trials.[81, 82, 92, 93, 95, 98, 107, 108, 111]There were very few statistically significant group differences at any followup timepoint on any mental health outcomes among study-reported adjusted analyses, although there were some additional statistically significant group differences among unadjusted results that we calculated based on reported means and standard deviations. A sample of mental health outcomes reported in the general prevention trials are shown in **Figure 2**, selecting the main followup (6–12 months, or the closest) for the most intensive or comprehensive intervention group in each trial, if there were multiple groups. These findings are representative of the larger body of evidence for mental health-related outcomes, with all followups, intervention groups, and subgroup analyses (**Appendix D Table 4).** Effect sizes shown include many difference types

of study-reported effects, including regression model parameter estimates, mean ratios, Cohen's Ds, and between-group differences in change or in post-test scores.

The next most commonly-reported health, social, or legal outcomes in the general prevention trials were related to family functioning, reported in three computer-based intervention trials among middle school-aged females and their mothers.[92, 107, 108] as well as the Familias Unidas trial[90] and one of the Strengthening Families Program trials.[93] Improvement in several family functioning outcomes (family communication, parental monitoring, and maternal closeness) were found in the three trials targeting middle school-aged females and their mothers[92, 107, 108] (**Figure 2, Appendix D Table 4**). Across all timepoints (up to 24 months), differences in change between groups most commonly ranged from 0.3 to 0.6 on a 5-point scale. The other two trials did not find group differences on measures of communication, [90, 93] parental monitoring,[90] or positive parenting.[90]

Three general prevention trials reported on scales measuring consequences of illicit drug use.[100, 114, 116] Two measured consequences on a scale that included items related to failure to maintain family and school responsibilities and difficulties with friends and family members due to illicit and nonmedical drug use, as well as symptoms of heavy or problematic use such as withdrawal symptoms and being unable to stop using.[100, 114] The other reported that participants were asked about four consequences related to cannabis use but specified only one of the items (trouble concentrating). One trial of a single-session online intervention for 17- to 19-year-olds with any cannabis use in the previous 3 months found no group differences at 3- or 6-month followups, with between-group differences in change ranging from 0.15 to 0.23 on a 72-point scale.[100] The trial of a primary care-based motivational intervention in youth with cannabis use in the previous year, found differences only at 3 months' followup (and not at 6 or 12 months) in the intervention group that completed their intervention entirely online (IG2), but no benefit for those with direct in-person counseling (IG1). At 3 months, the computer-only intervention group participants' scores had declined by a mean of 2.8 points (SD 15.3) while control participants' scores had declined by 0.4 points (SD 15.1, between-group $p<0.05$ for the study-reported treatment effect estimate). The range of this scale was not reported.[114] The final trial, another primary care-based intervention involving a single motivational interview, found a declining trajectory in the intervention group but an increasing trajectory in the usual care group, with statistically significant differences at the 12-month followup (Mean [SD] scores: IG: 0.9 [3.3]; CG: 2.4 [9.3], $p=0.04$).[116]

One trial each reported on health-related quality of life[82] and arrests.[88] For health-related quality of life, a trial of two very similar brief online interventions reported improved health-related quality of life at 4 months' followup for one group.[82] Compared with a mean 0.1-point increase in the control group, intervention group scores increased by 3.9 (SD 17.3) and 2.4 (SD 18.5) points on a 100-point scale in the two intervention groups, although the difference was statistically significant in only one group ($p<0.001$ and 0.35, respectively). For arrests, a trial that involved two 75-minute intervention sessions with truant youth, with or without an additional parent session, reported a lower proportion of participants with official arrest charges at 25 months' followup (but not at earlier followup assessments), but only for the intervention group that did *not* include a parent session.[88]

Among the Family Spirit intervention trials, all three reported depression symptoms. Only the largest and best-quality trial found group differences,[83] and only at the last (38-month) followup (**Figure 3**). In this trial, the mean intervention group CESD score had declined by 0.9 points on a 60-point scale while the control mean had increased by 0.3 points. This trial also reported internalizing, externalizing, overall mental health score from the Problem-Oriented Screening Instrument for Teens, and a total emotion and behavior problem T-score. While all point estimates were in the direction of benefit, the only statistically significant finding was for externalizing.[83] At the 38-month followup, the intervention group mean had declined of 0.6 points on a 100-point scale, compared with a 0.4-point increase in the control group. No other health, social, or legal outcomes pertinent to this review were reported, including mortality and disease onset.

KQ2. Do Primary Care-Feasible or Referable Interventions to Prevent Drug Use in Children, Adolescents, and Young Adults Improve Drug Use Outcomes?

Summary of Results

The effects of the general prevention interventions on illicit and nonmedical drug use were wide ranging, and the pooled effect was not statistically significant (pooled SMD=-0.08 [95% CI, -0.16 to 0.001], k=24 [from 23 studies], n=12,801, I^2=57.0%, **Figure 4, Table 8**), with results primarily reflecting 6 to 12 months of followup, primarily among adolescents**.** The pooled OR for any illicit drug use or any cannabis use was 0.82 (95% CI, 0.67 to 1.04, k=12 [11 studies], n=9031, I^2=38.2%, **Table 8**). Among trials reporting any use of either cannabis or all illicit drugs, absolute proportions using at followup ranged from 2.3 to 38.6 percent in the control groups and 2.4 to 33.7 percent in the intervention groups. The median absolute risk difference between groups was -2.8 percent, favoring the intervention group (range, -11.5% to +14.8%). When examining times used in the previous 3 months, the pooled mean difference (MD) between groups was -0.21 times (95% CI, -0.44 to 0.02, k=11, n=3651, I^2=51.0%, **Table 8**). Some interventions did show a benefit at one or more followups,[80, 90, 92, 96, 106-108, 110, 114, 115] but many showed no clear evidence of benefit and two reported *increased* illicit drug use in youth participating in the interventions for at least one drug-related outcome.[95, 97] 10 trials had less than 12 months' followup, which may be insufficient to find differences younger adolescents with low use levels. We investigated a number of possible effect modifiers (study, population, intervention, and control characteristics) and none appeared to explain variability in effect sizes (**Figure 2**), and there was no evidence of a small studies effect. Pooled effects for alcohol and tobacco use both showed statistically significant but very small benefits (alcohol pooled SMD= -0.11 [95% CI, -0.16 to -0.07], k=23 [from 22 studies], n=12,307, I^2=4.9%; tobacco pooled SMD=-0.09 [95% CI, -0.15 to -0.03], k=15, n=8366, I^2=35.0%, **Table 8, Figures 5 and 6**). Other behavioral outcomes reported included delinquent behavior (5 trials)[98, 88, 93, 95, 115] risky sexual behavior (3 trials),[82, 90, 106] and unsafe driving or riding (3 trials),[72, 106, 114] with most trials finding no differences between groups.

Detailed Results

Illicit and Nonmedical Drug Use Outcomes

All included trials reported on illicit and nonmedical drug use. The pooled effect of illicit and nonmedical drug use for the general prevention trials did not show a statistically significant benefit (pooled SMD=-0.08 [95% CI, -0.16 to 0.001], k=24 [from 23 studies], n=12,801, I^2=57.0%), **Figure 4, Table 8, Appendix D Table 5**). For this and all meta-analyses we included one observation per study (or per study site, if results were only reported separately for each site), preferentially selecting 6- to 12-month followup records if available (or closest, if not available), 1-month prevalence over lifetime use, and outcomes assessing the use of any illicit drug over the use of a single drug (e.g., cannabis)**.** This effect size (Hedge's g) can be interpreted as a Cohen's D, where a small effect is typically considered to be 0.20 to 0.50.[123] Five[81, 92, 93, 98, 108] of the general prevention trials reported longer-term outcomes, ranging from 20 to 38 months post-baseline, and three of these found statistically significant group differences in the long term.[92, 98, 108]

The pooled OR for any illicit drug use or any cannabis use (preferentially selecting any illicit drug use, if available) was 0.82 (95% CI, 0.67 to 1.04, k=12 [11 studies], n=9031, I^2=38.2%, **Table 8**), with ORs that ranged from 0.42 (95% CI 0.24, 0.72)[80] to 3.52 (95% CI 1.23, 10.10)[95] across all followup timepoints and intervention groups (even those not included in the meta-analysis). Recall periods (the time window during which participants' illicit drug use was assessed) ranged from lifetime[102] to 1 month,[81, 82, 103, 106] and, not surprisingly, there was a wide range of absolute rates of illicit drug use. At followup, the proportion reporting illicit or nonmedical drug use ranged from 2.3 to 38.6 percent in the control groups and 2.4 to 33.7 percent in the intervention groups, at followup ranging from 3 to 33 months. The median absolute risk difference between groups was -2.8 percent, favoring the intervention group (range, -11.5% to +14.8%). When examining times used in the previous 3 months, the pooled mean difference (MD) between groups was -0.21 times (95% CI, -0.44 to 0.02, k=11, n=3651, I^2=51.0%, **Table 8**). Across all followups and intervention groups, between-group differences in change from baseline ranged from -7.5 times (95% CI -16.9 to 1.9)[90] to +1.0 times (95% CI -1.0 to 3.0)[111] over the previous 3 months (range of followup: 3 to 36 months). Results were very similar when limited to cannabis outcomes only, except that the pooled effect was statistically significant for the proportion reporting any cannabis use (OR=0.78, 95% CI, 0.64 to 0.95, k=7 [6 studies], n=6520, I^2=1.3%, **Table 8**). Only four trials reported the impact of their interventions on misuse of prescription medications specifically, although the interventions were broadly targeted at substance use and other non-substance-related outcomes.[90, 92, 107, 108] All of these were computer-based interventions: Familias Unidas[90] and 3 targeting young adolescent girls and their mothers.[92, 108, 110] All reported greater reductions misuse of prescription medications with the intervention, ranging from 0.1 (95% CI NR)[90] to 11.3 (95% CI -22.6 to -0.08)[92] fewer times used over the previous 3 months, at up to 24 months' followup.

We found no evidence of a small-studies effect (**Figure 7**, Egger's test p=0.68) and no study or intervention characteristics that influenced effect size based on meta-regressions. Subgroup analyses for some of the potential effect modifiers are shown in **Figure 8**.

Some general prevention interventions did show a consistent benefit across multiple time points or multiple outcomes,[90, 92, 98, 106-108, 110] or at least had some positive findings on primary drug use outcomes.[80, 96, 114, 115] Two trials reported *increased* illicit drug use for at least one drug use outcome in youth participating in the interventions,[95, 97] and the remaining showed no clear evidence of benefit or harm. Among those showing the strongest evidence of benefit, five were computer-based interventions, of which four targeted middle-school aged girls (with 3 including both mothers and daughters in the intervention.[92, 107, 108] Effect sizes were generally very small in these trials targeting middle-school aged girls, typically differences between groups of less than one time used over the prior 3 months, among girls with very low use levels at baseline. Interestingly, a replication[111] of the successful computer-based trial among young adolescent girls that did not involve mothers[110] did not find reduced illicit drug use in their trial at either 3 or 15 months' followup.

The other effective computer-based program was the online version of Familias Unidas.[90] This trial found larger effects than the other computer-based trials, for example at 12 months' followup it found that participants had used cannabis an average of 2.7 fewer times (95% CI -3.7 to 0.5, p<0.01 in study-reported repeated measures analyses) over the previous 3 months, had misused prescription medications 0.2 fewer times (95% CI -1.8 to 1.6, study-reported p<0.01), and used inhalants 1.4 fewer times (95% CI -3.5 to 0.77, study-reported p<0.001). Dichotomous outcomes representing the proportion with any illicit or nonmedical drug use and prescription drug misuse were both statistically nonsignificant, but with fairly large point estimates favoring the intervention groups (any illicit drug use: 7.3% [6/82] in the intervention group vs. 14.3% [14/98] in the control group, OR=0.47 [95% CI 0.09 to 2.46]; prescription drug use: 2.4% [2/82] in the intervention group vs. 5.1% 5/98] in the control group, OR=0.47 [95% CI 0.09 to 2.46] at 12-month followup).

The remaining two general prevention trials showing a beneficial effect at multiple followups or for multiple outcomes were the primary care clinician training and QI intervention[106] and the 46-session program for foster youth and their foster parents.[98] In the clinician training intervention, 10.1 percent [38/377] of intervention group participants and 15.7 percent [82/524] of control group participants reported any illicit or nonmedical drug use in the previous month (OR=0.61, 95% CI 0.38 to 0.97) at 12 months' followup, and a slightly larger effect at 3 months (OR=0.55, 95% CI 0.33 to 0.90).[106] The trial among foster families reported a mean 1.04-point lower score (95% CI -1.74 to 0.34) on a 9-point cannabis use scale and 0.19-point lower score (95% CI -0.33 to -0.04) on a 9-point composite substance use score in the intervention than control participants at 36 months' followup.[98]

Among the Family Spirit trials, only the largest, best-quality trial found reductions in illicit drug use, and only at the final followup timepoint (**Table 9**). At 38 months' followup, 10.7 percent of intervention participants reported any cannabis use in the previous month, compared with 15.6 percent of the control group participants (OR=0.65 [95% CI 0.48 to 0.89], p=0.007). Findings were similar for any illicit drug use (12.3% in the intervention group vs. 17.3% in the control group, OR=0.67 [95% CI 0.50 to 0.91], p=0.01).

Other Substance Use Outcomes

Alcohol and tobacco use outcomes were commonly reported in the general prevention trials, which was not surprising since most also aimed to reduce alcohol and tobacco use in addition to illicit and nonmedical drug use. Pooled effects for alcohol and tobacco use both showed statistically significant but very small benefits (alcohol pooled SMD=-0.11 [95% CI, -0.16 to -0.07], k=23 [from 22 studies], n=12,307, I^2=4.9%; tobacco pooled SMD=-0.09 [95% CI, -0.15 to -0.03], k=15, n=8366, I^2=35.0%, **Table 8, Figures 5 and 6**). However, we did not consider these findings to be robust, because newly published findings could easily lead to a loss of statistical significance for these pooled effects, given how close the upper confidence intervals are to the null. The four computer-based trials targeting young adolescent females that showed reduced illicit and nonmedical drug use also found statistically significant reductions in alcohol use, but not tobacco use.[92, 107, 108, 110] In the trials that involved mothers, mean change in the number of times the girls used alcohol over the previous 3 months ranged from 0.0 (SD 0.6) to +0.3 (SD 0.9) in the intervention groups and +0.2 (SD 1.3) to +0.8 (SD 3.9) in the control groups at 12 months' followup.[92, 107, 108] The Familias Unidas trial,[90] the trial among foster girls and their caregivers,[98] and the clinician training trial[106] found no group differences in use of alcohol at followup, although the Familias Unidas and foster family trials did report reductions in tobacco use,[90, 98] as did another trial of a computer-based intervention in young adolescent females.[111]

Two of the Family Spirit trials report on alcohol use[83, 113] and one reported tobacco use,[113] with no group differences at any followup (**Table 10**).

Other Behavioral Outcomes

Few other behavioral outcomes were reported. Five general prevention trials reported on delinquent behavior[88, 93, 95, 98, 115] (**Appendix D Table 6**). In a primary care-based trial among youth with no use of cannabis in the previous year, those randomized to receive a computer-guided, in-person motivational intervention from a research interventionist reported lower scores than control participants on a composite measure of 10 different delinquent behaviors (raw proportions or scores not provided).[115] However group differences were present only at 3 months' followup, and disappeared at the 6- and 12-month assessments. The other four trials found no differences in self-reported delinquent behavior.

Three studies reported condom use, with no statistically significant group differences,[82, 90, 106] although one of these (the clinician training intervention) reported lower risk of unplanned pregnancy in the prior 3 months in the intervention group (7.0% [26/377]) than the control group (10.2% [53/524]).[106] The clinician training trial found no differences in the proportion reporting one or more road safety risks (71.4% [269/377] and 73.9% [387/524] in the intervention and control groups, respectively).[106] One primary care-based trial examining a brief motivational intervention found lower self-reported frequency of driving under the influence of cannabis in the intervention condition that included an in-person counseling session, but not for the intervention condition that was entirely computer-based.[114] In addition, another primary care-based trial reported reduced risk of riding with someone under the influence at 1 year followup among youth who had reported riding with someone under the influence at baseline (38% in the intervention group vs. 68% in the control group; aRR=0.58 [95% CI 0.37 to 0.91]), however this

effect was smaller and not statistically significant at earlier followups or among youth who had not reported a history of risky riding at baseline.[72]

None of the Family Spirit trials reported other behavioral outcomes.

Differential Effects Across Population Subgroups

We examined all 29 included studies to determine whether effect sizes differed with respect to age, gender, race/ethnicity, risk level, rural vs. urban residence, and substance used. We found interaction or subgroup analyses for gender;[81, 82, 88, 95, 103, 105] race/ethnicity;[82, 105] and risk level, based on having a family history of drug problems,[100] education level of the child[82] or parents,[81] family functioning,[81] family income,[81] nuclear vs. joint family type,[81] family history of migration,[81] baseline substance use,[72, 83] and high baseline psychosocial dysfunction, based on the Strengths and Difficulties Questionnaire.[95] The impact of gender on treatment effect ran the full gamut, from favoring females,[82, 88, 105] favoring males,[103] no differential effect,[81, 95] to tending toward *increased* illicit drug use in boys (but tending toward benefit in girls).[82] For race/ethnicity, one trial found a larger benefit among nonwhite than white participants for alcohol use,[105] and another found a benefit for condom use only for youth of Dutch ethnicity, in contrast to nonDutch participants.[82] Greater benefits were seen on illicit drug outcomes for youth with a family history of drug problems,[100] and young women with a personal history of drug use (in one of the Family Spirit trials) improved their internalizing symptom score, in contrast to the full sample.[83] In addition, one trial reported improvements on the Life Quality in Children and Adolescents composite score for those with high baseline Strengths and Difficulties Questionnaire scores.[81] One primary care-based trial found a benefit for participants who had used alcohol or illicit drugs at baseline but not among those with no substance use at baseline.[72] Most, but not all, of these trials explicitly examined interaction terms or stated that their subgroup analyses were preplanned.

KQ3. What Are the Harms of Primary Care-Feasible or Referable Interventions to Prevent Drug Use in Children, Adolescents, and Adults?

Only one of the included trials (a Family Spirit trial) directly reported on harm.[83] Adverse events identified by both assessment staff and home visitors were recorded and reviewed by the trial's data safety and monitoring board. The authors stated that the proportion of adverse events and serious adverse events was similar between groups after accounting for increased contact time within the intervention group, but did not provide detailed data.[83]

In addition, as mentioned above, two general prevention trials reported increased illicit drug use in intervention groups over the control groups.[95, 97] In one of these was conducted in Sweden and included at-risk youth aged 12 to 18 years and tested two different interventions that involved either 6- or 10-session group interventions for parents.[95]After 6 months, 17.1 and 25.9 percent of the intervention group youth reported any illicit drug use since baseline, compared with 11.1 percent of the control group youth. This study was rated as fair quality and had a number of methodological limitations, including an imbalance in the distribution of males and females

bewteen groups (58% of the control group were female, compared with 38% and 46% of the two intervention groups), a lack of objective intervention fidelity ratings, and lifetime illicit drug use reported at baseline was higher in the control than the intervention group (contrary to the findings at followup), although none of these factors seemed likely to explain the harmful result. The other trial involved community recruitment of 14 to 17-year-olds from several US cities and provided participants with two 8-hour workshops covering diet, physical activity, and illicit drug prevention topics.[97] Raw proportions of participants with illicit drug use at follow-up were not reported, but regression coeficients indicated that lifetime cannabis use has increased less in the control group than the intervention group. However, there were no group differences in 30-day cannabis use and the direction of effect was to the benefit of the intervention group. This was a large study (n=1654) with low attrition (10%) and generally good methods, however was rated as fair quality because they did not report whether allocation was concealed, did not show baseline characteristics by group (although the study did control for gender and baseline values of outcome variables in their analyses), and did not report intervention fidelity. Additionally, seven other trials reported statistically non-significant increases in illicit drug, alcohol, or tobacco use with SMD>0.20 or OR>2.0.[82, 85, 93, 102, 105, 113, 114]

Chapter 4. Discussion

Summary of Evidence

Among the 29 included trials (and 18,353individuals), findings were inconsistent for the primary outcome of illicit and nonmedical drug use, with some trials showing clear benefits, most showing no clear benefit or harm, and two showing *increased* use of illicit drugs in the intervention groups (see **Table 11** for a summary of evidence for each key question, including our strength-of-evidence rating). While some interventions were associated with reduced illicit and nonmedical drug use, they tended to either target a relatively narrow population (e.g., young adolescent females, or 8th grade girls in foster care) with unknown or likely limited generalizability to other populations, or to have not had their results replicated. There is a growing body of evidence on substance use prevention in primary care settings, using electronically-delivered interventions, typically along with a brief one-time motivational interview with a clinician, however these studies generally found benefits only in subgroup analyses and the pattern of results was not consistent across studies.[72, 80, 114-116] The previous USPSTF review on this topic concluded that there was inadequate evidence to determine whether preventive interventions were effective in reducing the likelihood of illicit drug use, based on six trials, all of which were also included in the current review.[80, 92, 105, 107, 108, 114] The current review added newly published literature and expanded the scope of this topic to include trials that were deemed feasible for implementation in a health care system even if the study was conducted in the community or other non-health care settings (i.e., clinicians and/or related staff in the primary care setting should have [or could have] the skills necessary to deliver the intervention, or could refer to others in the health system with the necessary skills). Despite this scope expansion and 23 additional included studies, we concluded that the strength of evidence that primary care-relevant interventions to prevent illicit and nonmedical drug use in children, adolescents and young adults reduce substance use was low, due to the inconsistency in effects, the relatively narrow target populations for most of the interventions that showed a benefit, and the overall lack of benefit among studies conducted in U.S. primary care settings, which were primarily limited to low-dose interventions.

Among the 26 general prevention trials (i.e., those that did not target pregnant youth), the pooled estimate for illicit and nonmedical drug use was a very small effect and was not statistically significant. Only 9 of these trials were conducted in healthcare settings. Further, despite the wide range of effect sizes, we found no study, population, or intervention characteristics that were clearly associated with effect size. These interventions typically addressed substance use in general (not just illicit and nonmedical drug use) and typically had broader goals as well, such as improving family functioning and adolescent mental health, and reducing behavior problems. Pooled effects showed that these interventions were associated with lower rates of alcohol and, to a lesser extent, tobacco use, but pooled effect sizes were very small. However, small effects may be expected in these trials composed predominantly of youth who had never or only rarely used illicit drugs or other substances. Ten of trials had less than 12 months' followup, which may be insufficient to find differences younger adolescents with low use levels. Health, social, and legal outcomes such as consequences of illicit and nonmedical drug use, health-related quality of life, depression, and other mental health symptom scales were sparsely reported in the general

prevention trials and generally showed mixed results or no beneficial effects, although three trials of a computer-based intervention for young adolescent girls and their mothers consistently improved family communication, closeness, and parental monitoring.

Two initial pilot trials of the Family Spirit intervention showed minimal effects on the outcomes of interest to this review, however the full-scale trial was effective in reducing illicit and nonmedical drug use, depression, and externalizing symptoms, and is a potentially important intervention in this very high-risk, underserved population of pregnant American Indian adolescents and young adults.[83] For most of these outcomes, benefits were seen only on long-term followup. This study also found potentially important improvements in other outcomes that were not in scope for this review, including parenting knowledge, parenting self-efficacy, home safety attitudes, and externalizing behaviors in their children.

Despite the overall conclusions, some interventions did prove effective. Among the general prevention interventions, these included the computer-based interventions targeting young adolescent females,[92, 107, 108, 110] the computer-based version of Familias Unidas targeting eighth-graders with behavior problems,[90] the primary care clinician training and QI intervention,[106] and the 46-session intervention for eighth-grade girls in foster care and their foster parents.[98] Effects were generally maintained through 12 months or beyond in these trials. All of these interventions involved nine or more intervention sessions, all but one[110] included components for parents or caregivers as well as the youth themselves, and all addressed a broad range of skills and topics. Meta-regressions did not show statistically significant associations between effect size and these or any other characteristics across all included general prevention studies; however, computer-based interventions targeting young adolescent females were tested with and without maternal involvement, and those with a maternal component were more consistently effective.

Findings in Related Existing Systematic Reviews

Our observation that effective intervention tended to be fairly intensive, include parents, and target a wide range of outcomes was supported by existing systematic reviews of family-based interventions to prevent substance use that had no restriction on study setting.[124-126] A systematic review of reviews concluded that the strongest evidence to support family-based interventions came from those that were designed to have an impact on a wide range of behaviors rather than focusing narrowly on substance use, those that required active participation of parents, and those among younger adolescents.[124] Another review concluded that the evidence of benefit was strongest in trials that intervened with young adolescents, but it noted that some programs had been effective in preventing or reducing use in older adolescents as well.[125] A third review also concluded that interventions targeting both parents and children were likely to be effective in preventing the use of cannabis, but noted a lack of impact on other illicit drug use.[126] A meta-analysis of intervention components in a large review of family-based prevention programs (k=116) further determined that youth-focused content to encourage more positive family relationships and a more positive orientation toward the future were associated with larger effect sizes, suggesting the value of the youth component as well as the parent component.[61] Many of the studies included in these review were excluded from our review because they were conducted in school settings, and many had school or community components in addition to the family-

based components. We found no systematic reviews addressing substance use prevention in *health care* settings other than the previous USPSTF review.[127]

Acceptability of the Included Interventions

We found minimal information on the acceptability of the included interventions to youth, parents, or clinicians. Among the included trials, four that were conducted in or recruited from health care settings reported some measure of acceptability among the youth, with generally favorable results.[80, 105, 106, 114] Among youth with previous-year cannabis use recruited from primary care waiting rooms and randomized to a single motivational interviewing session, 77 percent said they "liked" the intervention or liked it "a lot," with no difference in ratings between the computer-based and interventionist-delivered versions.[114] In the New England arm of a primary care-based trial exploring a brief computer-assisted primary care clinician screening and counseling intervention, 77 percent of youth rated the information they received from the clinicians as excellent or very good, and 59 percent said they were very likely to follow the clinician's advice.[80] Among youth in the intervention arm of the clinician training and QI study, 89% rated the screening and intervention process as a "good idea," 11 percent were unsure, and none rated it as a "bad idea." Youth ratings were very similar between the intervention and usual care groups on trust in the clinician (mean intervention score=74.6 [SD 13.6], usual care=76.7 [SD 12.3]) and likelihood of returning for future visits to discuss a wide range of complaints (intervention=96.7%, usual care=97.2%).[106] In the study of rural youth with asthma, 100 percent reported finding the CD-ROM program helpful, 87 percent found the role-playing helpful, and 100 percent found the decisionmaking model helpful.[105] In addition to these health care-based studies, one of the computer-based interventions reported that 83 percent of participants found the intervention messages easy to understand, 60 percent found them credible, and 66 percent found the program easy to use, and the average global rating of the program was 6.7 (SD 1.6) on a scale of 1 (worst rating) to 10 (best rating).[82]

No studies reported on how the clinicians felt about the interventions that were conducted in or recruited from healthcare settings, nor did we find other evidence related to the acceptability of illicit drug prevention interventions to primary care clinicians. Some of the healthcare-based studies provided some information on adherence, which provides insight into the feasibility of the interventions. A study that recruited adolescents from clinic waiting rooms and provided a single motivational session via either computer or in-person reported that 93 percent of participants completed their intervention within two weeks of their appointment, with most completing them the same day.[115] Another study that recruited adolescents from appointment rosters of primary care clinics reported the 72 percent of the intervention participants received at least part of the 3-session motivational intervention promoting youth development, and 60 percent completed all three.[96]

Extrapolation of Findings From Interventions in School Settings

Most of the studies of family-based interventions to prevent illicit and nonmedical drug use have been conducted in school classroom or after school settings, and other reviews have found these school-based prevention program to be effective in reducing illicit drug use.[128] Two interventions that have been primarily studied in schools settings are Familias Unidas and the Strengthening Families Program. Familias Unidas[129] is a family-based preventive intervention to improve family communication, positive parenting, and parental monitoring to reduce risky substance use and sexual behaviors in Hispanic adolescents. Participants were generally recruited from middle schools, and sessions occurred outside of school hours. The intervention generally included eight group sessions for parents and four family visits that included the adolescents.[130] The intervention has shown reductions in illicit drug, alcohol, and cigarette use, as well as improvements in family functioning. For example, an RCT among Hispanic eighth graders and their parents (n=746) found that 30-months after baseline, illicit drug use remained stable in the intervention group while it increased in the control group.[131] Similarly, an RCT in Hispanic ninth-graders (n=160) found that substance use initiation among girls was significantly lower at 24 months in the intervention versus control group (30.4% vs 64.0%, respectively).[132] The online version of Familias Unidas that was used in the trial we included in this review did not find a statistically significant effect on the proportion with illicit drug use. However, the relative effect was similar in magnitude to this study, but with shorter followup, a smaller sample size, and lower baseline use levels (e.g., any illicit drug use: 7.3% [6/82] in the intervention group vs. 14.3% [14/98] in the control group, OR=0.47 [95% CI 0.09 to 2.46]).[90] The included trial also reported statistically significant reductions in the number of use occasions over the prior 3 months for cannabis, inhalants, and misuse of prescription medications.

It is unknown whether the effects of the full in-person version of Familias Unidas would be comparable to those found in school settings if it was implemented in a health care setting. The effects of the intervention may be influenced, for example, by the fact that many of the families already know each other at the start of the intervention, the different expectations and capabilities surrounding confidentiality in schools versus primary care settings, and the role that school personnel play in participants' lives versus that played by health care clinicians. Interestingly, we included two trials that implemented the Strengthening Families Program 10-14 (SFP10-14) and a third that heavily borrowed from the SFP10-14 materials in their intervention, but these interventions did not prove to be effective outside of school settings.[81, 93, 95] The Strengthening Families Program is a widely studied intervention designed for high-risk families; several versions exist for different age groups (e.g., preschool, elementary, early teens, and high school).[133] The program consists of 14 sessions and includes training in parenting skills, family life skills, and children's social skills; can be implemented in various settings (e.g., schools, community centers, drug courts); and has been adapted to be culturally sensitive.[133] A 10-year followup (n=446 families) of an RCT originally conducted in Iowa in 1993 found long-term reduction in substance use (27.5% of SFP participants had initiated illicit substance use by age 21 versus 38.3 percent control group (β=−.14, P<.001).[134, 135] There was also evidence that this program could benefit friends of participants: nonparticipants with a higher cumulative proportion of friends who participated in the SFP intervention were less likely than their peers to

use drugs after 3 years.[136] The beneficial effects of this program appear to have emerged between the 18 and 30-month assessments in most studies, and since the SFP studies included in this review followed participants for a maximum of 24 months, the lack of findings could also be due to insufficient followup. Nevertheless, the fact that the success of this program did not clearly translate to the health care setting illustrates the importance of testing the feasibility and effectiveness of prevention programs in health care settings before recommending their full-scale implementation.

Potential Role of Primary Care in Promoting and Implementing Illicit Drug Prevention Interventions

Despite the successes of Family Spirit, Familias Unidas, SFP (outside of health care settings), and a number of other general parenting preventive interventions in schools and other settings (e.g., Family Foundations,[137] Triple P System,[138] Strong African American Families Program,[139, 140] New Beginnings[141]), these programs have not been widely adopted. Child wellness experts have posited primary care as an ideal home for these programs, once the benefits are established.[142] Primary care has the potential to substantially expand the reach of these programs and reduce the stigma associated with taking a parenting class if offered routinely through health care systems as childbirth education classes are now, with primary care providers as the point of engagement. Experts have outlined a number of calls for action and research to support broader acceptance and uptake of general parenting classes,[142] including:

- Creating an adequately funded research foundation to support integration of effective family-focused preventions programs into primary care
- Increasing public awareness of the effectiveness of family-focused prevention programs and change public norms regarding participation
- Increasing awareness, acceptance, and opportunities among primary care providers for the incorporation of preventive parenting into primary care
- Preparing a workforce that can effectively and efficiently deliver proven family-focused prevention programs in primary care settings
- Advocating for a specific focus on health in implementation efforts under the Affordable Care Act.

As valuable as these programs may be, however, such primary care-based early parenting classes may not provide support for a drug prevention counseling recommendation, since very long-term followup would be needed to determine whether these programs affect illicit drug use.

Limitations of the Literature

Most of the limitations of the literature center on outcomes reporting. First, reporting of health, social, and legal outcomes was sparse and heterogeneous, limiting our conclusions on these important outcomes. Second, drug use outcomes were very heterogeneous. The trials were almost evenly split between reporting dichotomous and continuous outcomes, limiting our confidence in the pooled effect sizes that combined disparate outcomes. In addition, several trials

did not report detailed information on the proportion of individuals in each group who used illicit drugs or the mean number of use occasions (with standard deviations) by group at each assessment. Reporting only parameter estimates without group means makes it difficult to impossible to understand the absolute effect sizes, and some trials had to be dropped from the meta-analysis altogether due to insufficient information.

The landscape in the United States is changing with regard to illicit drugs. Notably, cannabis use has been decriminalized in a growing number of states, and the infusion of fentanyl into the supply of illicit opioids has contributed to numerous accidental overdoses. It is difficult to know, for example, how the legalization of cannabis might impact effect sizes or mechanisms of change. Different approaches may be needed in states where cannabis is legally regulated, or in states that have been hit particularly hard by fentanyl and other illicit and nonmedical opioid use.

Another limitation is that almost all of the interventions were studied by the teams who developed the intervention and had not been replicated by independent researchers. This may be an especially important limitation in this field where outcomes are measured by self-report and are subject to socially desirability effects. Replication by independent investigators helps ensure that group differences are due to the intervention, rather than other factors.[143]. The importance of replication in this literature is highlighted by the fact that among the few replications by independent investigators that were included in this review, some did not replicate beneficial results.[93, 95]

The results for the alcohol and tobacco outcomes do not represent all available evidence on these topics, since we only included interventions that included a drug use prevention component. The USPSTF review on tobacco use prevention in children and adolescents,[4] for example, provides a better estimate of the potential impact of behavioral counseling interventions, with or without concomitant illicit and nonmedical drug use prevention counseling content, on tobacco use. This review found a 19 percent relative reduction in smoking initiation among participants in behavioral counseling interventions to reduce tobacco use compared to controls (risk ratio, 0.81 [95% CI, 0.70 to 0.93]).[144]

We found no evidence that included children younger than age 10, and minimal evidence on preventing illicit and nonmedical drug use in young adults. We also found very limited evidence on young adults. Most of the evidence we found in young adults focused on reduction of use in people who were regular users, hazardous users, or who had a likely substance use disorder, so were excluded from our review. These types of secondary prevention trials will be included in the USPSTF review on screening and interventions for drug misuse.

Limitations of Our Approach

We did not include trials that did not report a drug use outcome. The literature on the prevention of illicit and nonmedical drug use is a subset of a larger substance abuse prevention literature. Among these are quite few studies that report only composite substance use outcomes, combining tobacco, alcohol, and illicit drug use without providing information specifically about illicit and nonmedical drug use. Like most of the included interventions, they target substance

use broadly, usually along with other outcomes such as family functioning, mental health, behavioral problems, and other health behaviors such as risky sexual behavior, diet, and physical activity. However, they lack the specificity to support a recommendation on counseling for illicit and nonmedical drug use.

We excluded interventions that did not explicitly address prevention of illicit and nonmedical drug use in young people, although some broad prevention or resilience interventions may be effective in preventing illicit drug use. For example, some youth development interventions addressed career development, community service, academic achievement, or leadership skills, but had no direct content on illicit drug use prevention, but have been hypothesized to also prevent or reduce involvement with illicit drugs. Most of the positive youth development interventions we found were implemented in school settings, but some appeared to have been implemented in other community settings such as social service agencies. However, existing systematic reviews have not shown them to be clearly associated with illicit drug use prevention.[145, 146]

Similarly, there are a number of school-based universal resilience interventions targeting child and adolescent mental health, which have been effective in reducing outcomes such as depression symptoms, internalizing and externalizing problems, and general psychological distress.[147] Because we required a drug use outcome, we may have missed a study of a universal resilience intervention with drug-specific content that reported health outcomes but no drug use outcomes. However, in our searches, all of the interventions we found that specifically targeted illicit drug use also reported drug use outcomes.

In a similar vein, we excluded the trials of early prevention approaches in parents of young children that we found because they did not have drug-specific content in the intervention and did not report a drug use outcome; that is, we did not include studies with only intermediate outcomes such as academic achievement or behavior problems that may predict future illicit drug use. For these early childhood studies, 10 or more years of followup would have typically been needed before the children were at an age relevant for collecting illicit drug use outcomes. For example, we excluded an early intervention trial conducted in pediatric offices among families of toddlers who screened positive on a scale predictive of disruptive behavioral disorders.[148] This study reported improvements in parenting skill (reduced harsh parenting and inconsistent discipline, increased positive parenting) and reduced child behavior problems, likely precursors of substance use during adolescence. We did find studies of an early childhood nurse home visiting intervention with long-term followup; they found a reduction in a composite substance use outcome at age 12 (combining tobacco, alcohol, and illicit drug use) and no reduction in days used drugs for the full sample at ages 15 and 19, but did find improved academic performance at age 12 for the low-SES subgroup of participants, as well as fewer arrests at ages 15 and 19.[149-151]

Future Research Needs

Studies are needed that replicate, further refine, and broadly implement some of the interventions described in this review that showed reductions in illicit and nonmedical drug use. These include

the clinician training and QI intervention,[106] and the Familias Unidas intervention.[90] Several of the primary care-based interventions showed a benefit for some outcomes, for some subgroup, suggesting the combination of a clinician interview and an electronic-based intervention holds promise, however the relatively small overall evidence base and inconsistencies across studies indicates a need for further study of these interventions. It would also be valuable to conduct a trial of the full in-person version of the Familias Unidas intervention in a health care setting. In addition, long-term followup for the SFP trials[81, 93, 95] should be considered, as SFP trials in other settings generally found benefits only at 30 or more months of followup. Pragmatic implementation studies that integrate prevention programs into real-world practice settings are needed. Efforts to implement other proven school-based interventions that are feasible for implementation in healthcare systems would also be valuable.

It would also be valuable to continue to explore the influence of context and mechanisms of change. This information could provide insight into why some of the existing interventions were successful while other similar interventions were not. Relatedly, given the changing context in United States, understanding the impact of the legal status of cannabis on intervention effectiveness would be useful, for example.

Further work developing computer-based interventions, including as tools for primary care clinicians, is also needed. The included computer-based trials that showed a benefit were designed only for young adolescent females, so are unlikely to be helpful for (or at least have not been tested in) most youth. Results of a survey administered in an urban pediatrics department published in 2013 found that 76 percent of adolescents were interested in receiving a behavioral intervention on alcohol or illicit drugs, and 45 percent preferred technology-based (vs. in-person, telephone-based, or paper) interventions, with text messaging and internet-based modalities garnering the most votes.[152] As use of electronic devices has grown even more ubiquitous since this survey was administered, the proportion preferring technology-based interventions may have grown even higher. Technology-based interventions represent an opportunity for wide reach, yet, according to a recent review of computer-based interventions to reduce substance use, interventions have not been tested that reach youth through games, smartphone apps, social media, and widely accessible web-based interventions, and have included minimal customization to youths' individual demography, risk factors, and vulnerabilities.[62] In addition, studies of implementation of those computer-based interventions that have proven to be effective should be tested among families referred from primary care to determine uptake and effectiveness in this setting.

The landscape of illicit drug use is evolving, for example with normative beliefs changing with regard to cannabis use and the rising number of deaths associated with opioid use. Research is needed to determine the extent to which general prevention interventions are effective for different substances (e.g., cannabis and opioids), and to determine when interventions are needed that target specific substance.

Finally, while this was outside the scope of our review, we nevertheless believe it is important to conduct research on current provider behavior and beliefs with regard to prevention of illicit drug use in their patients. For example, it would be useful to understand as how often they discuss illicit drug use with their young patients, how they discuss it, their beliefs on the value of

discussing illicit drug use in their patients, and barriers and facilitators to such discussions. This type of formative work may provide a valuable foundation for developing interventions for delivery in healthcare systems and provide a basis for evaluating change in current practice over time.

Illicit drug use prevention outside of school settings is an emerging field. There are a number of relevant trials registered in clinicaltrials.gov (**Appendix F**), and we are optimistic that further research will clarify the effects of interventions to prevent illicit drug use.

Conclusions

We found low strength of evidence that behavioral counseling interventions to prevented illicit and nonmedical substance use in young people due to inconsistency and imprecision of findings. Health, social, and legal outcomes were sparsely reported and few showed improvement. Some interventions were associated with reductions in illicit and nonmedical drug use; however, others showed no benefit and two found paradoxical increases in use.

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Figure 1. Analytic Framework

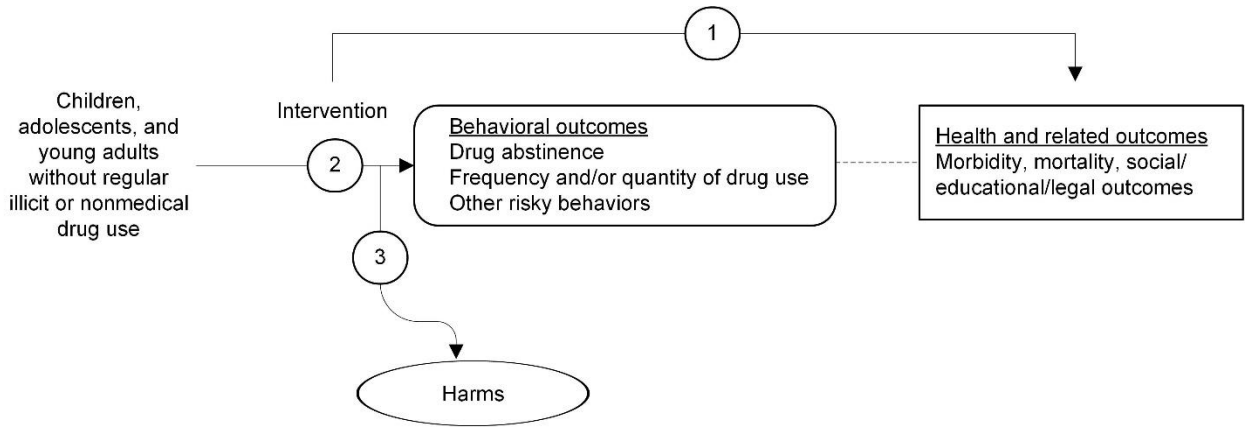
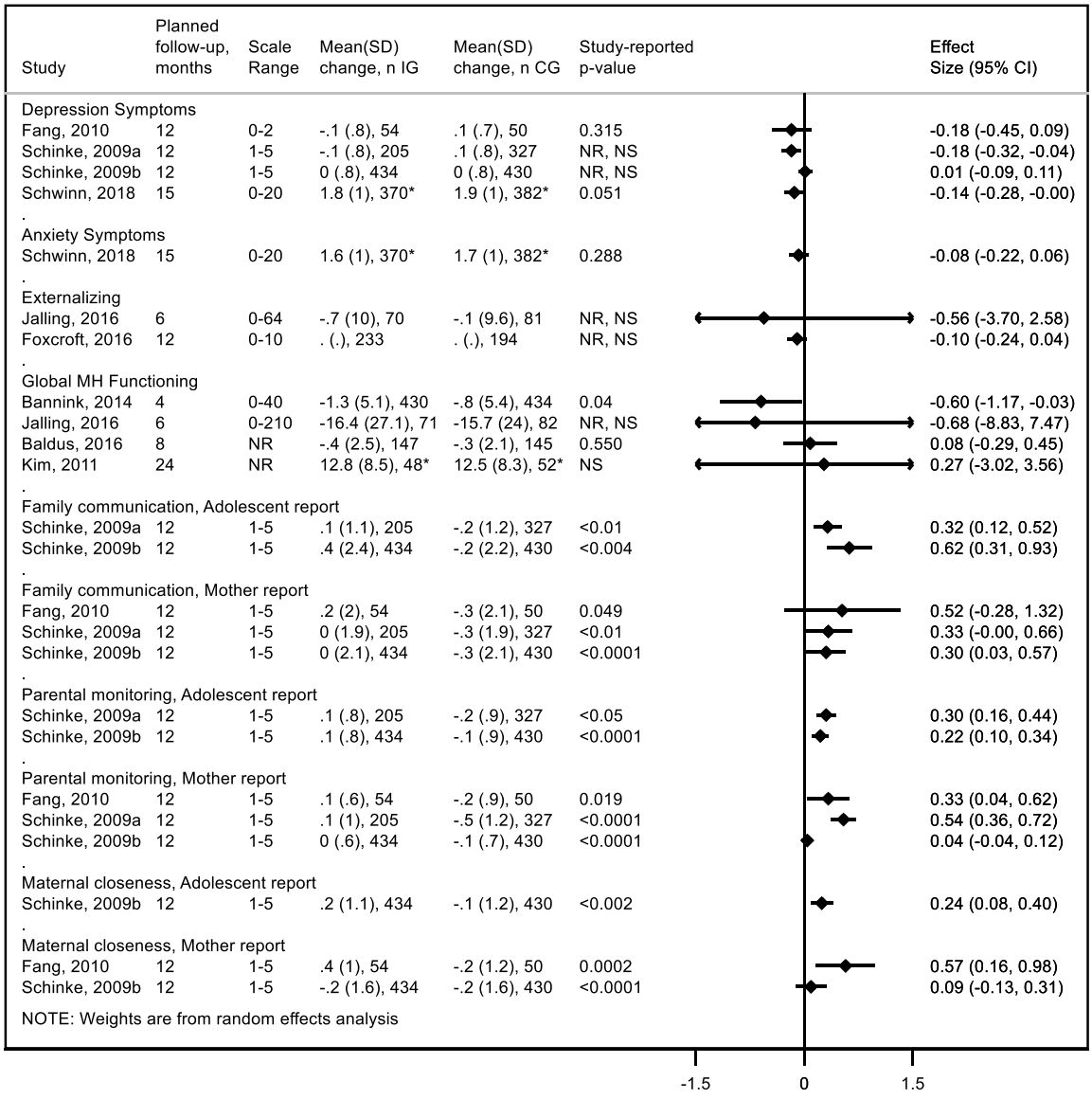


Figure 2. Mental Health and Family Functioning Outcomes Summary (KQ1) Among the General Prevention Trials, Standardized Mean Difference Between Intervention and Control Groups, by Outcome, for Main Timepoint Only

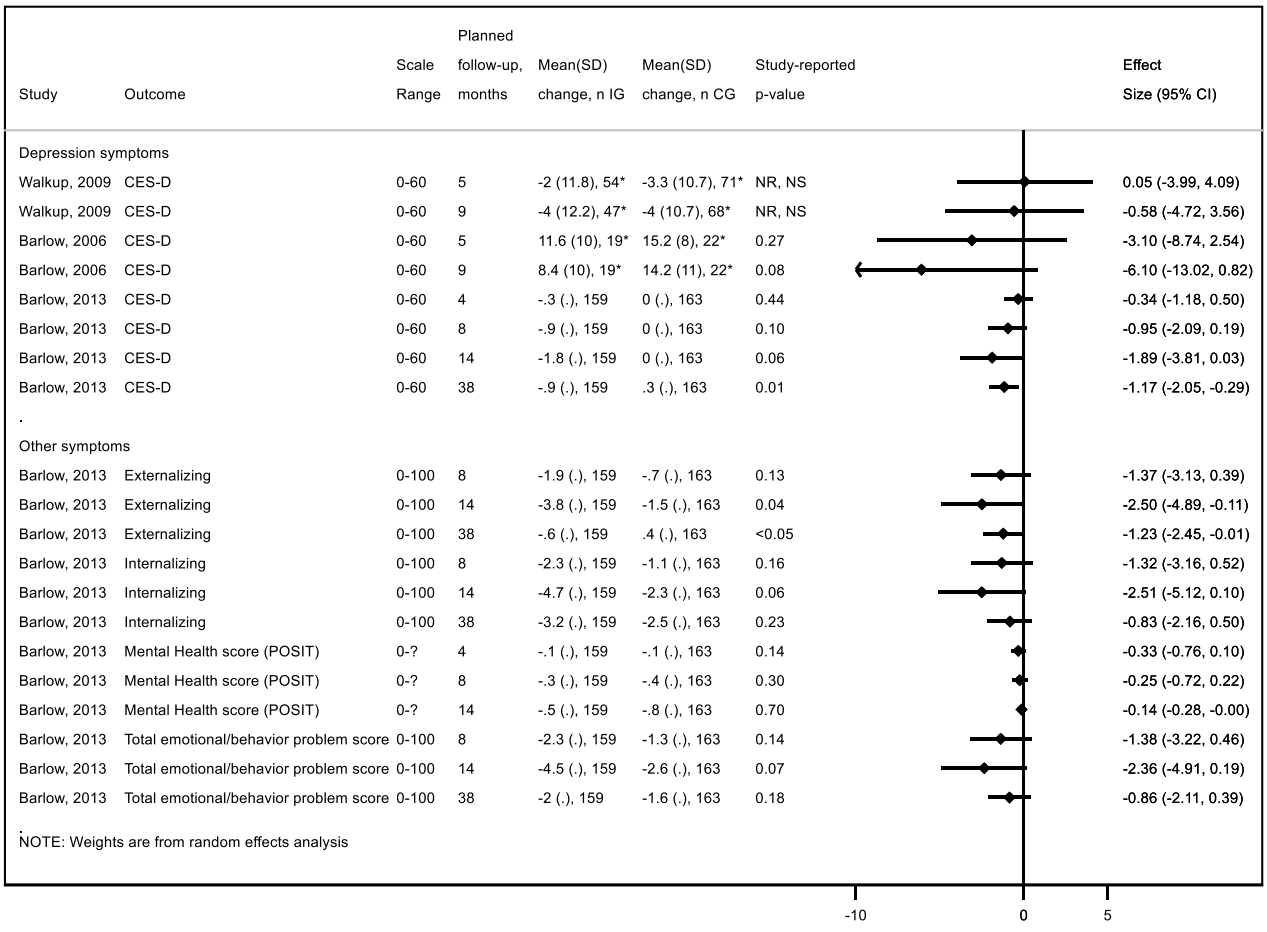


*Mean value at followup, rather than change from baseline.

Abbreviations: CG = control group; CI = confidence interval; IG = intervention group; MH = mental health; SD = standard deviation.

Note: Effect sizes include a variety of measures reported by studies, if available, or a calculated between-group difference if study-reported values were not reported; effects include mean difference in change between groups, mean difference between groups at followup, regression parameter estimates (e.g., beta-weights, b-weights), Cohen's d.

Figure 3. Mental Health Outcomes Summary (KQ1) Among the Family Spirit Trials, Mean Difference Between Intervention and Control Groups, by Outcome

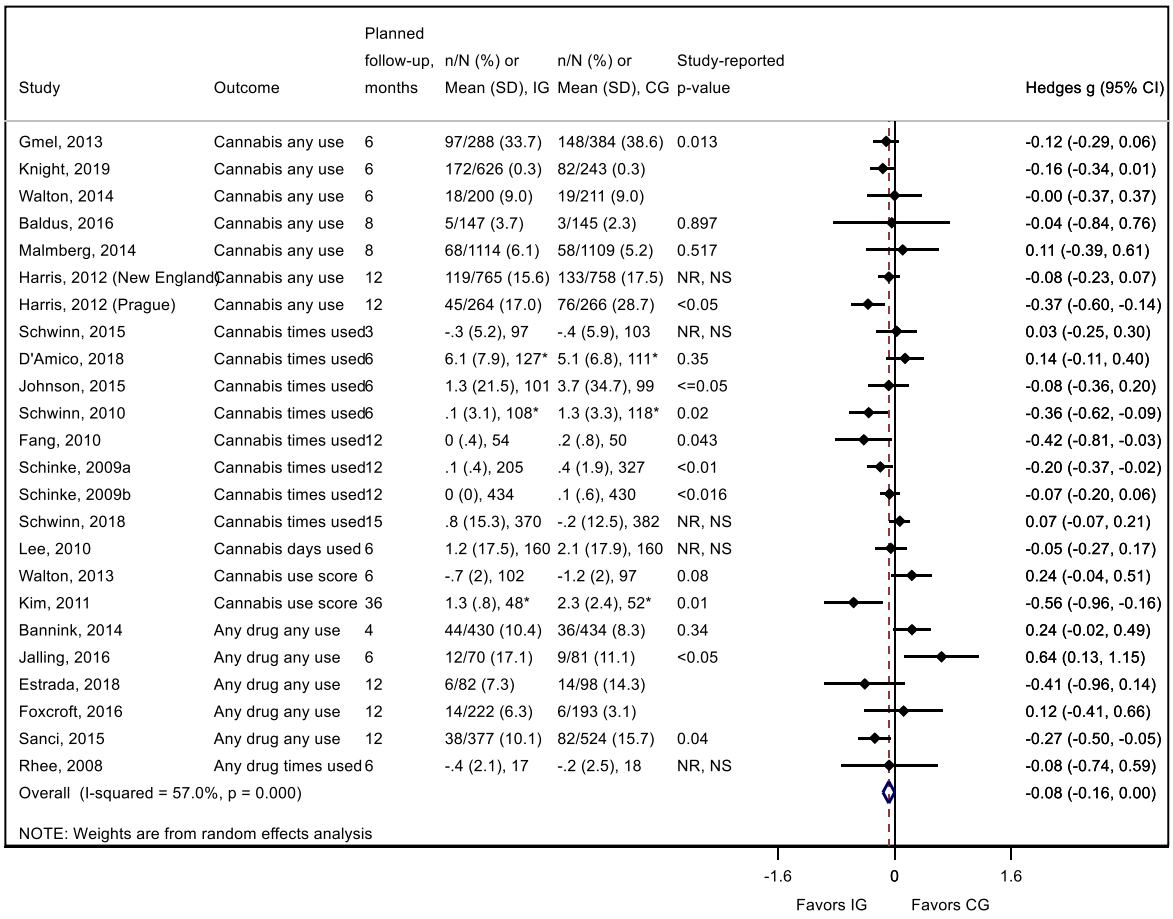


*Mean value at followup, rather than change from baseline.

Abbreviations: CES-D = Center for Epidemiologic Studies Depression Scale; CG = control group; CI = confidence interval; IG = intervention group; SD = standard deviation.

Note: Effect sizes are study-reported mean differences at followup (for Barlow, 2006, and Barlow, 2013) and beta-weight (Walkup, 2090).

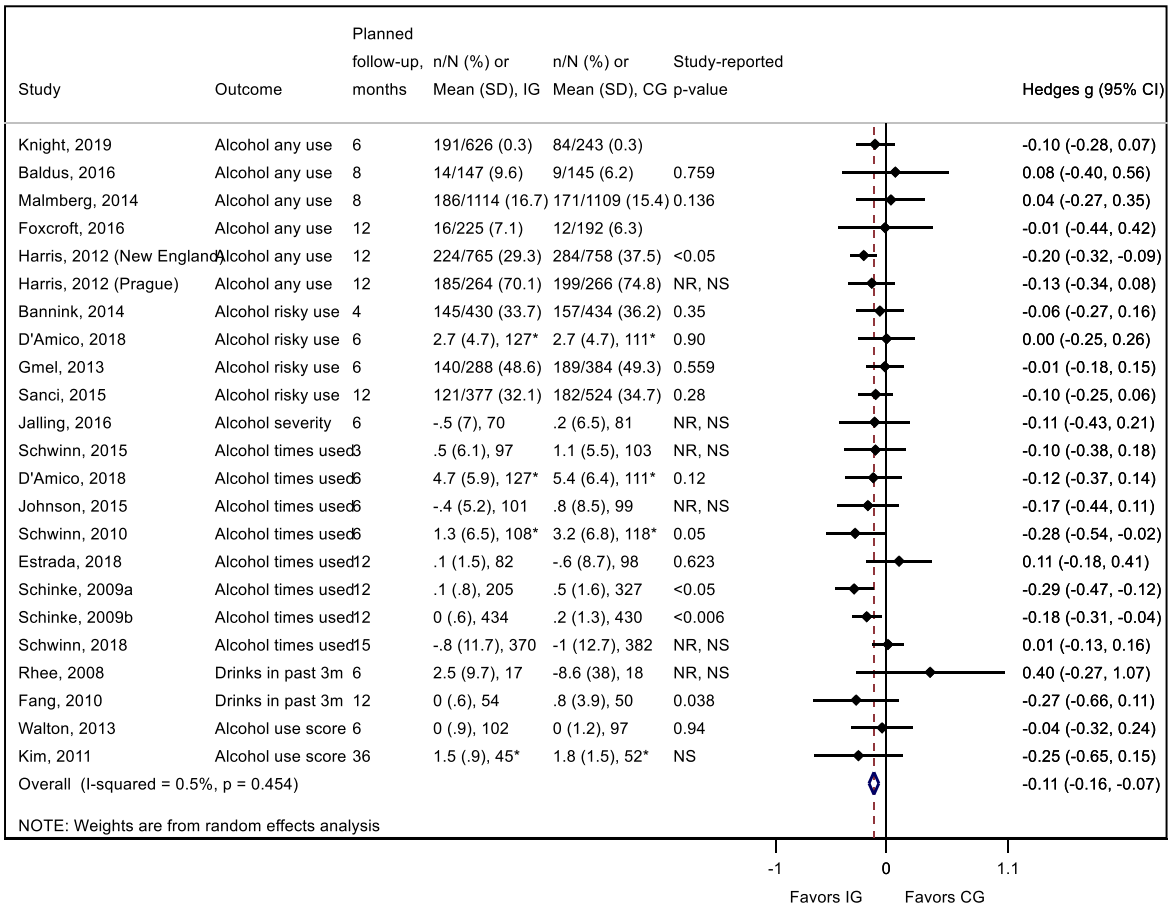
Figure 4. Primary Drug Use Outcome (KQ2) for General Prevention Trials, Standardized Mean Difference Between Intervention and Control Group, Sorted by Specific Outcome



*Mean value at followup, rather than change from baseline.

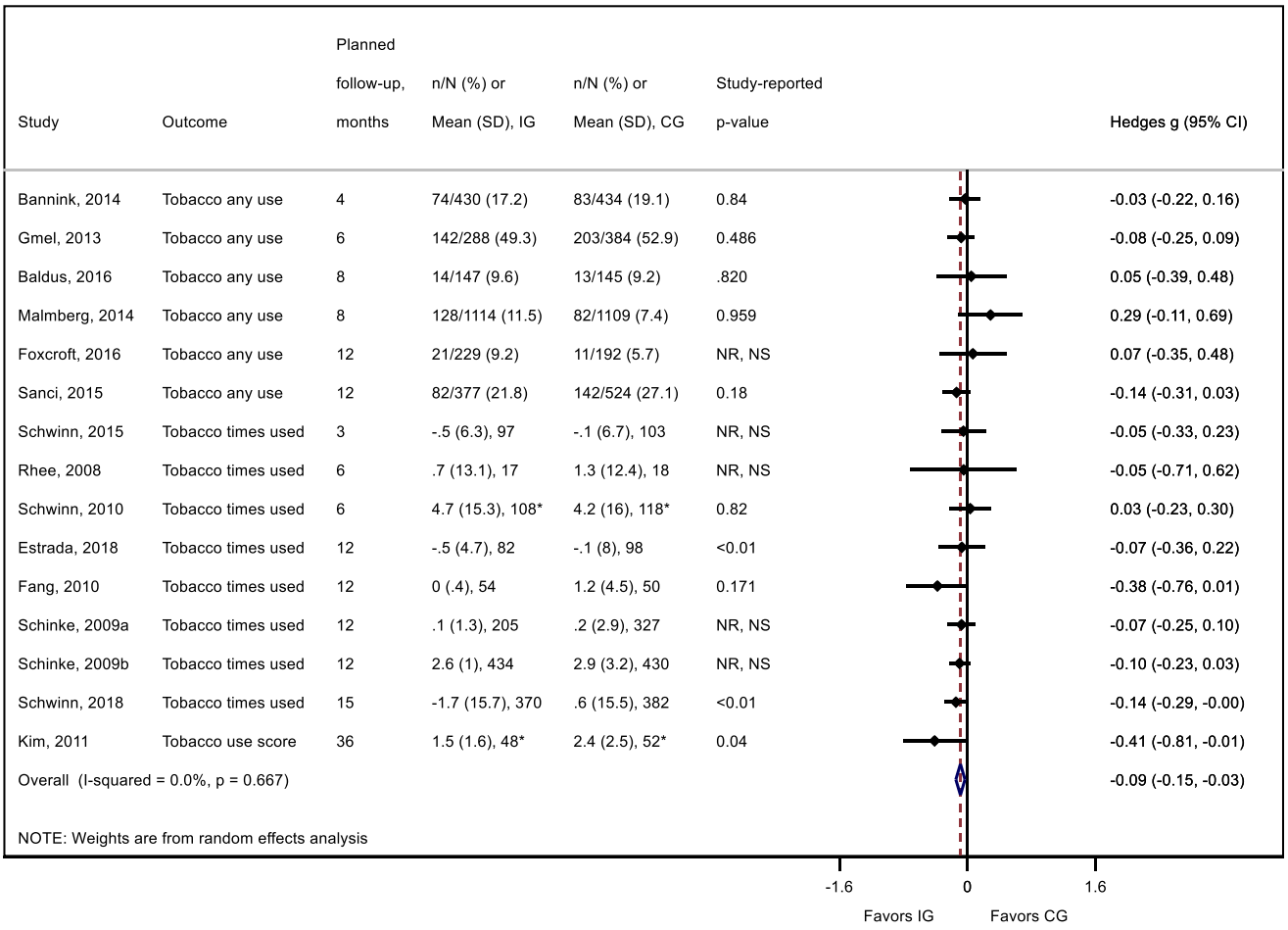
Abbreviations: CG = Control group; CI = Confidence interval; IG = Intervention group; NR = Not reported; NS = Not significant; SD = Standard deviation.

Figure 5. Primary Alcohol Use Outcome (KQ2) for General Prevention Trials, Standardized Mean Difference Between Intervention and Control Group, Sorted by Specific Outcome



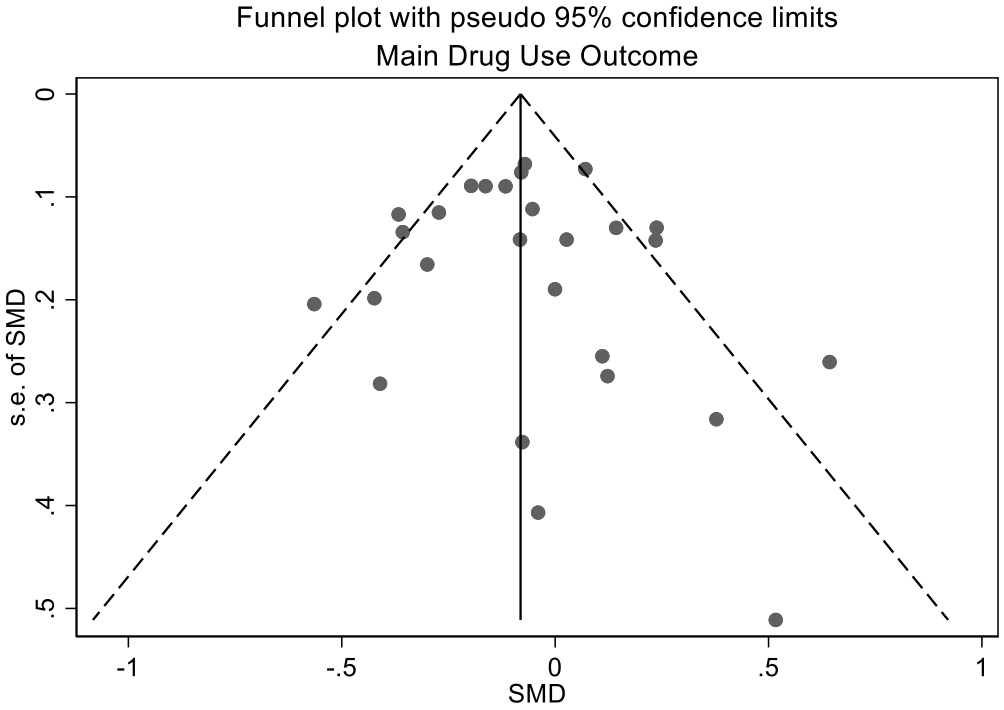
Abbreviations: CG = Control group; CI = Confidence interval; IG = Intervention group; NR = Not reported; NS = Not significant; SD = Standard deviation.

Figure 6. Primary Tobacco Use Outcome (KQ2) for General Prevention Trials, Standardized Mean Difference Between Intervention and Control Group, Sorted by Specific Outcome



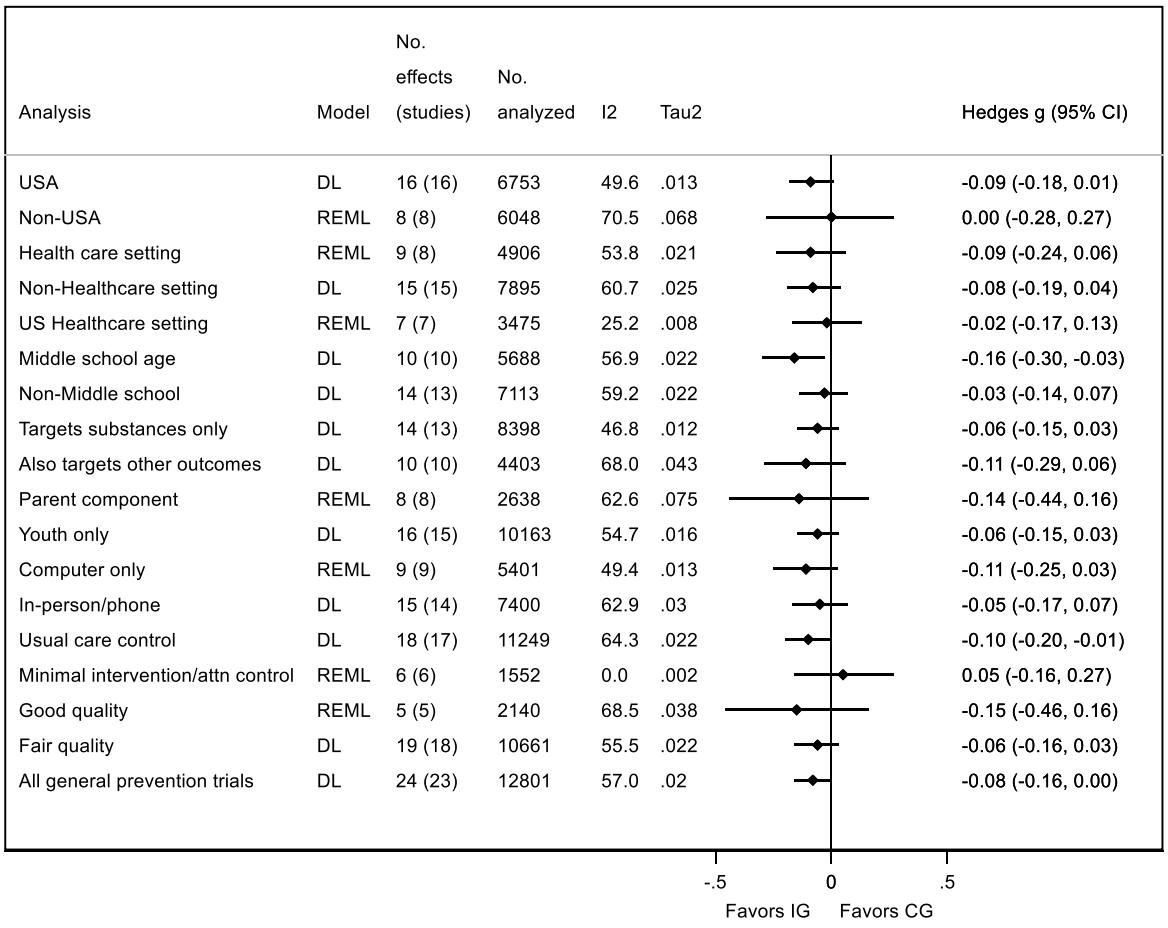
Abbreviations: CG = Control group; CI = Confidence interval; IG = Intervention group; NR = Not reported; NS = Not significant; SD = Standard deviation.

Figure 7. Funnel Plot Examining Small Studies Effect for Primary Drug Use Outcome (KQ2) for General Prevention Trials



Abbreviations: SMD = Standardized mean difference.

Figure 8. Summary of Sensitivity Analyses of Primary Drug Outcome (KQ2) for General Prevention Trials: Results of Meta-Analyses for Subgroups of Studies With the Indicated Characteristics



Abbreviations: CI = Confidence interval; DL = DerSimonian and Laird; REML = Restricted maximum likelihood; USA = United States of America.

Table 1. Stages of Illicit and Nonmedical Drug Use Among Children and Adolescents

Stage	Description
Abstinence	The time before an individual has ever used drugs
Sporadic use	The first 1-2 times that a substance is used and the adolescent wants to know how intoxication from using a certain drug(s) feels (sometimes also refers to extremely infrequent or non-persistent use)
Limited use	Use together with ≥ 1 friends in relatively low risk situations and without related problems; typically, use occurs at predictable time such as on weekends
Problematic/ harmful use	Use in a high-risk situation, such as when driving or babysitting; use associated with a problem such as a fight, arrest, or school suspension; or use for emotional regulation such as to relieve stress or depression
Substance use disorder (mild, moderate, or severe)	Drug use associated with recurrent problems or that interferes with functioning. Previously, the Diagnostic and Statistical Manual of Mental Disorders (DSM) system distinguished substance abuse from substance dependence (which includes loss of control or compulsive use)

Adapted from: Levy SJ, Kokotailo PK. Substance use screening, brief intervention, and referral to treatment for pediatricians. Pediatrics 2011 Nov;128(5):e1330-e1340[153] and Levy SJL, Williams JF, Committee on Substance Use and Prevention. Substance Use Screening, Brief Intervention, and Referral to Treatment [Clinical Report]. Pediatrics. 2016.[67]

Table 2. Current (Previous Month) Percentage of Illicit Drug Use, 2016 National Survey on Drug Use in Health[15]

Illicit drug	All adolescents (12-17 years)	Male adolescents (12-17 years)	Female adolescents (12-17 years)	12-13 years	14-15 years	16-17 years	18-25 years
Any illicit drug	7.9	7.9	7.8	2.0	6.7	14.5	23.2
Cannabis	6.5	6.8	6.1	0.8	5.3	12.9	20.8
Non-medical use of any prescription psychotherapeutic (pain relievers, specifically)	1.6 (1.0)	1.2 (0.6)	2.0 (1.3)	0.7 (0.6)	1.5 (0.9)	2.4 (1.3)	4.6 (1.8)
Cocaine	0.1	0.1	0.1	*	0.1	0.2	1.6
Hallucinogens	0.5	0.6	0.3	0.1	0.4	0.8	1.9
Inhalants	0.6	0.4	0.8	0.7	0.5	0.6	0.4

* Estimate suppressed due to low precision.

Table 3. Other Relevant Guidelines on Assessment and Prevention of Illicit and Nonmedical Substance Use in Children and Adolescents

Organization *Title (year)*	Recommendation(s)
American Academy of Pediatrics *Substance Use Screening, Brief Intervention, and Referral to Treatment (2016)*[66]	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.
Canadian Pediatric Society *Cannabis and Canada's children and youth (2017)*[154]	Screen all children and youth for cannabis exposure; be aware of and communicate the health risks related to cannabis use; and provide anticipatory guidance to parents and older children on the potential health risks of cannabis use.
Canadian Pediatric Society *Harm reduction: An approach to reducing risky health behaviours in adolescents (2008, reaffirmed 2016)*[155]	Screen all preadolescent and adolescent patients for potentially risky behaviors at regular health care visits; provide messages that encourage delay in initiation of potentially risky behaviors, and at the same time, promote risk-reduction strategies if adolescents choose to engage in the behavior; use principles of motivational interviewing in the assessment and discussion of risky health behaviors with adolescent patients; and become familiar with the resources in their communities that provide harm reduction programs for substance abuse, pregnancy prevention, and injury prevention.
National Institute for Health and Care Excellence *Drug misuse prevention: targeted interventions (2017)*[156]	Deliver drug misuse prevention activities to people at risk through a range of existing statutory, voluntary, or private services (e.g., primary care services, mental health services, dental services); at routine appointments and opportunistic contacts with statutory and other services, assess whether someone is vulnerable to drug misuse; and consider skills training for children and young people who are assessed as vulnerable to drug misuse. If skills training is delivered to children and young people, ensure that their carers or families also receive skills training. Offer older adolescents/young adults who are assessed as vulnerable to drug misuse clear information on drugs and their effects, advice and feedback on any existing drug use, and information on local services and where to find further advice and support; and offer information and advice both verbally and in writing.
United Nations Office on Drugs and Crime/World Health Organization *International Standards on Drug Use Prevention - Second updated edition*	Recommended services potentially relevant to health care settings include: Infancy/early childhood: prenatal and infancy visitation programs to provide support in accessing needed resources and in parenting skills. Middle childhood: parenting skills programs emphasizing warm child-reading style, clear rules, monitoring, role modeling; supporting children, adolescents and parents in addressing emotional and behavioral disorders as early as possible. Early adolescence: Skills-based prevention programs to encourage social competence, including substance and peer refusal skills; addressing individual psychological vulnerabilities as needed, such as coping with sensation-seeking, impulsivity, anxiety sensitivity and hopelessness. Adolescence: Brief interventions for those using substances but have not experienced important consequences and are unlikely to seek treatment

Abbreviations: SBIRT = Screening, Brief Intervention, and Referral to Treatment.

Table 4. Study Characteristics of All Included Studies of Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults (29 Studies)

Study	Quality	No. rand (% FU)	Country	Brief population description	Baseline drug use, % used	IG description	Number of sessions (est hrs)	Other target behaviors	Intervention setting: format
Baldus, 2016[81]	Fair	302 (88.7)	DEU	Aged 10-14 youth not diagnosed with substance use disorder	Cannabis: 1.7 Any Drug: NR	IG1: Strengthening Families Program 10-14: 11 x 2-hour family-based group sessions to reduce risk of substance abuse and behavior problems	11 (22)	Alc, Tob, Fam, SocLeg	Social services agency: Group (in-person)
Bannink, 2014[82]	Fair	1702 (73.8)	NLD	Aged 15-16	Cannabis: NR Any Drug: NR	IG1: 1 x 45-minute computer-based program to assess health-risk behavior and well-being with tailored messages; referred for consultation if at-risk of mental health problems or if youth self-refers	2 (1.2)	Alc, Tob, MH, RSex	School: Individual (in-person), Computer-based
						IG2: 1 x 45-minute computer-based program to assess health-risk behavior and well-being with tailored messages; option to self-refer to nurse	1 (0.8)	Alc, Tob, MH, RSex	School: Computer-based
Barlow, 2006[85]	Fair	53 (77.4)	US	Pregnant American Indian youth aged 12 to 19	Cannabis: NR Any Drug: NR	IG1: Family Spirit: 25 x 90-minute in-home sessions on parenting, substance abuse prevention, coping, and other maternal and infant health topics	25 (37.5)	Alc, Oth	Home: Individual (in-person)
Barlow, 2013[83]	Good	322 (92.0)	US	Pregnant American Indian youth aged 12-19	Cannabis: 78.88 Any Drug: NR	IG1: Family Spirit: 43 x 60-minute in-home sessions on parenting, substance abuse prevention, coping, and other maternal and infant health topics	43 (43)	Alc, Oth	Home: Individual (in-person)
D'Amico, 2018[116]	Fair	1702 (73.8)	US	Adolescents aged 12 to 18 at risk for alcohol abuse	Cannabis: NR Any Drug: NR	IG1: 1 x 15-20 minute individual brief motivational interview for youth focusing on motivation to change and substance use prevention	1 (0.3)	Alc	Primary Care: Individual (in-person)
Dembo, 2016[88]	Fair	300 (93.7)	US	Truant youth, aged 11-17	Cannabis: 82.3 Any Drug: NR	IG1: 2 x 75-min youth sessions on substance use and consequences 1 x 75-	3 (3.8)	SocLeg	Home: Individual (in-person)

Table 4. Study Characteristics of All Included Studies of Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults (29 Studies)

Study	Quality	No. rand (% FU)	Country	Brief population description	Baseline drug use, % used	IG description	Number of sessions (est hrs)	Other target behaviors	Intervention setting: format
						min parent session on parental attitudes of use			
	Fair	300 (93.7)	US	Truant youth, aged 11-17	Cannabis: 82.3 Any Drug: NR	IG2: 2 x 75-minute individual sessions on substance use and consequences	2 (2.5)	SocLeg	Home: Individual (in-person)
Estrada, 2018[90]	Fair	230 (75.2)	US	Eighth graders with behavior problems	Cannabis: NR Any Drug: NR	IG1: Online version of Familias Unidas (eHealth Familias Unidas); 8 x 30-min online recorded e-parent group sessions accessed via the internet and 4 x 45-min parent-adolescent family sessions delivered by a facilitator via web-based video conferencing software	12 (7)	Alc, Tob, Fam, RSex	Home: Computer-based, Video
Fang, 2010[92]	Good	108 (96.3)	US	Asian American girls, aged 10-14	Cannabis: 3.8 Any Drug: NR	IG1: 10 x 35-45-minute interactive online sessions for mother-daughter dyads on family functioning, self-efficacy, social skills, and drug use prevention	10 (7.5)	Alc, Tob, Fam, MH	Home: Computer-based
Foxcroft, 2016[93]	Fair	614 (75)	POL	Children ages 10 to 14	Cannabis: NR Any Drug: 4	IG1: Strengthening Families Program 10-14: 7 x 120-min group substance use prevention sessions for parent-youth dyads	7 (14)	Alc, Tob, Fam	NR: Group (in-person), Video
Gmel, 2013[94]	Fair	853 (79)	CHE	Male conscripts, age 19 or greater	Cannabis: 46 Any Drug: NR	IG1: 2 x 20-minute counseling sessions targeting multi-substance use behaviors in men ages 19 and older	2 (0.7)	Alc, Tob	Other Medical: Individual (in-person)
Harris, 2012[80]	Fair	2685 (76.5)	US, CZE	Aged 12-18 (New England) or 13-17 (Prague) with a routine primary care appointment	Cannabis: 13.2 Any Drug: NR	IG1: 1 x 7-8-minute computer and clinician-based screening and intervention to not start/stop substance use	1 (0.1)	Alc	Primary Care: Individual (in-person), Computer-based
Jalling, 2016[95]	Fair	271 (83.8)	SWE	At-risk youth not being treated for	Cannabis: NR Any Drug: 16.9	IG1: 6 x 120-min group sessions to increase parental understanding of youth	6 (12)	Alc, Fam, SocLeg	NR: Group (in-person)

Table 4. Study Characteristics of All Included Studies of Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults (29 Studies)

Study	Quality	No. rand (% FU)	Country	Brief population description	Baseline drug use, % used	IG description	Number of sessions (est hrs)	Other target behaviors	Intervention setting: format
				alcohol or drug use, aged 12-18		development & skill improvement			
	Fair	271 (83.8)	SWE	At-risk youth not being treated for alcohol or drug use, aged 12-18	Cannabis: NR Any Drug: 16.9	IG2: 10 x 150-minute group parent sessions to help to develop and enhance their skills and self-efficacy for parenting	10 (25)	Alc, Fam, SocLeg	NR: Group (in-person)
Johnson, 2015[96]	Fair	200 (85.0)	US	Aged 14 to 21 with a primary care appointment	Cannabis: 18.5 Any Drug: NR	IG1: 3 positive youth development motivational interview sessions with phone or email followup targeting career readiness and addressing risky behaviors (time NR)	6 (1.8)	RSex, SocLeg	Primary Care: Individual (in-person)
Kerr, 2013[97]	Fair	1654 (90.4)	US	Aged 14 to 17	Cannabis: NR Any Drug: NR	IG1: 2 x 8-hour group workshops covering diet, physical activity, and drug prevention	2 (16)	Alc, Oth	NR: Group (in-person)
Kim, 2011[98]	Good	100 (90.0)	US	Girls in foster care, aged 10-12	Cannabis: NR Any Drug: NR	IG1: 6 group sessions of caregiver training; 6 group sessions of skill-building and 40 individual coaching sessions for adolescent girls (time NR)	46 (86)	Alc, Tob, Fam, MH, RSex, SocLeg	NR: Individual (in-person), Group (in-person)
Knight, 2019[72]	Fair	871 (87.5)	US	Adolescents aged 12 to 18	Cannabis: 12.2 Any Drug: NR	IG1: 1 X 2 to 5-minute conversation about the risks of substance abuse using motivational interviewing strategies	1 (0.2)	Alc	Primary Care: Individual (in-person)
Lee, 2010[100]	Good	341 (94.4)	US	Incoming college freshmen with any use of cannabis in previous 3 months	Cannabis: NR Any Drug: NR	IG1: 1 computer-based individualized personalized feedback session (time NR)	1 (0.5)	--	Home: Computer-based
Malmberg, 2014[102]	Fair	2416 (92.0)	NLD	Aged 11 to 17	Cannabis: NR Any Drug: NR	IG1: 3 interactive modules (1 module per year for 3 years) on substance use prevention (time NR)	3 (1.5)	Alc, Tob	School: Computer-based
Mason, 2015[103]	Fair	119 (98)	US	Youth at risk for substance use	Cannabis: NR Any Drug: NR	IG1: 1 x 20-minute individual motivational interviewing	1 (0.3)	Alc	NR: Individual (in-person)

Table 4. Study Characteristics of All Included Studies of Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults (29 Studies)

Study	Quality	No. rand (% FU)	Country	Brief population description	Baseline drug use, % used	IG description	Number of sessions (est hrs)	Other target behaviors	Intervention setting: format
				disorder, aged 14-18		session with peer network counseling			
Rhee, 2008[105]	Fair	41 (85)	US	Youth with asthma, aged 14-20	Cannabis: NR Any Drug: NR	IG1: 3 x 30-min CD-ROM sessions covering decision-making and risk behaviors	3 (3.2)	Alc, Tob	Other Medical, Home: Individual (phone), Computer-based
Sanci, 2015[106]	Fair	901 (68.8)	AUS	Aged 14-24, attending a primary care visit	Cannabis: NR Any Drug: 26.5	IG1: Clinician training to screen for risky behaviors and discuss protective factors with youth, plus supported plan-do-study-act cycle.	1 (0.2)	Alc, Tob, MH, RSex, SocLeg	Primary Care: Individual (in-person)
Schinke, 2009a[107]	Fair	591 (90.0)	US	Females aged 11 to 13	Cannabis: 2.7 Any Drug: NR	IG1: 9 x 45-minute individual computer sessions for mother-daughter dyads aimed to reduce substance use through mother-daughter interactions	9 (6.8)	Alc, Tob, MH, Fam	Home: Computer-based
Schinke, 2009b[108]	Good	916 (94)	US	Females aged 11 to 13	Cannabis: NR Any Drug: NR	IG1: 9 X 45-minute weekly computer-based substance use prevention sessions plus two annual booster sessions for mother-daughter dyads	11 (8.2)	Alc, Tob, MH, Fam	Home: Computer-based
Schwinn, 2010[110]	Fair	236 (91)	US, CAN	Females aged 13-14	Cannabis: NR Any Drug: NR	IG1: RealTeen: 12 x web-based modules and homepage access to curated online community	12 (5)	--	Home: Computer-based
Schwinn, 2015[112]	Fair	236 (85)	US	Sexual-minority adolescents, aged 15-16	Cannabis: NR Any Drug: NR	IG1: 3 x 14-minute individual computer sessions for youth	3 (0.7)	--	Home: Computer-based
Schwinn, 2018[111]	Good	788 (96.5)	US	Females aged 13 to 14 residing in the United States	Cannabis: NR Any Drug: NR	IG1: RealTeen: 9 x 15-minute online substance use prevention sessions for girls aged 13-14	9 (2.8)	--	Home: Computer-based
Walkup, 2009[113]	Fair	167 (68.9)	US	Pregnant American Indian youth, aged 12-22	Cannabis: NR Any Drug: NR	IG1: Family Spirit: 25 x 60-minute in-home sessions on parenting, substance abuse	25 (25)	Alc, Oth	Home: Individual (in-person)

Table 4. Study Characteristics of All Included Studies of Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults (29 Studies)

Study	Quality	No. rand (% FU)	Country	Brief population description	Baseline drug use, % used	IG description	Number of sessions (est hrs)	Other target behaviors	Intervention setting: format
						prevention, and problem-solving and coping skills			
Walton, 2013[114]	Fair	328 (85)	US	Youth with previous-year cannabis use, aged 12 to 18, attending a primary care visit	Cannabis: 100 Any Drug: NR	IG1: 1 MI session (time NR)	1 (0.6)	Alc	Primary Care: Individual (in-person)
						IG2: 1 computer-based MI session (time NR)	1 (0.6)	Alc	Primary Care: Computer-based
Walton, 2014[115]	Fair	714 (88.1)	US	Youth with no cannabis use in previous year, aged 12-18, attending a primary care visit	Cannabis: 0 Any Drug: 6.9	IG1: 1 x 38-minute MI session	1 (0.6)	Alc	Primary Care: Individual (in-person)
						IG2: 1 x 33-minute computer-based MI session	1 (0.6)	Alc	Primary Care: Computer-based

Abbreviations: Alc = Alcohol; AUS = Australia; CAN = Canada; CHE = Switzerland; CZE = Czech Republic; DEU = Germany; Est hrs = Estimated hours; Fam = Family functioning; FU = Followup; IG = intervention group; MH = Mental health; NR = Not reported; NLD = Netherlands; Oth = Other health behavior; POL = Poland; RSex = Risky sexual behavior; SocLeg = Social-legal; SWE = Sweden; Tob = Tobacco; US = United States.

Table 5. Summary of Study Characteristics of All Included Studies of Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults (29 Studies, N=18,353)

Characteristics	No. studies	%
All studies	29	100
Study design		
RCT	24	83
Cluster RCT	4	14
CCT	1	3
Quality rating*		
Good	6	21
Fair	23	79
Conducted in the US	22	76
Recruitment setting		
Primary care	11	38
Other health care	1	3
School (only)	4	14
Online, media (only)	6	21
Other	7	24
Prevention type		
Universal	20	69
Selective	9	31
Drug focus		
Cannabis	5	17
Any drug use	24	83
Primary Intervention Outcomes		
Drug only	4	14
Drug and alcohol	6	21
Drug, alcohol, tobacco	3	10
Drug and nonsubstance	2	7
Substance use and nonsubstance	14	48
Non-substance outcomes†		
Family functioning	8	28
Risky sexual behavior	5	17
Mental health	6	21
Other	10	34
Control Group		
No. intervention/usual care	17	59
Minimal intervention	7	24
Attention control	5	17
Median sample size (IQR), Range	322 (230-853)	41-2685
Median % followup at 6 to 12 months (IQR), Range	87.5 (79.0-92.0)	68.8-98.0

*6 additional studies were rated as poor quality and excluded from the review.
†Interventions may have multiple non-substance-related primary outcomes.

Abbreviations: CCT = Controlled clinical trial; IQR = Interquartile range; No. = Number; RCT = Randomized controlled trial; US = United States.

Table 6. Summary of Population Characteristics of All Included Studies of Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults (29 Studies)

Characteristics	No. of trials	% of all trials or SD
Limited to pregnant adolescents	3	10
Age; Mean, SD[*]	14.9	2.0
Age group		
Middle school (~10-14)	10	35
High school (~14-17)	3	10
Young adults (~18-25)	2	7
Wide age range	14	48
Majority Hispanic or non-white[†]	15	68
	Total % across all trials	**IQR (No. trials reporting)**
Female	59.4	50-66.5 (29)
Race[†]		
% Black	38.9	8.1-63.7 (17)
% Asian	6.4	1.2-5.6 (8)
% Native American	20.0	0.1-0.3 (8)
% White	42.1	11.5-72.3 (15)
Hispanic ethnicity[†,‡]	16.5	8.6-23.1 (16)
Used cannabis, Median %	24.0	12.2-18.5 (11)
Used alcohol, Median %	37.7	32.3-53.1 (11)

[*]Mean across all trials, weighted by number randomized in each trial.
[†]Limited to trials conducted in the US (21 trials).
[‡]Assuming majority white, non-Hispanic if race and ethnicity were not reported.

Abbreviations: IQR = Interquartile range; SD = Standard deviation; US = United States.

Table 7. Summary of Intervention Characteristics of Included Studies of Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults (34 Intervention Arms)

Characteristics	Median (IQR)	Range
Median duration (IQR), Range	6 weeks (1 day - 26 weeks)	1 day – 3 years
Median no. sessions (IQR), Range	3 (1-10)	1-46
Median estimated planned contact hours (IQR), Range	2.8 (0.6-12)	0.1-86
	No. groups	**%**
Intervention participant		
Youth only	23	68
Youth and parent	8	23
Parent only	2	6
Clinician (for youth counseling)	1	3
Format		
Individual counseling (in person or phone-based)	17	50
Computer-based (entirely)	12	35
Group sessions offered	6	18
Group AND individual counseling	1	3
Setting		
Primary care	9	26
Other medical	2	6
School*	3	9
Other or NR	20	59
Primary care clinician involved in intervention delivery	3	9
Total number of intervention groups	34	100

*****Studies in school settings were only included if they used schools only for recruitment purposes, as long as they recruited from multiple schools and met at locations other than schools, or if they studied entirely online interventions that did not involve interactions among students at the same school or between students and teachers.

Abbreviations: IQR = Interquartile range; No. = Number; NR = Not reported.

Table 8. Summary of Meta-Analysis Results for Substance Use Outcomes for General Prevention Trials (KQ2)

Outcome	No. studies	Type of effect	Pooled result (95% CI)	No. studies (k) in MA	I^2, %	Tau^2	N	Range of effects*	Median (IQR) effects*
Primary drug outcome	26	SMD	-0.08 (-0.16, 0.001)	23 (24)	57.0	0.020	12,801	-0.58 to 0.69	-0.11 (-0.20 to 0.04)
% Any illicit drug use	11	OR	0.82 (0.67, 1.04)	11 (12)	38.2	0.041	9031	0.42 to 3.52	0.80 (0.64 to 0.95)
% Any illicit drug use	11	ARD	--	--	--	--	--	-11.5 to 14.8	-2.8 (-5.0 to -0.2)
% Any cannabis use	6	OR	0.78 (0.64, 0.95) ‡	6 (7)	1.3	0.000	6520	0.51 to 1.34	0.77 (0.71 to 0.86)
% Any cannabis use	6	ARD	--	--	--	--	--	-11.5 to 2.8	-3.0 (-5.0 to -1.3)
Times used in previous 3m	12	MD	-0.21 (-0.44, 0.02)	11 (11)	51.0	0.037	3651	ΔΔ: -7.5 to 1.0 Δ: -1.1 to 1.5	ΔΔ: -0.3 (-1.6 to 0.0) Δ: 0.7 (-0.4 to 1.3)
Times used cannabis in previous 3m	10	MD	-0.23 (-0.48, 0.01)	10 (10)	58.1	0.045	3616	ΔΔ: -2.7 to 1.0 Δ: -1.1 to 1.6	ΔΔ: -0.3 (-0.9 to 0.0) Δ: 0.7 (-0.4 to 1.3)
Primary alcohol outcome	24†	SMD	-0.11 (-0.16, -0.07)	22 (23)	4.9	0.001	12,307	-0.46 to 0.40	-0.08 (-0.18 to 0.05)
% Any alcohol use	6	OR	0.79 (0.64, 0.96)‡	5 (6)	0	0.009	5854	0.56 to 1.40	0.98 (0.81 to 1.18)
% Any alcohol use	6	ARD	--	--	--	--	--	-10.4 to 10.2	1.0 (-5.0 to 4.0)
% Risky alcohol use	5	OR	0.92 (0.72, 1.17)‡	5 (5)	0	0.0	5078	0.77 to 1.45	0.94 (0.88 to 1.20)
% Risky alcohol use	5	ARD	--	--	--	--	--	-4.7 to 8.9	0.8 (-2.4 to 4.6)
Times used alcohol in previous 3m	8	MD	-0.29 (-0.53 to -0.05)‡	8 (8)	20.7	0.014	3192	ΔΔ: -1.2 to 0.8 Δ: -1.9 to -0.5	ΔΔ: -0.2 (-0.4 to 0.2) Δ: -0.6 (-1.3 to -0.5)
Total drinks in previous 3m	3	MD	--	--	--	--	--	ΔΔ: -3.8 to 2.8 Δ: NA (0 trials)	ΔΔ: 1.4 (-2.2 to 2.5) Δ: NA (0 trials)
Primary tobacco outcome	16†	SMD	-0.09 (-0.15 to -0.03)	15 (15)	0	0.0	8366	-0.41 to 0.29	-0.06 (-0.14 to 0.04)
% Any tobacco use	7	OR	0.91 (0.73 to 1.14)‡	6 (6)	0	0.0	5373	0.63 to 1.69	1.08 (0.88 to 1.32)
% Any tobacco use	7	ARD	--	--	--	--	--	-8.6 to 8.5	0.8 (-2.1 to 5.8)
Times used tobacco in previous 3m	8	MD	-0.30 (-0.58 to -0.02)‡	8 (8)	0	0.0	2893	ΔΔ: -5.5 to -0.2 Δ: 0.54	ΔΔ: -1.0 (-2.2 to -0.3) Δ: NA (1 trial)

*Range of effects for all study arms and timepoints, i.e., not limited to records in the meta-analysis.

†Number of trials reporting the specific substance use outcomes (any use, risky use, times used, total drinks) does not add up to the total number of trials reporting any outcome because some trials reported only a continuous scale score and are not shown in this table.

‡Effect based on restricted maximum likelihood model. Remaining effects based on DerSimonian & Laird model.

Abbreviations: Δ = difference between group at followup; ΔΔ = difference between groups in change from baseline; ARD = absolute risk difference; IQR = interquartile range; k = number of effects in the meta-analysis; MD = mean difference between groups; OR = odds ration; obs. = observations; SMD = standardized mean difference (Hedges g).

Table 9. Drug Use Outcomes for Family Spirit Trials to Prevent Illicit Drug Use Among Pregnant American Indian Adolescents and Young Adults (3 Trials)

Outcome	Study	Planned followup, months	n/N (%) or Mean (SD), IG	n/N (%) or Mean (SD), CG	Study-reported p-value	OR or Group Diff. (95% CI)
Any cannabis use	Barlow, 2013[83]	4	33/159 (20.6)	34/163 (21.0)	0.68	0.87 (0.44 to 1.70)
		8	20/159 (12.4)	31/163 (18.8)	0.10	0.57 (0.29 to 1.11)
		14	30/159 (18.9)	32/163 (19.6)	0.57	0.83 (0.44 to 1.58)
		38	17/159 (10.7)	25/163 (15.6)	0.007	0.65 (0.48 to 0.89)
Any illicit drug use	Barlow, 2013[83]	4	36/159 (22.9)	36/163 (21.9)	0.84	1.03 (0.61 to 1.74)
		8	22/159 (13.8)	33/163 (20.2)	0.09	0.58 (0.31 to 1.10)
		14	34/159 (21.3)	36/163 (21.9)	0.55	0.83 (0.44 to 1.55)
		38	20/159 (12.3)	28/163 (17.3)	0.01	0.67 (0.50 to 0.91)
	Walkup, 2009[113]	5	7/54 (13.0)	5/71 (7.0)	NR, NS	2.02 (0.51 to 7.92)
		9	3/47 (7.0)	2/68 (3.0)	NR, NS	2.57 (0.37 to 18.00)
Severity score related illicit drug use (Range 0-17, lower indicates better outcome)	Barlow, 2013[83]	4	- 0.1 (NR), 159	0 (NR), 163	0.78	-0.1 (-0.4 to 0.3)
		8	-0.3 (NR), 159	-0.1 (NR), 163	0.34	-0.2 (-0.5 to 0.2)
		38	-0.5 (NR), 159	-0.2 (NR), 163	0.19	-0.3 (-0.8 to 0.2)
Use score for any illicit drug use (Range 8-32, directionality NR)	Barlow, 2006[85]	5	23.9 (8), 19*	22.5 (7), 22*	0.67	1.1 (-3.9 to 6.0)
		9	25.1 (6), 19*	22.4 (8), 22*	0.27	2.6 (-2.2 to 7.4)

*****Post-test score, rather than change from baseline.

Abbreviations: CG = Control group; CI = Confidence interval; IG = Intervention group; NR = Not reported; NS = Not significant; OR = Odds ratio; SD = Standard deviation.

Table 10. Alcohol and Tobacco Use Outcomes for Family Spirit Trials to Prevent Illicit Drug Use Among Pregnant American Indian Adolescents and Young Adults (3 Trials)

Outcome	Study	Planned followup, months	n/N (%) or Mean (SD), IG	n/N (%) or Mean (SD), CG	Study-reported p-value	OR or Group Diff. (95% CI)
Any alcohol use	Barlow, 2013[83]	4	28/159 (17.9)	29/163 (17.8)	0.60	0.8 (0.35 to 1.83)
		8	27/159 (16.9)	33/163 (20.0)	0.33	0.71 (0.36 to 1.4)
		14	41/159 (25.8)	35/163 (21.6)	0.67	1.14 (0.63 to 2.05)
		38	26/159 (16.5)	26/163 (15.7)	0.68	1.06 (0.8 to 1.41)
	Walkup, 2009[113]	5	6/54 (11.0)	5/71 (7.0)	NR, NS	1.52 (0.42 to 5.46)
		9	5/47 (12.0)	4/68 (6.0)	NR, NS	2.19 (0.55 to 8.78)
Any tobacco use	Walkup, 2009[113]	5	7/54 (13.0)	12/71 (17.0)	NR, NS	0.74 (0.24 to 2.3)
		9	9/47 (22.0)	8/68 (13.0)	NR, NS	2.06 (0.64 to 6.62)

Abbreviations: CG = Control group; CI = Confidence interval; IG = Intervention group; NR = Not reported; NS = Not significant; OR = Odds ratio; SD = Standard deviation.

Table 11. Summary of Evidence Among All 29 Included Trials (N=18,353) of Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults, by Key Question

Key question	No. of Studies, (No. of Observations)	Summary of findings	Consistency/ precision	Other limitations	EPC assessment of overall strength of evidence	Applicability
KQ1 (Health and social/legal outcomes)	19 (9042)	No single health, social, or legal outcome was widely reported. Family functioning was improved in 3 computer-based general prevention trials among middle school-aged females and their mothers; isolated group differences were found for delinquency (in 2 of 5 trials), global functioning (in 1 trial), and consequences of drug use (in 2 of 3 trials) in general prevention trials. Group differences were rarely found for a variety of mental health scales (9 general prevention trials, 3 Family Spirit trials).	Inconsistent, imprecise	Wide variety of instruments used; specific outcomes rarely reported by more than 4 trials; many trials limited to a narrow demographic or risk groups	Low evidence of small to no benefit	14 conducted in the U.S., 8 limited to females, including 3 that were limited to pregnant American Indians recruited through the Indian Health Service; 4 additional trials conducted in U.S. primary care settings
KQ2 (Behavioral outcomes)	29 (18,353)	Although some general prevention interventions were effective in reducing nonmedical and illicit drug use and other behavioral outcomes, the effects were very wide ranging and the pooled effect for drug use was not statistically significant (pooled SMD=-0.08 [95% CI, -0.16 to 0.001], k=24 [from 23 studies], n=12,801, I^2=57.0%). Pooled estimates showed very small beneficial effects on alcohol use (SMD=-0.11 [95% CI, -0.16 to -0.07], k=23 [from 22 studies], n=12,307, I^2=4.9%) and tobacco use SMD=-0.09 [95% CI, -0.15 to -0.03], k=15, n=8366, I^2=35.0%). Of the 3 Family Spirit intervention trials among pregnant adolescent Native Americans, only the largest and best-quality trial found reductions in drug use and only at long-term (38-month) followup.	Inconsistent, Imprecise	Heterogeneity in outcomes reported; only 6 were rating as good quality; 10 trials had less than 12 months' followup, which may be insufficient to find differences younger adolescents with low use levels; many trials limited to narrow demographic or risk groups	Low evidence of small to no benefit	22 of 29 trials conducted in the U.S., 15 of which included >50% racial or ethnic minority participants; primarily targeting adolescents (vs. young adults); only 12 trials were conducted in or recruited from health care settings, including 3 that were limited to pregnant American Indians recruited through the Indian Health Service
KQ3 (Harms)	Reported:1 (322) Paradoxical findings: 2 (1925)	One Family Spirit trial found no differences in adverse events or serious adverse events, after controlling for contact time. In addition, 2 general prevention trials reported statistically significant increases in drug use outcomes, and others reported statistically nonsignificant increases in drug, alcohol, or tobacco use.	Consistency NA, imprecise	Only directly reported in 1 trial, and raw proportions were not provided, nor details of how they adjusted for contact time.	Insufficient	Trial directly reporting harms limited to pregnant Native Americans; trials showing statistically significant harmful drug outcomes conducted in Sweden and the U.S.

Abbreviations: CI = Confidence interval; EPC = Evidence-based Practice Center; k = number of studies; KQ = Key Question; NA = Not applicable; SMD = Standard mean difference; US = United States.

Appendix A. Detailed Methods

Literature Search Strategies for Primary Literature

Sources searched:
Cochrane Central Register of Controlled Clinical Trials, via Wiley
Medline, via Ovid
PsycInfo, via Ovid
PubMed, publisher-supplied records
Key:
* = truncation
ab = word in abstract
ag= age group
id = keyword
kf = keyword heading [word not phrase indexed]
kw = keyword
md= methodology
ti = word in title

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#1 (drug or drugs or substance*):ti,ab,kw near/1 (use or using):ti,ab,kw

#2 (drug or drugs or substance*) near/5 (abuse* or abusing or misus* or overus* or overutili* or nonprescri* or (non next prescri*) or nonmedical or "non medical" or extramedical or "extra medical" or illicit* or illegal* or recreation*):ti,ab,kw

#3 (opioid* or opiate* or oxycodone or hydrocodone or ritalin or adderall or amphetamine* or methylphenidate or "laughing gas" or "nitrous oxide" or ketamine or dextromethorphan or GHB or gamma-hydroxybutyrate or inhalant* or stimulant* or sedative* or barbiturate* or benzodiazepine* or (sleep next medication*)):ti,ab,kw near/5 (use* or using or abuse* or abusing or misus* or overus* or overutili* or nonprescri* or (non next prescri*) or nonmedical or "non medical" or extramedical or "extra medical" or illicit* or illegal* or recreation*):ti,ab,kw

#4 ("pain relief" or (pain next reliever*) or (pain next medication*) or medicine* or "over the counter" or OTC):ti,ab,kw near/5 (abuse* or abusing or misus* or overus* or overutili* or nonprescri* or (non next prescri*) or nonmedical or "non medical" or extramedical or "extra medical" or illicit* or illegal* or recreation*):ti,ab,kw

#5 prescription*:ti,ab,kw near/5 (abuse* or abusing or misus* or overus* or overutili* or nonmedical or "non medical" or extramedical or "extra medical" or illicit* or illegal* or recreation*):ti,ab,kw

#6 (street* or designer* or club):ti,ab,kw next drug*:ti,ab,kw

#7 (legal next high*):ti,ab,kw

#8 nmupd:ti,ab,kw

#9 marijuana:ti,ab,kw

#10 (Cannabi* or hash or hashish):ti,ab,kw

#11 (cocaine or methamphetamine* or khat or "Catha edulis"):ti,ab,kw

#12 (heroin or opium or kratom or "mitragyna speciosa" or "manufactured fentanyl"):ti,ab,kw

#13 (mdma or ecstasy or flunitrazepam or rohypnol or "bath salts" or "synthetic cathinone"):ti,ab,kw

#14 (salvia or phencyclidine):ti,ab,kw

#15 (hallucinogen* or dimethyltryptamine or lsd or mescaline or psilocybin):ti,ab,kw

#16 {or #1-#15}

#17 counsel*:ti,ab,kw or advice:ti,ab,kw or advise*:ti,ab,kw

#18 (behavio* next chang*):ti,ab,kw

#19 (behavio* next intervention*):ti,ab,kw

#20 (behavio* next modification*):ti,ab,kw

#21 motivational next interview*:ti,ab,kw

#22 (cognitive next behavio*):ti,ab,kw or (behavio* next therap*):ti,ab,kw or CBT:ti,ab,kw

#23 (brief next intervention*):ti,ab,kw or "computer based":ti,ab,kw or "self help":ti,ab,kw

#24 SBIRT:ti,ab,kw

#25 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

#26 (reduc* or decreas* or prevent* or delay or avoid):ti,ab,kw near/3 initiation*:ti,ab,kw

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

#28 intervention*:ti or prevention:ti or preventive:ti or psychosocial:ti

#29 {or #17-#28}

#30 #16 and #29

#31 ((reduc* or decreas* or prevent* or delay or avoid):ti,ab,kw near/3 (drug* or substance* or marijuana* or cannabi* or opioid* or opiate* or heroin or oxycodone or hydrocodone or crack or cocaine or "pain relief" or pain reliever* or pain medication* or prescription* or medicine* or over the counter or OTC):ti,ab,kw) near/5 (abuse* or abusing or misuse* or misusing or overus* or overuitili* or use* or using or experiment*):ti,ab,kw

#32 #30 or #31

#33 (child* or teen or teens or teenage* or adolescen* or youth or youths or "young people" or pediatric* or paediatric* or school age* or juvenile*):ti,ab,kw

#34 #32 and #33 Publication Year from 2013 to 2018 899

#35 (young or emerging or early):ti,ab,kw next adult*:ti,ab,kw

#36 late:ti,ab,kw next (teen* or adolescen*):ti,ab,kw

#37 (college* or universit*):ti,ab,kw

#38 (undergraduate or graduate):ti,ab,kw next student*:ti,ab,kw

#39 "high school":ti,ab,kw near/2 senior*:ti,ab,kw

#40 (12th next grade):ti,ab,kw

#41 {or #35-#40}

#42 #32 and #41 Publication Year from 1992 to 2018 1219

#43 #34 or #42 in Trials

MEDLINE

Ovid MEDLINE(R) <1946 to January Week 4 2019>, Ovid MEDLINE(R) Daily Update <January 30, 2019>, Ovid MEDLINE(R) Epub Ahead of Print <January 30, 2019>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to January 28, 2019>

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1 substance-related disorders/

2 Drug misuse/

3 Prescription drug misuse/

4 Prescription drug overuse/

5 amphetamine-related disorders/

6 cocaine-related disorders/

7 inhalant abuse/ (183)

8 marijuana abuse/ (5652)

9 opioid-related disorders/

10 phencyclidine abuse/

11 substance abuse, intravenous/

12 substance abuse, oral/

13 street drugs/

14 hallucinogens/

15 ((drug or drugs or substance$) adj1 ("use" or using)).ti,ab,kf.

16 ((drug or drugs or substance$) adj5 (abuse$ or abusing or misus$ or overus$ or overutili$ or nonprescri$ or non prescri$ or nonmedical or non medical or extramedical or extra medical or illicit$ or illegal$ or recreation$)).ti,ab,kf.

17 ((opioid$ or opiate$ or oxycodone or hydrocodone or ritalin or adderall or amphetamine$ or methylphenidate or laughing gas or nitrous oxide or ketamine or dextromethorphan or GHB or gamma-hydroxybutyrate or inhalant$ or stimulant$ or sedative$ or barbiturate$ or

benzodiazepine$ or sleep medication$) adj5 (use$ or using or abuse$ or abusing or misus$ or overus$ or overutili$ or nonprescri$ or non prescri$ or nonmedical or non medical or extramedical or extra medical or illicit$ or illegal$ or recreation$)).ti,ab,kf.

18 ((pain relief or pain reliever$ or pain medication$ or medicine$ or over the counter or OTC) adj5 (abuse$ or abusing or misus$ or overus$ or overutili$ or non prescript$ or nonmedical or non medical or extramedical or extra medical or illicit$ or illegal$ or recreation$)).ti,ab,kf.

19 (prescription$ adj5 (abuse$ or abusing or misus$ or overus$ or overutili$ or nonmedical or non medical or extramedical or extra medical or illicit$ or illegal$ or recreation$)).ti,ab,kf.

20 ((street$ or designer$ or club) adj drug$).ti,ab,kf.

21 legal high$.ti,ab,kf

22 nmupd.ti,ab,kf.

23 marijuana.ti,ab,kf.

24 (Cannabi$ or hash or hashish).ti,ab,kf.

25 (cocaine or methamphetamine$ or methamphetamine$ or khat).ti,ab,kf.

26 (Heroin or opium or kratom or mitragyna speciosa or manufactured fentanyl).ti,ab,kf.

27 (mdma or ecstasy or flunitrazepam or rohypnol or bath salts or synthetic cathinone).ti,ab,kf.

28 (salvia or phencyclidine).ti,ab,kf.

29 (hallucinogen$ or dimethyltryptamine or lsd or mescaline or psilocybin).ti,ab,kf.

30 or/1-29

31 Behavior Therapy/

32 Cognitive Therapy/

33 Counseling/

34 Directive Counseling/

35 Distance Counseling/

36 Patient Education as Topic/

37 Risk Reduction Behavior/

38 Feedback, psychological/

39 Health education/

40 Health promotion/

41 Motivation/

42 Internet/

43 Motivational interviewing/

44 Persuasive communication/

45 Preventive health services/
46 Primary prevention/
47 Self-help groups/
48 Text messaging/
49 Therapy, computer-assisted/
50 counsel$.ti,ab,kf.
51 advice.ti,ab,kf.
52 advise$.ti,ab,kf.
53 behavio?r$ chang$.ti,ab,kf.
54 behavio?r$ intervention$.ti,ab,kf.
55 behavio?r$ modification$.ti,ab,kf.
56 motivational interview$.ti,ab,kf.
57 (cognitive behavio$ or behavio$ therap$ or cbt).ti,ab,kf.
58 brief intervention$.ti,ab,kf.
59 computer based.ti,ab,kf.
60 self help.ti,ab,kf.
61 email$.ti,ab,kf.
62 internet.ti,ab,kf.
63 text messag$.ti,ab,kf.
64 (web or website).ti,ab,kf.
65 ((reduc$ or decreas$ or prevent$ or delay or avoid) adj3 initiation$).ti,ab,kf.
66 (intervention$ or prevent$ or psychosocial).ti.
67 or/31-66
68 30 and 67
69 substance-related disorders/pc
70 amphetamine-related disorders/pc
71 cocaine-related disorders/pc
72 inhalant abuse/pc
73 marijuana abuse/pc
74 opioid-related disorders/pc
75 phencyclidine abuse/pc

76 substance abuse, intravenous/pc

77 substance abuse, oral/pc

78 ((reduc* or decreas* or prevent* or delay or avoid) adj3 (drug$ or substance$ or marijuana* or cannabi* or opioid* or opiate* or heroin or oxycodone or hydrocodone or crack or cocaine or pain relief or pain reliever$ or pain medication$ or prescription$ or medicine$ or over the counter or OTC) adj5 (abuse$ or abusing or misuse$ or misusing or overus$ or overuitili$ or use$ or using or experiment$)).ti,ab,kf.

79 or/68-78

80 adolescent/ or child/

81 (child$ or teen or teens or teenage$ or adolescen$ or youth or youths or young people or pediatric$ or paediatric$ or school age$ or juvenile$).ti,ab,kf.

82 79 and (80 or 81)

83 (clinical trial or controlled clinical trial or randomized controlled trial or adaptive clinical trial or equivalence clinical trial or pragmatic clinical trial or meta analysis).pt.

84 clinical trials as topic/ or controlled clinical trials as topic/ or randomized controlled trials as topic/ or adaptive clinical trials as topic/ or equivalence clinical trials as topic/ or pragmatic clinical trials as topic/

85 Meta-Analysis as Topic/

86 Random allocation/

87 clinical trial$.ti,ab,kf.

88 (control$ adj3 (study or studies or trial$)).ti,ab,kf.

89 random$.ti,ab,kf.

90 (metaanaly$ or meta analy$).ti,ab,kf.

91 trial.ti.

92 or/83-91

93 82 and 92 (3022)

94 limit 93 to (english language and yr="2013 -Current")

95 remove duplicates from 94

96 Young adult/

97 Universities/

98 Student Health Services/

99 ((young or emerging or early) adj adult$).ti,ab,kf.

100 (late adj (teen$ or adolescen$)).ti,ab,kf.

101 (college$ or universit$).ti,ab,kf.
102 ((undergraduate or graduate) adj student$).ti,ab,kf.
103 (high school adj2 senior$).ti,ab,kf.
104 12th grade.ti,ab,kf.
105 or/96-104
106 79 and 92 and 105
107 limit 106 to (english language and yr="1992 -Current")
108 remove duplicates from 107
109 95 or 108
110 Animals/ not (Humans/ and Animals/)
111 109 not 110

PsycINFO
Database: PsycINFO <1806 to January Week 3 2019>

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1 Drug Abuse/
2 "substance use disorder"/
3 Drug Usage/
4 Inhalant Abuse/
5 Glue Sniffing/
6 Polydrug Abuse/
7 Drug Abstinence/
8 Intravenous Drug Usage/
9 Marijuana Usage/
10 Cocaine/
11 Opiates/
12 Hallucinogenic Drugs/
13 Phencyclidine/
14 Methamphetamine/
15 Methylenedioxymethamphetamine/
16 Lysergic Acid Diethylamide/
17 ((drug or drugs or substance$) adj1 ("use" or using)).ti,ab,id.

18 ((drug or drugs or substance$) adj5 (abuse$ or abusing or misus$ or overus$ or overutili$ or nonprescri$ or non prescri$ or nonmedical or non medical or extramedical or extra medical or illicit$ or illegal$ or recreation$)).ti,ab,id.

19 ((opioid$ or opiate$ or oxycodone or hydrocodone or ritalin or adderall or amphetamine$ or methylphenidate or laughing gas or nitrous oxide or ketamine or dextromethorphan or GHB or gamma-hydroxybutyrate or inhalant$ or stimulant$ or sedative$ or barbiturate$ or benzodiazepine$ or sleep medication$) adj5 (use$ or using or abuse$ or abusing or misus$ or overus$ or overutili$ or nonprescri$ or non prescri$ or nonmedical or non medical or extramedical or extra medical or illicit$ or illegal$ or recreation$)).ti,ab,id.

20 ((pain relief or pain reliever$ or pain medication$ or medicine$ or over the counter or OTC) adj5 (abuse$ or abusing or misus$ or overus$ or overutili$ or non prescript$ or nonmedical or non medical or extramedical or extra medical or illicit$ or illegal$ or recreation$)).ti,ab,id.

21 (prescription$ adj5 (abuse$ or abusing or misus$ or overus$ or overutili$ or nonmedical or non medical or extramedical or extra medical or illicit$ or illegal$ or recreation$)).ti,ab,id.

22 ((street$ or designer$ or club) adj drug$).ti,ab,id.

23 legal high$.ti,ab,id.

24 nmupd.ti,ab,id.

25 marijuana.ti,ab,id.

26 (Cannabi$ or hash or hashish).ti,ab,id.

27 (cocaine or methamphetamine$ or methamphetamine$ or khat).ti,ab,id.

28 (Heroin or opium or kratom or mitragyna speciosa or manufactured fentanyl).ti,ab,id.

29 (mdma or ecstasy or flunitrazepam or rohypnol or bath salts or synthetic cathinone).ti,ab,id.

30 (salvia or phencyclidine).ti,ab,id.

31 (hallucinogen$ or dimethyltryptamine or lsd or mescaline or psilocybin).ti,ab,id.

32 or/1-31

33 Health Promotion/

34 Motivation/

35 behavio?r$ chang$.ti,ab,id.

36 behavio?r$ intervention$.ti,ab,id.

37 behavio?r$ modification$.ti,ab,id.

38 behavior therapy/

39 cognitive behavior therapy/

40 cognitive therapy/

41 Cognitive Techniques/

42 (cognitive behavio$ or behavio$ therapy or cbt).ti,ab,id.
43 brief intervention$.ti,ab,id.
44 SBIRT.ti,ab,id.
45 Behavior Modification/
46 Behavior Change/
47 Persuasive Communication/
48 Motivational Interviewing/
49 motivational interview$.ti,ab,id.
50 Health Knowledge/
51 Health Behavior/
52 Health Education/
53 Client Education/
54 Feedback/
55 Online Therapy/
56 Computer Assisted Therapy/
57 Computer Mediated Communication/
58 Internet/
59 computer based.ti,ab,id.
60 text messag$.ti,ab,id.
61 email$.ti,ab,id.
62 internet.ti,ab,id.
63 (web or website).ti,ab,id.
64 Self Help Techniques/
65 self help.ti,ab,id.
66 counseling/
67 Group Counseling/
68 counsel$.ti,ab,id.
69 counselling.ti,ab,id.
70 advice.ti,ab,id.
71 advise$.ti,ab,id.
72 (intervention$ or prevention or preventive or psychosocial).ti.

73 ((reduc$ or decreas$ or prevent$ or delay or avoid) adj3 initiation$).ti,ab,id.

74 or/33-73

75 32 and 74

76 Drug Abuse Prevention/

77 ((reduc* or decreas* or prevent* or delay or avoid) adj3 (drug$ or substance$ or marijuana* or cannabi* or opioid* or opiate* or heroin or oxycodone or hydrocodone or crack or cocaine or pain relief or pain reliever$ or pain medication$ or prescription$ or medicine$ or over the counter or OTC) adj5 (abuse$ or abusing or misuse$ or misusing or overus$ or overuitili$ or use$ or using or experiment$)).ti,ab,id.

78 75 or 76 or 77

79 (adolescence 13 17 yrs or childhood birth 12 yrs).ag.

80 (child$ or teen or teens or teenage$ or adolescen$ or youth or youths or young people or pediatric$ or paediatric$ or school age$ or juvenile$).ti,ab,id.

81 79 or 80

82 78 and 81

83 (treatment outcome or clinical trial).md.

84 Experiment Controls/

85 (control$ adj3 (study or studies or trial$)).ti,ab,id.

86 clinical trial$.ti,ab,id.

87 random$.ti,ab,id.

88 meta analy$.ti,ab,id.

89 metaanaly$.ti,ab,id.

90 trial.ti.

91 or/83-90

92 82 and 91

93 limit 92 to (english language and yr="2013 -Current")

94 young adulthood 18 29 yrs.ag.

95 emerging adulthood/

96 colleges/ or community colleges/ or college students/

97 ((young or emerging or early) adj adult$).ti,ab,id.

98 (late adj (teen$ or adolescen$)).ti,ab,id.

99 (college$ or universit$).ti,ab,id.

100 ((undergraduate or graduate) adj student$).ti,ab,id.

101 (high school adj2 senior$).ti,ab,id.

102 12th grade.ti,ab,id.

103 or/94-102

104 78 and 103

105 78 and 91 and 103

106 limit 105 to (english language and yr="1992 -Current")

107 93 or 106

PubMed, publisher-supplied records

#26	(#22 OR #25) AND publisher[sb]
#25	#24 AND ("1992/01/01"[Date - Publication] : "3000"[Date - Publication]) AND English[Language]
#24	#9 AND #18 AND #20 AND #23
#23	young adult*[tiab] OR emerging adult*[tiab] OR early adult*[tiab] OR late teen*[tiab] OR late adolescen*[tiab] OR college*[tiab] OR university*[tiab] OR undergraduate student*[tiab] OR graduate student*[tiab] OR high school senior*[tiab] OR 12th grade[tiab]
#22	#21 AND ("2013/01/01"[Date - Publication] : "3000"[Date - Publication]) AND English[Language]
#21	#9 AND #18 AND #19 AND #20
#20	random*[tiab] OR clinical trial*[tiab] OR controlled trial*[tiab] OR “controlled study”[tiab] OR “controlled studies”[tiab] OR trial*[title] or meta analy*[tiab] OR metaanaly*[tiab]
#19	child*[tiab] OR teen[tiab] OR teens[tiab] OR teenage*[tiab] OR adolescen*[tiab] OR youth[tiab] OR youths[tiab] OR "young people"[tiab] OR pediatric*[tiab] OR paediatric*[tiab] OR school age*[tiab] OR juvenile*[tiab]
#18	#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17
#17	intervention*[ti] OR prevention[ti] OR preventive[ti] OR psychosocial[ti]
#16	"patient education"[tiab] OR "health education"[tiab] OR "health promotion"[tiab]
#15	email*[tiab] OR internet[tiab] OR text messag*[tiab] OR web[tiab] OR website[tiab]
#14	brief intervention*[tiab] OR SBIRT[tiab]
#13	cognitive behavio*[tiab] OR behavio* therap*[tiab] OR cbt[tiab]

#12	motivational interview*[tiab]
#11	behavio* chang*[tiab] OR behavio* intervention*[tiab] OR behavio* modification*[tiab]
#10	counsel*[tiab] OR advice[tiab] OR advise*[tiab]
#9	#3 OR #4 OR #5 OR #6 OR #7 OR #8
#8	marijuana[tiab] OR Cannabi*[tiab] OR hash[tiab] OR hashish[tiab] OR cocaine[tiab] OR methamphetamine[tiab] OR khat[tiab] OR "Catha edulis”[tiab] OR Heroin[tiab] OR opium[tiab] OR kratom[tiab] OR “mitragyna speciosa”[tiab] OR “manufactured fentanyl” [tiab] OR mdma[tiab] OR ecstasy[tiab] OR flunitrazepam[tiab] OR rohypnol[tiab] OR “bath salts”[tiab] OR “synthetic cathinone”[tiab] OR salvia[tiab] OR phencyclidine[tiab] OR hallucinogen*[tiab] OR dimethyltryptamine[tiab] OR lsd[tiab] OR mescaline[tiab] OR psilocybin[tiab]
#7	nmupd[tiab]
#6	legal high*[tiab]
#5	street drug*[tiab] OR designer drug*[tiab] OR club drug*[tiab]
#4	drug use*[tiab] OR substance use*[tiab] OR using drug*[tiab]
#3	#1 AND #2
#2	abuse*[tiab] OR abusing[tiab] OR misus*[tiab] OR overus*[tiab] OR overutili*[tiab] OR nonprescri*[tiab] OR non prescri*[tiab] OR nonmedical[tiab] OR "non medical"[tiab] OR extramedical[tiab] OR "extra medical"[tiab] OR illicit*[tiab] OR illegal*[tiab] OR recreation*[tiab]
#1	drug[tiab] OR drugs[tiab] OR substance*[tiab] OR opioid*[tiab] OR opiate*[tiab] OR oxycodone[tiab] OR hydrocodone[tiab] OR ritalin[tiab] OR adderall[tiab] OR Adderall[tiab] OR amphetamine*[tiab] OR methylphenidate[tiab] OR “laughing gas”[tiab] OR “nitrous oxide” [tiab] OR ketamine[tiab] OR dextromethorphan[tiab] OR GHB[tiab] or “gamma-hydroxybutyrate”[tiab] OR inhalant*[tiab] OR stimulant*[tiab] OR sedative*[tiab] OR barbiturate*[tiab] OR benzodiazepine*[tiab] OR sleep medication*[tiab] OR “pain relief”[tiab] OR pain reliever*[tiab] OR pain medication*[tiab] OR medicine*[tiab] OR “over the counter”[tiab] OR OTC[tiab] prescription*[tiab]

Appendix A Table 1. Inclusion and Exclusion Criteria

	Included	Excluded
Aim	Preventing illicit and nonmedical drug use is a primary study aim, with or without addressing other substances or behaviors (e.g., addressing drug use *and* alcohol and tobacco use, addressing drug use *and* risky sexual behaviors)	Change in drug use is not a stated aim but is a reported outcome
Condition	*Any* use of psychoactive illicit drugs and nonmedical use of psychoactive prescription or over-the-counter medications, e.g.: • Cannabinoids (marijuana, hashish, synthetic cannabinoids) • Club drugs (3,4-methylenedioxymethamphetamine [MDMA or ecstasy], flunitrazepam [Rohypnol], gamma-hydroxybutyrate [GHB], synthetic cathinone [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	• Children, adolescents, and young adults (age ≤25 years), including pregnant females who do not regularly use illicit drugs or medications for nonmedical psychoactive effects. • A priori subpopulations of interest will be examined based on: age (early childhood, preadolescent, adolescent, young adult), sex, race/ethnicity, risk level, rural vs. urban residence, and substance used	• Young persons who regularly use illicit drugs or prescription drugs nonmedically, including those with harmful or hazardous use, or with drug abuse or dependence (*DSM-IV-TR*) or a drug use disorder (*DSM-5*)[1] • Children and adolescents seeking treatment for drug-related issues[1] • Children and adolescents who are referred to treatment for drug-related issues by the juvenile justice system, a social or health agency, or their parents, or otherwise directly referred for substance abuse treatment in a specialty setting[1] • Trials limited to young persons with health issues (e.g., schizophrenia, HIV) that would limit generalizability to general primary care patients
Interventions	• Counseling interventions designed to prevent and/or reduce illicit and nonmedical prescription drug use, with or without referral, including interventions targeting parents or caregivers to prevent and/or reduce drug use in young persons • Counseling interventions can vary in their approach (e.g., 12-step programs, cognitive behavioral therapy, motivational enhancement therapy), specific strategies (e.g., action plans, diaries), delivery method (e.g., in person, electronic, individual, group-based), length of contact (e.g., brief, extended), and number of contacts (e.g., single, multiple)	• Detoxification, medically managed withdrawal, or medication-assisted treatment (e.g., methadone maintenance programs, buprenorphine, naltrexone) • Maintaining abstinence after substance use treatment for dependence or drug use disorder (i.e., secondary abstinence) • Broad public health, media, or policy interventions • Inpatient/residential treatment • Contingency management/vouchers • Vocational rehabilitation/customized employment supports • Outward Bound/life skills training

Appendix A Table 1. Inclusion and Exclusion Criteria

	Included	Excluded
Comparators	• No intervention • Usual care • Waitlist • Attention control (e.g., intervention is similar in format and intensity but on a different content area) • Minimal intervention (no more than one brief contact [i.e., <5 minutes] per year or brief written materials, such as pamphlets)	Active intervention (i.e., more than one brief contact per year or brief written materials)
Outcomes	**KQ 1: Health, social, educational, and other outcomes** *Health outcomes* • All-cause mortality • Drug-related mortality (intentional and unintentional) • Drug-related morbidity (including but not limited to: mental health disorders; STI/HIV transmission; hepatitis B or C virus transmission; unintended pregnancy/pregnancy complications; deep bacterial abscesses; endocarditis; respiratory infections; cardiovascular complications; stroke; seizures) • Drug-related injury or accidents • Nonfatal overdose • Quality of life • Pain • Other drug-related consequences *Social, educational, or other outcomes:* • Health care utilization • Global functioning • Educational attainment/school performance • Social/legal outcomes (e.g., incarceration, out-of-home juvenile placement, criminal activity, violence, driving under the influence) • Family functioning • Other related social or educational outcomes **KQ 2: Behavioral outcomes** • Drug use (**required**) (self-reported and/or biologic measures): o Abstinence (use/no use) o Frequency and/or quantity of use o Severity of substance 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) o Meeting criteria for substance use disorder • Composite substance use outcome • Other risky behaviors (e.g., alcohol, tobacco, or other drug use; risky sexual behaviors) **KQ 3: Harms** • Serious treatment-related harms at any time point after the intervention began (e.g., death (including suicide), seizure, cardiovascular event, or other medical issue requiring urgent medical treatment) • Demoralization due to failed quit attempt • Harms associated with parents finding out about their children's drug use • Discontinuation of effective treatment due to fears of addiction (e.g., ADHD medication)	• Attitudes, knowledge, or beliefs related to drug use • Intention to change behavior • Intervention participation/compliance

Appendix A Table 1. Inclusion and Exclusion Criteria

	Included	Excluded
Outcome assessment timing	At least 3 months after baseline measurement (except for studies in pregnant women, for which shorter length of follow-up will be included)	Less than 3 months after baseline measurement
Setting	• Primary care settings • Other primary care–relevant settings, including other health care clinics, emergency departments, research clinics/offices, school health clinics, community centers, homes, and virtual settings (e.g., online support groups)	• Substance abuse treatment centers • School classrooms • Worksites • Inpatient/residential settings • Other institutions (e.g., juvenile detention facility)
Study design	• Randomized, controlled trials • Cluster randomized, controlled trials • Nonrandomized, controlled trials	• Prospective or retrospective cohort studies • Case-control studies • Time-series studies • Before-after studies • Cross-sectional studies • Editorials, commentaries, case studies, case series
Study geography	Studies conducted in countries categorized as “Very High” on the United Nations Human Development Index (based on 2015 indicators)	Studies conducted in countries not categorized as “Very High” on the 2015 Human Development Index
Publication language	English	Languages other than English
Quality rating	Fair- or good-quality studies	Poor-quality studies (according to design-specific USPSTF criteria)

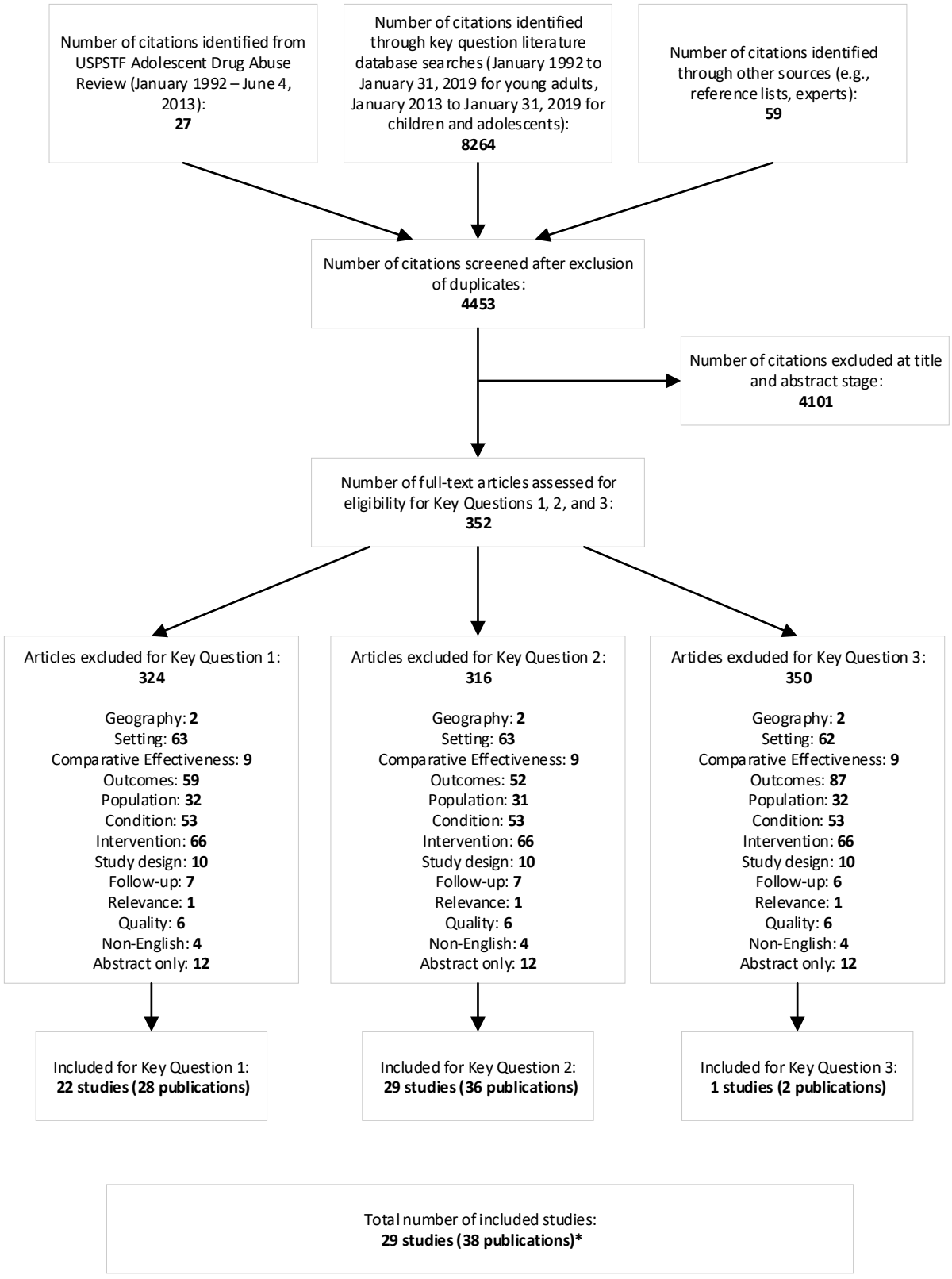
Abbreviations: KQ = Key Question; USPSTF = U.S. Preventative Services Task Force.

Appendix A Table 2. Study Design-Specific Quality Rating Criteria

Study Design	Adapted Quality Criteria
Randomized and non-randomized controlled trials, adapted from the U.S. Preventive Services Task Force methods[74]	**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 inferential statistics **Bias in reporting results selectively** • No evidence that the measures, analyses, or subgroup analyses are selectively reported

* Good quality studies generally meet all quality criteria. Fair quality studies do not meet all the criteria but do not have critical limitations that could invalidate study findings. Poor quality studies have a single fatal flaw or multiple important limitations that could invalidate study findings. Critical appraisal of studies using *a priori* quality criteria are conducted independently by at least two reviewers. Disagreements in final quality assessment are resolved by consensus, and, if needed, consultation with a third independent reviewer.

Appendix A Figure 1. Literature Flow Diagram



*Studies may appear in more than one Key Question.

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

Baldus, C, Thomsen, M, et al. Evaluation of a German version of the Strengthening Families Programme 10-14: a randomised controlled trial. Eur J Public Health. 26(6): 953-959. 2016. https://dx.doi.org/10.1093/eurpub/ckw082

Broning, S, Sack, PM, et al. Implementing and evaluating the German adaptation of the "Strengthening Families Program 10 - 14"- a randomized-controlled multicentre study. BMC Public Health. 14. 83. 2014. https://dx.doi.org/10.1186/1471-2458-14-83

Broning, Sonja, Baldus, Christiane, et al. Children with elevated psychosocial risk load benefit most from a family-based preventive intervention: Exploratory differential analyses from the German "Strengthening Families Program 10-14" adaptation trial. Prevention Science. 18(8): 932-942. 2017. http://dx.doi.org/10.1007/s11121-017-0797-x

Bannink, R, Broeren, S, et al. Effectiveness of a Web-based tailored intervention (E-health4Uth) and consultation to promote adolescents' health: randomized controlled trial. J Med Internet Res. 16(5): e143. 2014. https://dx.doi.org/10.2196/jmir.3163

Barlow, A, Varipatis-Baker, E, et al. Home-visiting intervention to improve child care among American Indian adolescent mothers: a randomized trial. Arch Pediatr Adolesc Med. 160(11): 1101-7. 2006. PMID: 17088511. https://dx.doi.org/10.1001/archpedi.160.11.1101

Barlow, Allison, Mullany, Britta, et al. Effect of a paraprofessional home-visiting intervention on American Indian teen mothers' and infants' behavioral risks: A randomized controlled trial. Am J Psychiatry. 170(1): 83-93. 2013. http://dx.doi.org/10.1176/appi.ajp.2012.12010121

Barlow, A, Mullany, B, et al. Paraprofessional-delivered home-visiting intervention for American Indian teen mothers and children: 3-year outcomes from a randomized controlled trial. Am J Psychiatry. 172(2): 154-62. 2015. https://dx.doi.org/10.1176/appi.ajp.2014.14030332

Mullany, Britta, Barlow, Allison, et al. The Family Spirit Trial for American Indian teen mothers and their children: CBPR rationale, design, methods and baseline characteristics. Prevention Science. 13(5): 504-518. 2012. http://dx.doi.org/10.1007/s11121-012-0277-2

D'Amico, EJ, Parast, L, et al. Brief motivational interviewing intervention to reduce alcohol and marijuana use for at-risk adolescents in primary care. J Consult Clin Psychol. 86(9): 775-786. 2018. PMID: 30138016. https://dx.doi.org/https://dx.doi.org/10.1037/ccp0000332

Dembo, Richard, Briones-Robinson, Rhissa, et al. Brief intervention impact on truant youths' marijuana use: Eighteen-month follow-up. J Child Adolesc Subst Abuse. 25(1): 18-32. 2016. http://dx.doi.org/10.1080/1067828X.2013.872068

Dembo, Richard, Cervenka, KathleenA, et al. Engaging high risk families in community based intervention services. Aggress Violent Behav. 4(1): 41-58. 1999. http://dx.doi.org/10.1016/S1359-1789%2897%2900028-1

Estrada, Y, Lee, TK, et al. eHealth Familias Unidas: Efficacy Trial of an Evidence-Based Intervention Adapted for Use on the Internet with Hispanic Families. Prevention Science. 10. 10. 2018. https://dx.doi.org/10.1007/s11121-018-0905-6

Fang, L, Schinke, SP, et al. Preventing substance use among early Asian-American adolescent girls: initial evaluation of a web-based, mother-daughter program. J Adolesc Health. 47(5): 529-532. 2010.

Fang, L, Schinke, SP. Two-year outcomes of a randomized, family-based substance use prevention trial for Asian American adolescent girls. Psychol Addict Behav. 2012.

Foxcroft, DR, Callen, H, et al. Effectiveness of the strengthening families programme 10-14 in Poland: cluster randomized controlled trial. Eur J Public Health. 27(3): 494-500. 2017. https://dx.doi.org/10.1093/eurpub/ckw195

Gmel, G, Gaume, J, et al. Effectiveness of a brief integrative multiple substance use intervention among young men with and without booster sessions. J Subst Abuse Treat. 44(2): 231-40. 2013. https://dx.doi.org/10.1016/j.jsat.2012.07.005

Harris, SK, Csemy, L, et al. Computer-facilitated substance use screening and brief advice for teens in primary care: an international trial. Pediatrics. 129(6): 1072-1082. 2012.

Jalling, Camilla, Bodin, Maria, et al. Parent programs for reducing adolescent's antisocial behavior and substance use: A randomized controlled trial. J Child Fam Stud. 25(3): 811-826. 2016. http://dx.doi.org/10.1007/s10826-015-0263-y

Johnson, Sarah Lindstrom, Jones, Vanya, et al. Promoting "healthy futures" to reduce risk behaviors in urban youth: A randomized controlled trial. Am J Community Psychol. 56(1-2): 36-45. 2015. http://dx.doi.org/10.1007/s10464-015-9734-y

Kerr, JC, Valois, RF, et al. Effects of Promoting Health Among Teens on Dietary, Physical Activity and Substance Use Knowledge and Behaviors for African American Adolescents. American Journal of Health Education. 44(4): 191-202. 2013.

Kim, HK, Leve, LD. Substance use and delinquency among middle school girls in foster care: a three-year follow-up of a randomized controlled trial. J Consult Clin Psychol. 79(6): 740-750. 2011. https://dx.doi.org/22004305

Kim, HK, Pears, KC, et al. Intervention Effects on Health-Risking Sexual Behavior Among Girls in Foster Care: The Role of Placement Disruption and Tobacco and Marijuana Use. J Child Adolesc Subst Abuse. 22(5): 370-387. 2013.

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Appendix C. Excluded Studies

Reason for Exclusion*
E1. Geography: Not a country with a very high HDI ranking
E2. Setting: Excluded on the basis of setting alone (e.g., substance abuse treatment centers, school classrooms, worksites, inpatient/residential, other institutions (e.g., juvenile detention facilities)
E3. Comparative Effectiveness (control group received active intervention)
E4. No relevant outcomes
E5. Population: **E5a.** Does not target youth or young adults, or average age of study sample >22 years old **E5b.** Youth with health conditions that limit generalizability (schizophrenia/psychosis, HIV), individuals in juvenile justice system, court-mandated
E6. Condition **E6a.** Non-psychoactive drugs **E6b.** >50% with regular drug use (weekly use, injection use, positive screener), harmful/hazardous use, or diagnosable disorder
E7. Intervention **E7a.** Not a primary care-relevant behavioral counseling intervention **E7b.** Drug misuse is not a primary target of the intervention
E8. Study Design: Not an RCT or CCT
E9. Followup: <3 months (12 weeks) followup post baseline (does not apply to harms)
E10. Study Relevance
E11. Poor Quality Rating
E12. Non-English
E13. Conference abstract

*Assigned at full-text phase.

Abbreviations: E = exclude

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Appendix D Table 1. Population Characteristics, Sorted by Author

Author, year	Population	Mean age (range)	Female, %	Race/ Ethnicity, %	SES	BL drug use	BL alcohol use	BL mental health	BL other comorbidities
Baldus, 2016[81]	Aged 10-14 youth not diagnosed with substance use disorder	12 (10-14)	41.4	NR	Financial strain, n (%): No: 155 (53.1%) Yes: 137 (46.9%) Participating parent's education, n (%): High school graduate: 148 (95.5%) Other: 5 (3.2%) None: 2 (1.3%) Living with both biological parents: 51%	% Used Cannabis: 1.7 % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: Lifetime	% Used: 21.6 Frequency: Other: Over: Lifetime	NR	Problem behavior, n (%): Self-reported score above cut-off (>85th percentile of norm): 20 (6.8%) Parent-reported score above cut-off (93rd percentile of norm): 25 (8.6%)
Bannink, 2014[82]	Aged 15-16	15.9 (15-16)	45.3	NR	Ethnicity classified as Dutch/non-Dutch where Dutch = person whose parents were born in the Netherlands regardless of where you were born. Dutch = 957/1256; Non-Dutch 299/1256.	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: NR	% Used: Frequency: Other: Over:	NR	NR
Barlow, 2006[85]	Pregnant American Indian youth aged 12 to 19	17 (14-20)	100	AI/AN: 100	Education <12 years:41 (77%) >=12 years: 12 (23) Currently employed: 7 (13%)	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: NR	% Used: 87 Frequency: Other: Over: Lifetime	Depression, mean: IG: 17.7 CG: 18.4	NR

Appendix D Table 1. Population Characteristics, Sorted by Author

Author, year	Population	Mean age (range)	Female, %	Race/ Ethnicity, %	SES	BL drug use	BL alcohol use	BL mental health	BL other comorbidities
Barlow, 2013[83]	Pregnant American Indian youth aged 12-19	18.12 (12-19)	100	AI/AN: 100	n (%) Currently unmarried: 311 (96.58%) Currently in school: 131 (40.68%) Currently employed: 23 (7.14%) Completed high school/GED: 88 (27.33%)	% Used Cannabis: 78.88 % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: Lifetime	% Used: 84.16 Frequency: Other: Over: Lifetime	CES-D score for depressive symptoms, n (%) (score of 16+ = depressive symptoms) ≤16: 218 (67.70%) >16: 104 (32.30%)	NR
D'Amico, 2018[116]	Adolescents aged 12 to 18 at risk for alcohol abuse	16.0 (12-18)	56.8	White: 11.5 Black: 16.7 Hisp: 66.3 Other: 5.4	n (%) Maternal education some college or more: 65 (22.1)	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: 9.8 Times used any drug: NR Over: 1 year	% Used: NR Frequency: 10.0 Other: Over: 1 year	NR	NR
Dembo, 2016[88]	Truant youth, aged 11-17	14.80 (11-17)	37.0	White: 37.3 Black: 25.7 Asian: 1.0 AI/AN: 0.3 Hisp: 28.7 Other: 7.0	Family annual income level % (n=297): <$5000: 5.1% $5000-10,000: 8.1% $10,000-25,000: 26.3% $25,000-40,000: 27.9% $40,000-75,000: 22.9% >$75,000: 9.8%	% Used Cannabis: 82.3 % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: 1 month	% Used: NR Frequency: Other: Over:	NR	Legal problem resulting in jail time or detention: 26.4%
Estrada, 2018[90]	Eighth graders with behavior problems	13.6 (NR)	37	Hisp: 100	% yearly household incomes below $20,000 = 55.7 Majority of adolescents born outside USA mainly from Cuba (20%), Honduras (6%), and Colombia (3%)	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: 0.61 Times used any drug: NR Over: 3 months	% Used: Frequency: 0.64 Other: Over: 3 months	NR	NR

Appendix D Table 1. Population Characteristics, Sorted by Author

Author, year	Population	Mean age (range)	Female, %	Race/ Ethnicity, %	SES	BL drug use	BL alcohol use	BL mental health	BL other comorbidities
Fang, 2010[92]	Asian American girls, aged 10-14	13.10 (10-14)	100	Asian: 100	Single mothers % (n): 16.67 (18) Foreign born mothers % (n): 58.33 (63) Foreign born girls % (n): 19.44 (21) Mother's education % (n) High school: 27.78 (30) College: 31.7 (33) Graduate school: 32.41 (35)	% Used Cannabis: 3.8 % Used Any Drug: NR Times used cannabis: 0.03 Times used any drug: NR Over: 1 month	% Used: 6.7 Frequency: 0.16 Other: Over: 1 month	Depression: CDI = 1.51	NR
Foxcroft, 2017[93]	Children ages 10 to 14	11.9 (10-14)	40	NR	Highest parent education level, primary = 14.0 Highest parent education level, secondary = 28.1 Highest parent education level, college = 24.4 Highest parent education level, university = 33.6 Family structure, % dual parent = 74.3 Parent employment status, % employed full time = 57.3	% Used Cannabis: NR % Used Any Drug: 4 Times used cannabis: NR Times used any drug: NR Over: 1 year	% Used: 15 Frequency: Other: Over: 1 month	NR	NR
Gmel, 2013[94]	Male conscripts, age 19 or greater	20.1 (NR)	0	NR	Mandatory (9 years of schooling), 40.7% Apprenticeship, professional school, 31.8% High school preparing for eligibility for universities, 27.5%	% Used Cannabis: 46 % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: 6 months	% Used: 55 Frequency: Other: heavy use (binge episode) >1 Over: 1 month	NR	NR

Appendix D Table 1. Population Characteristics, Sorted by Author

Author, year	Population	Mean age (range)	Female, %	Race/ Ethnicity, %	SES	BL drug use	BL alcohol use	BL mental health	BL other comorbidities
Harris, 2012[80]	Aged 12-18 (New England) or 13-17 (Prague) with a routine primary care appointment	15.6 (12-18)	55.8	NR	Parents' highest education level (%): College/Uni or higher: 1165 (43.4); High school/secondary school graduate: 1049 (39.1); Did not complete HS/SS: 171 (6.4); Don't know: 222 (8.4)	% Used Cannabis: 13.2 % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: 3 months	% Used: 32.3 Frequency: Other: Over: 3 months	NR	NR
Jalling, 2016[95]	At-risk youth not being treated for alcohol or drug use, aged 12-18	14.60 (12-18)	47.2	NR	Foreign born mother, %: IG2: 19.8 IG1: 20.0 CG: 20.9 Single-parent family, %: IG2: 43.7 IG1: 50.7 CG: 41.5 Parent has university degree, %: IG2: 28.4 IG1: 17.1 CG: 28.0 Parent is employed, %: IG2: 86.4 IG1: 84.5 CG: 84.1	% Used Cannabis: NR % Used Any Drug: 16.9 Times used cannabis: NR Times used any drug: NR Over: 6 months	% Used: 70 Frequency: Other: Over: Lifetime	NR	95.4% of the adolescents reported having engaged in any delinquent behavior in previous 6 months.
Johnson, 2015[96]	Aged 14 to 21	17 (14-21)	60	Black: 96.0 Other: 4.0	Maternal education Some college: 39% HS grad/GED: 40 Dropout, no GED: 21 Participant education Drop out: 5% HS student: 68 HS grad/GED: 27	% Used Cannabis: 18.5 % Used Any Drug: NR Times used cannabis: 2.4 Times used any drug: NR Over: 30 days	% Used: 22 Frequency: 0.7 Other: Over: 30 days	NR	NR

Appendix D Table 1. Population Characteristics, Sorted by Author

Author, year	Population	Mean age (range)	Female, %	Race/ Ethnicity, %	SES	BL drug use	BL alcohol use	BL mental health	BL other comorbidities
Kerr, 2013[97]	Aged 14 to 17	NR (12-18)	60	White: 0.2 Black: 92.0 Asian: 1.2 AI/AN: 0.1 Hisp: 4.7 Other: 6.6	Free or reduced lunch: 73%	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: NR	NR	NR	NR
Kim, 2011[98]	Girls in foster care, aged 10-12	11.54 (10-12)	100	White: 63.0 Black: 9.0 AI/AN: 4.0 Hisp: 10.0 Other: 14.0	Caregiver family income, n (%): $24,999 or below: 20 (20%) $25,000-59,999: 50 (50%) $60,000 or more: 30 (30%)	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: NR	NR	Psychological adjustment (ASEBA) Internalizing behavior, mean (SD): CG 11.56 (9.42) IG 11.96 (8.19) Externalizing behavior, mean (SD): CG 14.38 (11.65) IG 16.06 (11.05)	NR
Knight, 2019[72]	Aged 12 to 18	14.8 (12-18)	50.6	White: 44.5 Hisp: 29.5 Other: 26.0	Two parents at home (%): 76.8 College-graduated parents or guardians (%): 64.2 In grades 9-12 (%): 57.2	% Used Cannabis: 12.2 % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: 1 year	NR	NR	NR

Appendix D Table 1. Population Characteristics, Sorted by Author

Author, year	Population	Mean age (range)	Female, %	Race/ Ethnicity, %	SES	BL drug use	BL alcohol use	BL mental health	BL other comorbidities
Lee, 2010[100]	Incoming college freshmen with any use of marijuana in previous 3 months	18 (17-19)	54.6	White: 75.7	NR	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: 9.86 Times used any drug: NR Over: 90 days	NR	NR	NR
Malmberg, 2014[102]	Aged 11 to 15 years	13.0 (11-15)	50.0	NR	Ethnicity classified as Dutch/non-Dutch where Dutch = person whose parents were born in the Netherlands regardless of where you were born. Dutch = 2332/2416; Non-Dutch 84/2416.	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: NR	NR	NR	NR
Mason, 2015[103]	Youth at risk for substance use disorder, aged 14-18	16.4 (14-18)	71	Black: 84	NR	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: 1 month	% Used: Frequency: 0.9 Other: Score from 0 (0 days) to 7 (all 30 days) Over: 1 month	NR	NR
Rhee, 2008[105]	Youth with asthma, aged 14-20	16.05 (14-20)	68	White: 63 Black: 29 AI/AN: 2 Hisp: 2 Other: 2	Family income <$30,000, 54%	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: NR	NR	NR	Asthma severity: Mild intermittent, 43% Mild persistent, 33% Moderate persistent, 24%

Appendix D Table 1. Population Characteristics, Sorted by Author

Author, year	Population	Mean age (range)	Female, %	Race/ Ethnicity, %	SES	BL drug use	BL alcohol use	BL mental health	BL other comorbidities
Sanci, 2015[106]	Aged 14-24	NR (14-24)	75.7	NR	Born in Australia, n (%): 756 (83.9%) Employment/Study status, n (%): Studying only: 237 (26.3%) Working only: 223 (24.8%) Both working and studying: 373 (41.4%) Neither working or studying: 65 (7.2%)	% Used Cannabis: NR % Used Any Drug: 26.5 Times used cannabis: NR Times used any drug: NR Over: 1 year	% Used: NR Frequency: NR Other: Risky use 364/901 (40.4%) Over: 1 year	Emotional distress (in last month): 264/901 (29.3%)	NR
Schinke, 2009a[107]	Females aged 11 to 13	12.7 (11-13)	100	White: 26.4 Black: 48.9 Hisp: 24.7	NR	% Used Cannabis: 2.7 % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: Lifetime	% Used: 34.2 Frequency: Other: Over: Lifetime	Depression score, mean: 1.67 (scale of 1-5 where lower scores are better)	NR
Schinke, 2009b[108]	Females aged 11 to 13	13 (11-13)	100	White: 23.2 Black: 40.6 Asian: 10.8 Hisp: 23.1 Other: 1.7	Single-parent household: 43.7% Two-parent household: 56.3% Mother's education, < High school: 6.3% Mother's education, High school: 9.1% Mother's education, Some college: 28.3% Mother's education, A.A. or B.A. degree: 42.6% Mother's education, Graduate degree: 13.7%	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: 0.09 Times used any drug: NR Over: 1 month	% Used: Frequency: 0.16 Other: Over: 1 month	3.35 on 5-point scale, higher scores better	NR

Appendix D Table 1. Population Characteristics, Sorted by Author

Author, year	Population	Mean age (range)	Female, %	Race/ Ethnicity, %	SES	BL drug use	BL alcohol use	BL mental health	BL other comorbidities
Schwinn, 2010[110]	Females aged 13-14	14 (13-14)	100	White: 61 Black: 16 Asian: 7 Hisp: 7 Other: 9	Live with mother and father, 53.0 %	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: NR	NR	NR	NR
Schwinn, 2015[112]	Sexual-minority adolescents, aged 15-16	16 (15-16)	50	White: 62.1 Black: 9.6 Asian: 7.4 Hisp: 13.2 Other: 7.5	NR	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: 1.8 Times used any drug: NR Over: 30 days	% Used: Frequency: 0.92 Other: Over: 30 days		
Schwinn, 2018[111]	Females aged 13 to 14 residing in the United States	13.7 (13-14)	100	White: 64.5 Black: 24.5 Hisp: 15.0 Other: 18.5	More than 80% of girls resided in urban areas, 9% in large towns, 10% in small towns/rural areas. The most recent average letter grade earned in school was 1.68 (where “mostly A’s” = 1 and “mostly B’s” = 2). One-half of parents had 2 or more years of college.	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: 0.82 Times used any drug: NR Over: 1 month	% Used: Frequency: 1.09 Other: Over: 1 month		
Walkup, 2009[113]	Pregnant American Indian youth, aged 12-22	18 (14-22)	100	AI/AN: 100	HS/GED/some college: 39% Current employment: 12%	% Used Cannabis: NR % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: NR	NR		

Appendix D Table 1. Population Characteristics, Sorted by Author

Author, year	Population	Mean age (range)	Female, %	Race/ Ethnicity, %	SES	BL drug use	BL alcohol use	BL mental health	BL other comorbidities
Walton, 2013[114]	Youth with past year cannabis use, aged 12 to 18	16.3 (12-18)	66.5	Black: 60.7 Hisp: 11.0	Dropped out of school: 5.8% Failing grades: 25.9%	% Used Cannabis: 100 % Used Any Drug: NR Times used cannabis: NR Times used any drug: NR Over: 3 months	% Used: 53.1 Frequency: 0.4 Other: Score from 0-4 where lower is better Over: 3 months		
Walton, 2014[115]	Youth with no cannabis use in past year, aged 12-18	14.9 (12-18)	57	Black: 63.7 Hisp: 9.2	Failing grades: 17.1%	% Used Cannabis: 0 % Used Any Drug: 6.9 Times used cannabis: NR Times used any drug: NR Over: 3 months	% Used: 12.0 Frequency: 0.2 Other: Score from 0-13 where lower is better Over: 3 months		

Abbreviations: AI/AN = American Indian/Alaska Native; ASEBA = Achenbach System of Empirically Based Assessment; BL = Baseline; CDI = Children's Depression Inventory; CES-D = Center for Epidemiologic Studies Depression Scale; CG = Control group; GED = General Education Development; HS = High School; IG = Intervention group; NR = Not reported; SES = Socioeconomic status; SD = Standard Deviation; SS = Secondary school.

Appendix D Table 2. Intervention Characteristics, Sorted by Author

Author, year	IG	Int target	Brief IG description	Int dur., wks	No. of sess.	Est hours	Int. format	Int. setting	Int. provider	CG category	Brief CG description
Baldus, 2016[81]	IG1	Youth, Parent	Strengthening Families Program 10-14: 11 x 2-hour family-based group sessions to reduce risk of substance abuse and behavior problems	26	11	22	Group (in-person)	Social services agency	Educator or Counselor NOS	Minimal	2-hour parent session on physical and mental changes effecting teenagers.
Bannink, 2014[82]	IG1	Youth	1 x 45-minute computer-based program to assess health-risk behavior and well-being with tailored messages; referred for consultation if at-risk of mental health problems or if youth self-refers	NR	2	1.2	Individual (in-person), Computer-based	School	Nurse, Self-Admin	Usual care	Usual care, briefer assessment of risk behaviors, option to self-refer to nurse
	IG2	Youth	1 x 45-minute computer-based program to assess health-risk behavior and well-being with tailored messages; option to self-refer to nurse	0.14	1	0.8	Computer-based	School	Self-Admin	Usual care	Usual care, briefer assessment of risk behaviors, option to self-refer to nurse
Barlow, 2006[85]	IG1	Youth	Family Spirit: 25 x 90-minute in-home sessions on parenting, substance abuse prevention, coping, and other maternal and infant health topics	39	25	37.5	Individual (in-person)	Home	Educator or Counselor NOS	Attention control	Breast-feeding/nutrition education during 23 1- to 1.5-hour home visits
Barlow, 2013[83]	IG1	Youth	Family Spirit: 43 x 60-minute in-home sessions on parenting, substance abuse prevention, coping, and other maternal and infant health topics	168	43	43	Individual (in-person)	Home	Educator or Counselor NOS	Minimal	Transportation assistance to regularly scheduled, clinic-based 7 prenatal and 9 well-baby visits, provision of pamphlets about child care and community resources for parents, and referrals to local services as needed.

Appendix D Table 2. Intervention Characteristics, Sorted by Author

Author, year	IG	Int target	Brief IG description	Int dur., wks	No. of sess.	Est hours	Int. format	Int. setting	Int. provider	CG category	Brief CG description
D'Amico, 2018[116]	IG1	Youth	1 x 15-20 minute individual brief motivational interview for youth focusing on motivation to change and substance use prevention	0.14	1	0.3	Individual (in-person)	Primary Care	Research staff NOS	Usual care	Brochure that included information on the effects of AOD use, how to prepare for risky situations, and online and telephone resources to obtain additional information.
Dembo, 2016[88]	IG1	Youth, Parent	2 x 75-min youth sessions on substance use and consequences 1 x 75-min parent session on parental attitudes of use	3	3	3.8	Individual (in-person)	Home	Research staff NOS	Attention control	Usual truancy services plus 3 weekly 1-hour visits to project staff with information on local services.
	IG2	Youth	2 x 75-minute individual sessions on substance use and consequences	2	2	2.5	Individual (in-person)	Home	Research staff NOS	Attention control	Usual truancy services plus 3 weekly 1-hour visits to project staff with information on local services.
Estrada, 2018[90]	IG1	Youth, Parent	Online version of Familias Unidas (eHealth Familias Unidas); 8 x 30-min online recorded e-parent group sessions accessed via the internet and 4 x 45-min parent-adolescent family sessions delivered by a facilitator via web-based video conferencing software	13	12	7	Computer-based, Video	Home	Research staff NOS, Self-Admin	Usual care	HIV prevention curriculum in health science class

Appendix D Table 2. Intervention Characteristics, Sorted by Author

Author, year	IG	Int target	Brief IG description	Int dur., wks	No. of sess.	Est hours	Int. format	Int. setting	Int. provider	CG category	Brief CG description
Fang, 2010[92]	IG1	Youth, Parent	10 x 35-45-minute interactive online sessions for mother-daughter dyads on family functioning, self-efficacy, social skills, and drug use prevention	26	10	7.5	Computer-based	Home	Self-Admin	Assessment only	No access to intervention
Foxcroft, 2017[93]	IG1	Youth, Parent	Strengthening Families Program 10-14: 7 x 120-min group substance use prevention sessions for parent-youth dyads	7	7	14	Group (in-person), Video	NR	Research staff NOS	Minimal	Leaflets
Gmel, 2013[94]	IG1	Youth	2 x 20-minute counseling sessions targeting multi-substance use behaviors in men ages 19 and older	0.28	2	0.7	Individual (in-person)	Other Medical	Psychologist	Assessment only	
Harris, 2012[80]	IG1	Youth	1 x 7-8-minute computer and provider based screening and intervention to not start/stop substance use	13	1	0.1	Individual (in-person), Computer-based	Primary Care	PCP	Usual care	NR
Jalling, 2016[95]	IG1	Parent	6 x 120-min group sessions to increase parental understanding of youth development & skill improvement	6	6	12	Group (in-person)	NR	Social Worker	Waitlist	6-month wait-list
	IG2	Parent	10 x 150-minute group parent sessions to help to develop and enhance their skills and self-efficacy for parenting	9	10	25	Group (in-person)	NR	Social Worker	Waitlist	6-month wait-list
Johnson, 2015[96]	IG1	Youth	3 positive youth development motivational interview sessions with phone or email followup targeting career readiness and addressing risky behaviors (time NR)	26	6	1.8	Individual (in-person)	Primary Care	Educator or Counselor NOS	Minimal	Invitation to bi-annual job and college fairs at the clinic, monthly newsletters with information about local opportunities to build their resume.

Appendix D Table 2. Intervention Characteristics, Sorted by Author

Author, year	IG	Int target	Brief IG description	Int dur., wks	No. of sess.	Est hours	Int. format	Int. setting	Int. provider	CG category	Brief CG description
Kerr, 2013[97]	IG1	Youth	2 x 8-hour group workshops covering diet, physical activity, and drug prevention	2	2	16	Group (in-person)	NR	NR	Attention control	Focus on Youth, a sexual risk reduction HIV/STI-prevention intervention. Similar frequency, length, and structure as the IG.
Kim, 2011[98]	IG1	Youth, Parent	6 group sessions of caregiver training; 6 group sessions of skill-building and 40 individual coaching sessions for adolescent girls (time NR)	43	46	86	Individual (in-person), Group (in-person)	NR	Research staff NOS, Lay provider	Usual care	Usual child welfare agency services
Knight, 2019[72]	IG1	Youth	1 2 to 5-minute conversation about the risks of substance abuse using motivational interviewing strategies	0.14	1	0.25	Individual (in-person)	Primary Care	PCP	Usual care	Self-administered computer screening
Lee, 2010[100]	IG1	Youth	1 computer-based individualized personalized feedback session (time NR)	0.14	1	0.5	Computer-based	Home	Self-Admin	Assessment only	No intervention
Malmberg, 2014[102]	IG1	Youth	3 interactive modules (1 module per year for 3 years) on substance use prevention (time NR)	156	3	1.5	Computer-based	School	Self-Admin	Usual care	Control schools agreed not to start any substance-related interventions in target group during study period, but could continue with already established programs.

Appendix D Table 2. Intervention Characteristics, Sorted by Author

Author, year	IG	Int target	Brief IG description	Int dur., wks	No. of sess.	Est hours	Int. format	Int. setting	Int. provider	CG category	Brief CG description
Mason, 2015[103]	IG1	Youth	1 x 20-minute individual motivational interviewing session with peer network counseling	0.14	1	0.3	Individual (in-person)	NR	Educator or Counselor NOS	Attention control	20-min review of handout on health behaviors (e.g., exercise, nutrition, weight management, life skills)
Rhee, 2008[105]	IG1	Youth	3 x 30-min CD-ROM sessions covering decision-making and risk behaviors	17	3	3.2	Individual (phone), Computer-based	Other Medical, Home	Nurse, Self-Admin	Minimal	Study skills CD-ROM, comparable time and duration
Sanci, 2015[106]	IG1	Youth, Practitioner	Provider training to screen for risky behaviors and discuss protective factors with youth, plus supported plan-do-study-act cycle.	NR	1	0.2	Individual (in-person)	Primary Care	Nurse, PCP	Assessment only	3-hour clinician seminar on youth-friendly care, including recommendations to discuss health risks with young people.
Schinke, 2009a[107]	IG1	Youth, Parent	9 x 45-minute individual computer sessions for mother-daughter dyads aimed to reduce substance use through mother-daughter interactions	9	9	6.8	Computer-based	Home	Self-Admin	Assessment only	No intervention
Schinke, 2009b[108]	IG1	Youth, Parent	9 X 45-minute weekly computer-based substance use prevention sessions plus two annual booster sessions for mother-daughter dyads	104	11	8.2	Computer-based	Home	Self-Admin	Assessment only	
Schwinn, 2010[110]	IG1	Youth	RealTeen: 12 x web-based modules and homepage access to curated online community	4	12	5	Computer-based	Home	Self-Admin	Assessment only	No intervention
Schwinn, 2015[112]	IG1	Youth	3 x 14-minute individual computer sessions for youth	4	3	0.7	Computer-based	Home	Self-Admin	Assessment only	None

Appendix D Table 2. Intervention Characteristics, Sorted by Author

Author, year	IG	Int target	Brief IG description	Int dur., wks	No. of sess.	Est hours	Int. format	Int. setting	Int. provider	CG category	Brief CG description
Schwinn, 2018[111]	IG1	Youth	RealTeen: 9 x 15-minute online substance use prevention sessions for girls aged 13-14	14	9	2.8	Computer-based	Home	Self-Admin	Assessment only	No intervention
Walkup, 2009[113]	IG1	Youth	Family Spirit: 25 x 60-minute in-home sessions on parenting, substance abuse prevention, and problem-solving and coping skills	38	25	25	Individual (in-person)	Home	Lay provider	Attention control	Breast-feeding/nutrition education during 23 1-hour home visits
Walton, 2013[114]	IG1	Youth	1 MI session (time NR)	0.14	1	0.6	Individual (in-person)	Primary Care	Educator or Counselor NOS	Minimal	
	IG2	Youth	1 computer-based MI session (time NR)	0.14	1	0.6	Computer-based	Primary Care	Self-Admin	Minimal	
Walton, 2014[115]	IG1	Youth	1 x 38-minute MI session	0.14	1	0.6	Individual (in-person)	Primary Care	Educator or Counselor NOS	Minimal	Brochure with warning signs of problematic cannabis use and community resources
	IG2	Youth	1 x 33-minute computer-based MI session	0.14	1	0.6	Computer-based	Primary Care	Self-Admin	Minimal	Brochure with warning signs of problematic cannabis use and community resources

Abbreviations: CG = Control group; STI = Sexually transmitted infection; IG = Intervention group; MI = Motivational interviewing; NOS = Not otherwise specified; NR = Not reported; PCP = Primary care provider.

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
Baldus, 2016[81]	IG1	Youth, Parent	Manual-based, 7 weekly sessions plus another 4 booster sessions that are conducted 4–6 months after the 7th session. In each session, at least three group facilitators work with 8–12 families, at first separately with parents and children, later with the whole family. Children sessions aim at improving children's self-efficacy and their ability to cope with stress and peer pressure. Parent sessions encourage caregivers to reflect their parenting style, to develop a more consistent form of parenting ("using love and limits"), and to express positive affect more openly. After each session, a family meal is provided to strengthen support and sharing between families. Families receive a €15 voucher after each session. Per clinical trial register: During the first hour of the training, parents and adolescents are separated and attend individual groups. In the second hour, families are reunited for the family session.	26 wks; 11; sessions 1320 min	Social services agency; Group (in-person); Educator or Counselor NOS	Minimal	Developed for 'assessment reactivity effects'. The programme gives information about the physical and mental changes affecting teenage youth. Parents are informed how they best can react to these changes and keep a trusting relationship. Video segments are used to show typical conflict situations at home and different ways to react to them. Material for this intervention came from a brochure with information about parenting for parents of adolescents (Starke Kinder - Ein Magazin für Eltern, BZgA; www.bzga.org) while the video segments came from another video-based prevention programme ("Freiheit in Grenzen"). A presentation with instructions along with video segments was sent to the cooperating agencies. At each agency, a

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
							staff member was assigned to deliver the event adhering closely to the slide show and instructions. Families allocated to the control condition are invited to a one-evening-only event, at which the two-hour programme was delivered. The event is closed with a complementary meal.
Bannink, 2014[82]	IG1	Youth	A 45-minute computer program covering 9 topics related to health risk behavior and well-being: alcohol consumption, drugs use, smoking, sexual behavior, bullying, mental health status, suicidal thoughts, suicidal attempts and unpleasant sexual experience. The messages were tailored for ages 12-18. For each topic a score is computed and compared to Dutch norms. Based on the score, a message related a message is presented that reflects the person's current behavior or well-being, the Dutch health norm, and offers advise to change unhealthy behavior or to talk to a person they trust, and links to websites. Immediately following completion of the program, adolescents are invited to join a Facebook group with further information. Adolescents can check a box for a	NR wks; 2; sessions 75 min	School; Individual (in-person),Computer-based; Nurse,Self-Admin	Usual care	Completed the same questionnaire assessing health-risk behaviors and well-being as adolescents in the intervention groups, with the exception of the questions on unpleasant sexual experience, suicidal thoughts, and suicidal attempts. The control group received care as usual (i.e., adolescents could check a box for a self-referral with the nurse or could send an email to the nurse with any question or request for information or care).

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			self-referral with the nurse, or can send an e-mail to the nurse. Those who report/score mental health problems are invited to have a consultation with the school nurse. After one month the adolescents receive a reminder of the tailored messages. Optional nurse consultation The consultation took place at school and was provided by school nurses who were already working at the schools and who had already provided consultations to adolescents at approximately 13 years of age. These nurses were trained to apply motivational interviewing with adolescents at age 15-16 years. They received the results of the assessment for each referred adolescent before the consultation. During the consultation, the nurses focused on specific risk areas and on mental health in particular. Furthermore, they either initiated a further consultation with themselves or referred adolescents to another professional if they deemed this necessary.				
	IG2	Youth	A 45-minute computer program covering 9 topics related to health risk behavior and well-being: alcohol consumption, drugs use, smoking, sexual behavior, bullying, mental health status, suicidal thoughts, suicidal attempts and	0.14 wks; 1; sessions 45 min	School; Computer-based; Self-Admin	Usual care	Completed the same questionnaire assessing health-risk behaviors and well-being as adolescents in the intervention groups, with the

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			unpleasant sexual experience. The messages were tailored for ages 12-18. For each topic a score is computed and compared to Dutch norms. Based on the score, a message related a message is presented that reflects the person's current behavior or well-being, the Dutch health norm, and offers advise to change unhealthy behavior or to talk to a person they trust, and links to websites. Immediately following completion of the program, adolescents are invited to join a Facebook group with further information. Adolescents can check a box for a self-referral with the nurse, or can send an e-mail to the nurse. After one month the adolescents receive a reminder of the tailored messages.				exception of the questions on unpleasant sexual experience, suicidal thoughts, and suicidal attempts. The control group received care as usual (i.e., adolescents could check a box for a self-referral with the nurse or could send an email to the nurse with any question or request for information or care).
Barlow, 2006[85]	IG1	Youth	The home-visiting intervention was modeled on "Healthy Families America." Healthy Families America is a national program founded on 12 research-based principles to ensure quality of home-visiting interventions for at-risk families. The content of the home-visiting intervention was derived from extensive community input on what teen parents needed to learn and was based on the American Academy of Pediatrics Guide to Baby Care: Caring for Your Baby and Young Child: Birth to Age 5. Lessons covered prenatal care, labor, delivery,	39 wks; 25; sessions 2250 min	Home; Individual (in-person); Educator or Counselor NOS	Attention control	Control participants received a breastfeeding education program that was developed in 1996-1997 by Johns Hopkins Center for American Indian Health and the participating communities. Participants assigned to the control arm were scheduled to receive 23 home visits covering 20 breastfeeding

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			breastfeeding, nutrition, parenting, home safety, immunizations, well-baby care, family planning, sexually transmitted disease prevention, and maternal goal setting for personal and family development. The curricular content was scheduled chronologically to provide key instruction at developmentally appropriate times for participants' children. The protocol included 25 home visits and 41 discrete lessons taught from 28 weeks' gestation until 6 months post-partum (about 9 months total) by the educators using tabletop flip charts. Home visits were scheduled to last approximately 1.5 hours. Cultural adaptations—including style, graphics, delivery, and content—were achieved through a community-based participatory process.				lessons. The expected visit duration was 1 to 1.5 hours.
Barlow, 2013[83]	IG1	Youth	Family Spirit: consists of 43 highly structured lessons delivered by Native paraprofessionals. Content targets three domains: parenting skills across early childhood (0–3 years); maternal drug abuse prevention; and maternal life skills and positive psychosocial development. Home visitors deliver lessons one-on-one in participants' homes using tabletop flip charts. The flip chart is designed so that the participant views illustrated content that often includes a real-life scenario while the home visitor	168 wks; 43; sessions 2580 min	Home; Individual (in-person); Educator or Counselor NOS	Minimal	OSC consists of transportation assistance to regularly scheduled, clinic-based prenatal and well-baby visits as recommended by the HIS and American Academy of Pediatrics, provision of pamphlets about child care and community resources for parents, and referrals to local

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			reviews an outline of key points relating to the scenario and illustration. Each home visit was designed to last ≤1 hour, including a brief warm-up conversation, conducting the lesson, a question/answer period, and providing summary handouts. Home visits occurred weekly through the end of pregnancy, biweekly until 4 months postpartum, monthly between 4 and 12 months postpartum, and bimonthly between 12 and 36 months postpartum. Staff also distribute quarterly study newsletters, birthday cards for mothers and their babies and annual certificates of program completion. Incentives in the form of Walmart gift cards are given for assessments, and increase with duration of participation in the study (i.e., start at $10 for initial assessment and increase by $5 per time point for maximum of $50 for final assessment). Optimized Standard Care (OSC, offered to both IG and CG, not counted in total session count): consists of transportation assistance to regularly scheduled, clinic-based prenatal and well-baby visits as recommended by the IHS and American Academy of Pediatrics, provision of pamphlets about child care and community resources for parents, and				services as needed. OSC visits include seven prenatal visits, nine well-baby visits during the first 3 years of life. 1 week, 2 weeks, and 2, 4, 6, 9, 12, 24 and 36 months postpartum), and four social support visits between years 2 and 3.

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			referrals to local services as needed. OSC visits include seven prenatal visits, nine well-baby visits during the first 3 years of life. 1 week, 2 weeks, and 2, 4, 6, 9, 12, 24 and 36 months postpartum), and four social support visits between years 2 and 3.				
D'Amico, 2018[116]	IG1	Youth	CHAT is a 15- to 20-min brief MI intervention that first focuses on assessing motivation for change by discussing adolescents' personal pros and cons of AOD use and determining what their friends think about AOD use and how this might affect their own use. The facilitator then provides normative information for AOD use. Next, adolescents are asked to discuss what they think might happen if they continue to use AOD in the same way. Depending on where adolescents are at in terms of wanting to make changes in their behavior, a discussion that addresses their willingness and confidence to cut back and/or stop their use follows. Finally, if adolescents are willing, they discuss a plan to prepare for high-risk situations where AOD might be present and how they could make a healthy choice in those situations. Facilitators delivered CHAT after adolescents completed their baseline survey	0.14 wks; 1; sessions 20 min	Primary Care: Individual (in-person); Research staff NOS	Usual care	Usual care participants received a brochure that included information on the effects of AOD use, how to prepare for risky situations, and online and telephone resources to obtain additional information.

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Dembo, 2016[88]	IG1	Youth, Parent	Youths were administered two BI sessions, and their parents/guardians were administered one BI session. Each BI session lasted for 1-1/4 hours, and occurred about a week apart. Each youth and parent/guardian was paid $15 for completing the baseline interview and each followup session. Youth The first BI session with the youth focused on discussing the youth's substance use and related consequences, the level of willingness to change, the causes and benefits of change, and what goals for change the youth wanted to select and pursue. The youth was encouraged to pursue goals of drug abstinence or reduction in drug use. In the second session with the youth, the counselor reviewed the youth's progress with the agreed upon goals, identified risk situations associated with difficulty in achieving goals, discussed strategies to overcome barriers toward goal achievement, reviewed where the youth was in the process of change, and negotiated either continuation or advancement of goals. Informed by an integrated behavioral and family therapy approach. Parent/guardian The parent BI session addressed	3 wks; 3; sessions 225 min	Home; Individual (in-person); Research staff NOS	Attention control	In addition to the normal truancy services provided, CG youths/families received a referral service overlay of three weekly hour long visits by a project staff member. The point of the CG condition was to provide publicly available contact information on local services available to the youth's family. No form of counseling or therapy was offered.

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			the youth's substance use issues, parent attitudes and behaviors regarding this use, parent monitoring and supervision to promote progress towards their child's intervention goals, and parent communication skills to enhance youth-parent connectedness.				
	IG2	Youth	Each BI session lasted for 1-1/4 hours, and occurred about a week apart. Each youth was paid $15 for completing the baseline interview and each followup session. The first BI session with the youth focused on discussing the youth's substance use and related consequences, the level of willingness to change, the causes and benefits of change, and what goals for change the youth wanted to select and pursue. The youth was encouraged to pursue goals of drug abstinence or reduction in drug use. In the second session with the youth, the counselor reviewed the youth's progress with the agreed upon goals, identified risk situations associated with difficulty in achieving goals, discussed strategies to overcome barriers toward goal achievement, reviewed where the youth was in the process of change, and negotiated either continuation or advancement of goals. Informed	2 wks; 2; sessions 150 min	Home; Individual (in-person); Research staff NOS	Attention control	In addition to the normal truancy services provided, CG youths/families received a referral service overlay of three weekly hour long visits by a project staff member. The point of the CG condition was to provide publicly available contact information on local services available to the youth's family. No form of counseling or therapy was offered.

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			by an integrated behavioral and family therapy approach.				
Estrada, 2018[90]	IG1	Youth, Parent	Eight online pre-recorded e-parent group sessions that are accessed via a website (Parental Investment in Adolescent Worlds, Enhancing Communication Skills, Family Support and Behavior Management, Parent Monitoring of Peer World, Adolescent Drug Use, Parent Investment in Adolescent's School, Adolescent Sexual Risk Behaviors, Prevention Has To Be Acheived All Over Again Everyday), and four parent-adolescent family sessions (Engagement and Orientation, Family Communication, Parental Monitoring of Peer World and Adolescent Drug Use, Adolescent Sexual Risk Behaviors) that are delivered by a trained facilitator. E-parent group sessions consisted of video recordings with three components: simulated parent group discussions, a culturally syntonic telenovela (soap opera) series, and interactive exercises. Sessions were designed so that parents were unable to fast forward or skip through sessions. Each participant was assigned a unique login name and password. The login procedure facilitated close monitoring of participants, particularly as it related to session participant rates. The research team was able to track who, when, how long, and for what purpose	13 wks; 12; sessions 420 min	Home; Computer-based,Video; Research staff NOS,Self-Admin	Usual care	Prevention as usual consisted of the HIV prevention curriculum provided by MDCPS via health science classes. The curriculum has six lessons delivered in a classroom setting and aim to provide information about HIV/AIDS and other sexually transmitted infections. Given that prevention as usual represents current community prevention activities, it is likely that participants from the experimental condition also received this curriculum.

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			the intervention website was accessed.				
Fang, 2010[92]	IG1	Youth, Parent	Nine 35-45 minute interactive online sessions (each including three to five modules) completed by mother-daughter dyads covering. Aiming to preventing girls' substance use through enhancing mother-daughter interactions, the program helped mothers establish clear rules about consequences for substance use, manage conflict, monitor their daughters' behavior and activities, improve their children's self-esteem, and gain competency in empathizing with their daughters and assisting them in coping with stress. At the same time, the program assisted girls to manage stress and interpersonal conflict, build refusal skills, enhance self-efficacy, increase their social supports and prosocial activities, and maintain close relationships with their mothers. (Titles of sessions: my mom and me; conflict management; substance use opportunities; body image; mood management; stress management; problem solving; social influences; and self efficacy.) One booster session reviewing initial program material and highlighting the issue on self-efficacy, problem solving, refusal skills, parent monitoring, parent-	26 wks; 10; sessions 450 min	Home; Computer-based; Self-Admin	Assessment only	No access to intervention

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			child communication, and parent-child closeness one year after initial program completion.				
Foxcroft, 2017[93]	IG1	Youth, Parent	Strengthening Families Program 10-14; the video based program was delivered by trained facilitators where parents/guardians and children learned together. In the first hour of each session parallel groups of children and parents develop their understanding and skills, led by parent and child group facilitators; in the second hour, parents and children come together in family units to practice principles they have learned.	7 wks; 7; sessions 840 min	NR; Group (in-person),Video; Research staff NOS	Minimal	Communities in the control arm of the trial received information leaflets for families
Gmel, 2013[94]	IG1	Youth	Conscripts were invited to a counseling session on tobacco, cannabis, and alcohol use lasting approximately 20 minutes in order to reinforce motivation to change using motivational interviewing. Interviewing involved exploring the use of tobacco, cannabis, alcohol and other substances by introducing and discussing behavior change perspectives in a non-judgmental, empathic and collaborative manner. Interviewing consisted of the following components to focus on the main problem(s) of each individual: (a) establish a collaborative rapport to enable elicitation of multiple substance use; (b) ensure confidentiality; (c) ask permission to talk about behaviors; (d) ask with open questions about	0.28 wks; 2; sessions 40 min	Other Medical; Individual (in-person); Psychologist	Assessment only	

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			substance use and focus on areas that the conscript considers problematic; (d) explore pros and cons; (f) reflect and affirm change talk and enhance values that might be incompatible with present substance use; (g) explore the importance, confidence and readiness to change; (h) evoke commitment to a change plan; and (i) support the conscript's self-efficacy.				
Harris, 2012[80]	IG1	Youth	1 session that included a computer-based self-administered screening about substance use including CRAFFT questions and score and 1o pages information materials; a 5-min computer-based intervention immediately following screening; and a 2-3 min provider discussion to not start/stop substance use. Providers received a report showing CRAFFT results, risk level, and 6-10 points to use as a basis for discussion.	13 wks; 1; sessions 8 min	Primary Care; Individual (in-person), Computer-based; PCP	Usual care	NR
Jalling, 2016[95]	IG1	Parent	ParentSteps is conveyed and practiced by means of video vignettes, group discussions, and home assignments. The themes for the six sessions and home assignments are Love and limits; Encouragement and consequences; Risks and protection; Stress, fights and different points of view; Youth, parents and alcohol; and Youth, parents and drugs. ParentSteps has a highly structured format, and	6 wks; 6; sessions 720 min	NR; Group (in-person); Social Worker	Waitlist	6-month wait-list

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			the video film for each session also provides the time-points for the starting and ending of group discussions and the assignments for that session.				
	IG2	Parent	Comet 12-18. overall aim is to help parents to develop and enhance their skills and self-efficacy for parenting. Principle program components are rehearsals of the use of reinforcement principles (e.g. encouragement and praise and ignoring minor problems) through role-play and home-assignments where parents practice and develop the principles in their daily lives. Parents keep a diary to document their interactions with their adolescent and home assignments are followed-up in subsequent sessions. Video vignettes are used in each session to enhance learning. Examples of themes covered during the nine group sessions include taking initiatives for spending time together with the adolescent, dealing with rejection, basic interactional (behavioral) analysis, positive communication and encouragement, problem solving, and rules and consequences.	9 wks; 10; sessions 1500 min	NR; Group (in-person); Social Worker	Waitlist	6-month wait-list
Johnson, 2015[96]	IG1	Youth	The Healthy Futures intervention takes a positive youth development (PYD) perspective, which is based on the belief that successful adult development is not the absence of involvement in	26 wks; 6; sessions 105 min	Primary Care; Individual (in-person); Educator or Counselor NOS	Minimal	All participants were invited to participate in bi-annual job and college fairs held at the clinic and received a monthly

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			risk behaviors, but the presence of developmentally appropriate skills. The Healthy Futures intervention seeks to understand additional health implications of career readiness intervention taking advantage of the strengths of locating such an intervention in a pediatric primary care clinic. Building on the Social Cognitive Theory, the intervention focuses on identifying and overcoming environmental and behavioral barriers to future plans as well as improving self-efficacy through skill-building activities. These activities are facilitated through motivational interviewing (MI). Participants received 3 in-person MI sessions (approximately 1 every other month), which took place at the clinic with follow-up contact via phone or email after each session (i.e., in the in-between month). The MI sessions were facilitated by master's level educators trained in MI. Intervention activities were not part of a clinic visit, although clinicians were informed if their patient was taking part in the Healthy Futures intervention. Activities in each session provided opportunities for the youth to discuss their goals for the future, identify barriers to accomplishing these goals (including involvement in risk behaviors), practice the skills				newsletter containing information about local opportunities to build their resume.

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			necessary to accomplish these goals (e.g., research careers, explore jobs and educational programs, develop their resume, complete applications), and link them to community resources. Explicit efforts were made to create cognitive dissonance around involvement with violence, substance use, and unsafe sexual practices and stated future plans, as the research team identified these behaviors as both prevalent and possibly negatively influencing vocational plans. For example, the MI coach might ask youth about the barriers to accomplishing their future plans. This conversation could be facilitated by a statement such as "I sometimes see in the youth that I work with that having a child before they are ready, their involvement with the law, and their drug use preventions them from accomplishing their goals. Why might some of these be/not be a problem for you?". All participants (IG and CG) were invited to participate in bi-annual job and college fairs held at the clinic and received a monthly newsletter containing information about local opportunities to build their resume.				

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
Kerr, 2013[97]	IG1	Youth	PHAT is a culturally tailored intervention for African American adolescents, focusing on three dimensions of health behavior (dietary behavior, physical activity, and substance use) for premature cancer and cardiovascular disease prevention. The intervention used various interactive learning activities to increase health knowledge, develop health behavior skills, change attitudes, increase self-efficacy, and explore beliefs regarding personal health behaviors. PHAT utilized cultural pride, goal setting, and instruction in dietary behaviors, physical activity, nutrition cognition, proper sleeping habits, and substance abuse. PHAT is designed to increase healthy behaviors of adolescents through the following: knowledge building, reexamination of beliefs regarding risk and consequences, development of skills to delineate and execute behaviors that reduce health risk, increasing self-efficacy to engage in health-beneficial behavior, and increasing motivation to implement healthy behaviors. PHAT was conducted using group facilitation, role-playing, games, and classroom multimedia messages. Based on Social Cognitive Theory (SCT). The PHAT curriculum was designed to modify intrapersonal attributes that affect health	2 wks; 2; sessions 960 min	NR; Group (in-person); NR	Attention control	Focus on Youth, a sexual risk reduction HIV/STI-prevention intervention. Similar frequency, length, and structure as the IG.

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			behavior such as knowledge, self-efficacy, and perceived susceptibility. Furthermore, the program was designed to modify expectancies regarding health behaviors and subsequent health outcomes. It also promoted self-efficacy to perform healthy dietary, physical activity, and drug use behaviors. In particular, activities in this intervention were designed to increase confidence to conduct healthy behaviors and overcome barriers that prevent their execution. The program was also designed to raise awareness concerning how behaviors affect the community as well as how the community influences behaviors and personal beliefs. Finally, PHAT was designed to increase skills to execute behaviors that prevent cardiovascular disease and cancer.				
Kim, 2011[98]	IG1	Youth, Parent	Delivered the summer prior to entering middle school. Both interventions met twice a week for 3 weeks. Caregiver intervention 6 group-based sessions on caregiver management training for foster parents focusing on establishing and maintaining stability in the foster home, preparing girls for the start of middle school, and preventing early adjustment problems during the transition to	43 wks; 46; sessions 5160 min	NR; Individual (in-person), Group (in-person); Research staff NOS,Lay provider	Usual care	Received the usual services provided by the child welfare system, including services such as referrals to individual or family therapy, parenting classes for biological parents, and case monitoring. Child Welfare caseworkers managed each case and were responsible

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			middle school to develop a behavioral reinforcement system to encourage adaptive behaviors across home, school, and community settings. A 10-min phone interview with caregivers about behavioral and emotional issues and the types of discipline and supervision used during the past 24 hr, to connect the planned curriculum to the daily challenges the foster parents were facing. Facilitators used items on the PDR to review specific problem behaviors that occurred during the day, and these behaviors were then used as the week's examples of the curriculum. Weekly home practice assignments were provided to encourage foster parents to apply new skills. When a participant missed a session, the interventionist either went to the family's home to deliver the content in person or delivered the content via a telephone call. Caregiver sessions were led by 2 facilitators. Follow-up services/support was available for 2 hours per week throughout the first year of middle school (up to 40 sessions). Adolescent intervention 6 group sessions on skill-building to prepare for the middle school transition by increasing their social skills for establishing and maintaining positive relationships				for making all decisions on referrals to community resources, including individual and family therapy and parenting classes.

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			with peers, increasing their self-confidence, and decreasing their receptivity to initiation from deviant peers. Each session typically included an introduction to the session topic, role plays, and a game or activity during which girls practiced the new skill. In addition, the girls engaged in overt discussions about self-image and the personal characteristics and behaviors (e.g., being a good friend, getting good grades, and abstaining from substance use) they wished to project as they entered middle school. During the final summer session, each girl proclaimed and solidified her goals and commitments in a small ceremony. The ceremony included members of the girl's session group and their foster parents; it was designed to help the girls build confidence in who they are and who they want to become and to build supportive ties between the girls and their foster parents by "publicizing" their goals and commitments. Girls sessions were led by 1 facilitator and 3 assistants to allow for more individualized attention, one-on-one modeling/practicing of new skills, and frequent reinforcement of positive behaviors. During the school year each girl had individual weekly coaching sessions delivered by female				

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			college grads serving as role models. These sessions continued to focus on establishing and maintaining positive peer relations, increasing knowledge of accurate norms for problem behaviors, and increasing self-competence in academic and social areas. Coaches also emphasized the risks of substance use and discussed issues around dating and partner relations.				
Knight, 2019[72]	IG1	Youth	Patient self-administered a tablet-based screening questionnaire that assessed the number of days of alcohol, cannabis, and other drug use in the past 12 months and the 6 CRAFFT questions. The tablet then immediately displayed to patients their CRAFFT score and level of risk, followed by 10 interactive pages of scientific information and true-life vignettes illustrating the health risks of substance use. This took on average 4 minutes to complete in a private location before the visit. Practitioners then logged into the tablet to see the patient's screen results, risk level, talking points designed to prompt a 2- to 5-minute conversation using motivational interviewing strategies, and the recommended follow-up plan. Practitioners gave a printed Contract for Life to all patients (and parents or guardians, if present) as a prevention strategy for high- and low-risk patients. The	0.14 wks; 1; sessions 15 min	Primary care; Individual (in-person); PCP	Usual care	Patients in the UC group self-administered the computer screening but did not receive any other intervention components.

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			Contract for Life asks youths to agree never to drive after substance use or accept a ride from a substance-impaired driver and instead to call a parent, guardian, or other trusted adult for a safe ride home. Parents or guardians agree to provide safe and sober transportation home and postpone discussion until the following day. Practitioners instructed patients to discuss the Contract for Life with their parent(s) or guardian(s) and to follow up if additional discussion was needed. Practitioners also gave all patients a flyer for a 20-minute family-centered online educational program, Teen-Safe, on preventing adolescent substance use.				
Lee, 2010[100]	IG1	Youth	Individualized personalized feedback based on the baseline survey. The individual PFI intervention is based on the MI approach described by Miller and Rollnick and the brief PFI approach pioneered by Marlatt and colleagues for alcohol prevention. The approach was also informed by recent work by Walker and colleagues regarding PFI for adolescent marijuana smokers and studies of computerized normative feedback for alcohol prevention. The feedback was primarily text based, but incorporated pictures to enhance interest and appeal as well as figures/graphs representing	0.14 wks; 1; sessions 30 min	Home; Computer-based; Self-Admin	Assessment only	No feedback or information. Asked to complete assessments.

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			normative information and comparisons. Participants were presented with feedback about their marijuana use (e.g., frequency and quantity of use), perceived and actual descriptive norms for marijuana use (e.g., how frequently they believe the typical student uses marijuana), and perceived pros and cons of using marijuana. Self-reported negative consequences were included in the feedback, as well as ways in which reducing or eliminating marijuana use might be associated with reduced social and academic harm and participants own cost-benefit scale for use. Finally, skills training tips for avoiding marijuana and making changes in one's use were provided, as well as limited alcohol feedback. Perceived high-risk contexts and alternative activities around campus and in the community were provided.				
Malmberg, 2014[102]	IG1	Youth	E-learning module about alcohol (4 lessons) between April and July 2009; tobacco (3 lessons) between April and July 2010; and marijuana (3 lessons) between April and July 2011. Lessons based on ASE model. The lessons consist of small films, animations and several types of interactive tasks. Also, adolescents are able to discuss relevant topics or to exchange their opinions through chatrooms and forums.	156 wks; 3; sessions 90 min	School; Computer-based; Self-Admin	Usual care	Control schools agreed not to start any substance-related interventions in target group during study period, but could continue with already established programs.

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Mason, 2015[103]	IG1	Youth	Adolescents assigned to the intervention condition received a 20-minute intervention referred to as Peer Network Counseling. The intervention is guided by five key MI clinical issues: rapport, acceptance, collaboration, reflections, and non-confrontation. The intervention follows Motivational Enhancement procedures with age-matched substance use normative data presented as feedback. The intervention is 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 between current use and future goals and values, (c) introduction of peer network information and graphical feedback, and (d) summary, change talk, and plans. The peer network component begins by introducing the concept of peer network and its influence on health using the laptop to illustrate this concept. Next, the teen's peer network is reviewed for risks and protection. Peer networks are reviewed for support, prosocial activities, and encouragement for healthful behavior as well as for substance use, influence/ offers to use	0.14 wks; 1; sessions 20 min	NR; Individual (in-person); Educator or Counselor NOS	Attention control	Adolescents 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.

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Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			substances, and risky/dangerous activities. Adolescents are shown the composition of their peer network in graphic form, such as a bar graph representing levels of risk and protection for each their closest three peers. Teens are 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				
Rhee, 2008[105]	IG1	Youth	After baseline data collection, a family nurse practitioner, conducted a 10- minute brief counseling session guided by the Risk Behavior Facts Sheet with information about the harmful effect of risk behaviors within the context of asthma and its treatment. Then participants completed a 1-hour CD-ROM intervention that included decision-making and risk behavior prevention modules via a laptop computer. The decision-making module discussed the basic principles of the decision-making model as the basis for understanding the consequences of poor decision making. At the 2-month contact, the decision-making module CD-ROM was mailed to the intervention group along with a workbook to provide	17 wks; 3; sessions 190 min	Other Medical,Home; Individual (phone),Computer-based; Nurse,Self-Admin	Minimal	Received a sham CD-ROM program about study skills which ran for a comparable time duration to the intervention program

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			reinforcement and an opportunity to apply the information in real-life situations and required approximately 1.5 hours to complete. The intervention group was mailed another intervention booster on risk behavior prevention by interactive CD-ROM at 4 months which required 30 minutes to complete. NPs called intervention participants to ask about the content of the CD-ROM to determine adherence. Further encouragement, guidance and follow-ups were provided to those of suspected noncompliance.				
Sanci, 2015[106]	IG1	Youth, Practitioner	Provider screened for risky behaviors (tobacco use, alcohol use, drug use, risky sex, road safety) and discussed protective health behaviors using the HEADSS framework. From supplemental material: Workshops covered 3 topics of 3 hours each: youth-friendly care; screening for and discussing health risks using the HEADSS framework; and providing a response to detected risky behaviours with a brief intervention based on motivational interviewing principles, including health promotion advice. Adolescent actors allowed clinicians to practice new skills by role play and provided feedback and coaching in youth-friendly communication skill. Two to three hours of interactive	NR wks; 1; sessions 15 min	Primary Care; Individual (in-person); Nurse, PCP	Assessment only	3-hour clinician seminar on youth-friendly care, including recommendations to discuss health risks with young people.

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			training in youth-friendly care was also provided to practice support staff (PSS: receptionists and practice managers). Training was delivered to each practice by an expert in adolescent primary care either at the practice or a local venue. During workshops, clinicians were introduced to the study screening tool designed to prompt them to raise and discuss health risk behaviours and also protective factors and strengths with their patients. After the workshops, two practice visits were conducted two weeks apart. Using the plan-do-study-act (PDSA) cycle of continuous quality improvement, practices were assisted with integrating screening into office and clinical procedures. The RA also assisted with updating practice referral lists with local youth specialist services, and provided posters and pamphlets addressing youth-friendly care (e.g. confidentiality) and health risk behaviours (e.g. road safety). Data collected from the profile exit interviews were presented to participating clinicians and PSS to help them identify aspects of care that could be improved. These data included patients' risk profile, whether clinicians discussed health behaviours during the consultation, and the young				

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			person's satisfaction, trust, and likelihood to return to the practice.				
Schinke, 2009a[107]	IG1	Youth, Parent	Guided by family interaction theory, the intervention program aimed to reduce girls' substance use through mother-daughter interactions. The program helped mothers learn to better communicate with their daughters, monitor their daughters' behavior and activities, build their daughters' self-image and self-esteem, establish rules about and consequences for substance use, create family rituals, and refrain from communicating unrealistic expectations. In the program, girls acquired skills for managing stress, conflict, and mood, for refusing peer pressure, and for enhancing body esteem and self-efficacy. Working together in their homes and at times convenient to them, mother-daughter dyads interacted with the program's nine sessions. Though participants were advised to complete one session per week, completion time varied somewhat. On average, participants required roughly 45 minutes to complete each intervention session. Session content was delivered by voice-	9 wks; 9; sessions 405 min	Home; Computer-based; Self-Admin	Assessment only	No intervention

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			over narration, skills demonstrations, and interactive exercises for mothers and daughters to complete jointly.				
Schinke, 2009b[108]	IG1	Youth, Parent	Computer intervention with sessions focused on building daughters' self-image and self-esteem, establish rules about and consequences for substance use, create family rituals, and refrain from placing unrealistic expectations on their daughters. Mothers learned to better communicate with their daughters, and monitor their daughters' activities. Girls learned to manage stress, conflict, and mood; refuse peer pressure; enhance body esteem and self-efficacy; and accurately assess prevalence of cigarette, alcohol, and drug use among their age-mates.	104 wks; 11; sessions 495 min	Home; Computer-based; Self-Admin	Assessment only	
Schwinn, 2010[110]	IG1	Youth	RealTeen program; comprised of two components: the homepage and 12 intervention sessions. The homepage features, available for access anytime, included news feeds, horoscopes, beauty tips, quotes of the day, fortunes, and access to their blog, pen pal, and the chat forum girls used optionally as a response to intervention session questions. The sessions incorporated not only general personal and social skills (self-efficacy, communication, asserting one's self), but also skills specific to dealing with drug use	4 wks; 12; sessions 300 min	Home; Computer-based; Self-Admin	Assessment only	Girls in the control group completed measures at designated intervals but did not receive the gender-specific drug abuse prevention program.

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			opportunities. Girls sequentially completed nine theory-based sessions on: goal setting, decision making, coping (particularly with stress, puberty, and bodily changes), self-esteem, assertion, communication, media influences, peer pressure, and drug facts. The first session served as an introduction; the final two sessions reviewed material and provided additional quizzes. Across sessions, an older female animated character guided girls through the content and practice exercises.				
Schwinn, 2015[112]	IG1	Youth	The three-session intervention was guided by a social competency skill-building strategy and minority stress theory. An animated young adult narrator led youths through the tailored content and practice scenarios that included interactive games, role-playing, and writing activities. Session 1 focused on skills for identifying and managing stress; session 2 provided a five-step guide for making decisions; and session 3 addressed drug use rates and refusal skills.	4 wks; 3; sessions 42 min	Home; Computer-based; Self-Admin	Assessment only	None
Schwinn, 2018[111]	IG1	Youth	RealTeen; Intervention sessions were held within the online program RealTeen, and focused on goal setting, decision making, puberty, body image, coping, drug knowledge, refusal skills (two sessions), and a review. Sessions were delivered sequentially and	14 wks; 9; sessions 165 min	Home; Computer-based; Self-Admin	Assessment only	Completed posttest measures 14 weeks after pretest date, and completed 1-year follow-up measures 12 months after posttest completion date

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			guided by an animated female narrator. Frequently, girls were also asked to generate a brief, written response to session content (i.e., a short- and long-term goal, feelings elicited from an ad for cigarettes, reframing a negative thought). Once responses were entered online, girls had the option to keep their responses private or to make them public. Private responses were stored in a girl's online journal. Public responses, posted to the social feed, were accessible to all girls in the intervention condition. For Each session reinforced how to help girls make healthier decisions around drug use, and all sessions were structured similarly by being a skills-based lesson, followed by interactive exercises to enhance skills acquisition, and ending with a review and short quiz. Subsequent sessions were available 1 week after girls completed the previous session.				
Walkup, 2009[113]	IG1	Youth	The curricular content for the Family Spirit intervention was based on recommendations and standards documented in the American Academy of Pediatrics' Caring for Your Baby and Child: Birth to Age 5. The curriculum includes developmentally timed prenatal and infant-care parenting lessons, as well as family planning, substance abuse prevention, and problem solving and coping-skills	38 wks; 25; sessions 1500 min	Home; Individual (in-person); Lay provider	Attention control	The control group's curricular content included a previously developed breast-feeding/nutrition education program. Mothers were to receive 23 home visits, each lasting approximately 1 hour. The control condition was selected to

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			lessons. Mothers were expected to receive 25 home visits, each lasting approximately 1 hour. The Family Spirit curriculum was carefully crafted to reflect local native practices but not community-specific traditions or spiritual beliefs. Tribal stakeholders emphasized that there is a broad spectrum of cultural beliefs and practices within and across tribal sites and supported that the Family Spirit curriculum address the shared needs of all of the participants. In addition, the interventionists were trained to interact in ways that respected the participants' cultural orientation and living situation. For example, some participants preferred to do the lesson in their native language, whereas others preferred English. Some participants expressed interest in traditional ceremonies and practices covered in the curriculum, whereas others preferred more Western approaches. Intervention was delivered by trained Native paraprofessionals.				provide participants a valuable home-visiting experience and hold constant the amount of supportive contact for mothers, so between-group differences could be linked to intervention content.
Walton, 2013[114]	IG1	Youth	The BIs incorporated MI, 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)	0.14 wks; 1; sessions 38 min	Primary Care; Individual (in-person); Educator or Counselor NOS	Minimal	Participants in the control were handed a tri-fold brochure containing warning signs of cannabis problems, resources (substance use treatment, suicide

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			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 therapists who were trained in MI conducted the TBI, which was facilitated by a computer which displayed screens to prompt content. The therapist used an elicit-provide-elicit framework when reviewing tailored feedback, using summaries and open-ended questions to evoke change talk. For example, for those who did not want to stop using, therapists focused on reducing use and avoiding consequences. During role plays, therapists elicited tools to reduce use and avoid consequences.				hotlines, employment services, leisure activities), and cannabis information websites. This "enhanced usual care" control (clinics did not routinely provide this information) was chosen for ethical reasons.
	IG2	Youth	The BIs incorporated MI, 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	0.14 wks; 1; sessions 33 min	Primary Care; Computer-based; Self-Admin	Minimal	Participants in the control were handed a tri-fold brochure containing warning signs of cannabis problems, resources (substance use treatment, suicide hotlines, employment services, leisure activities), and

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			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 CBI was a stand-alone interactive animated program, with touch screens. Research staff started the CBI, handed the tablet to participants, and showed them how to adjust the audio. A selected virtual buddy guided participants through the program and provided audio feedback (via headphones). For example, during the decisional balance exercise, the participant selected reasons to stay away from cannabis and the buddy provided affirmations and summaries. During the role-plays, 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				cannabis information websites. This "enhanced usual care" control (clinics did not routinely provide this information) was chosen for ethical reasons.

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			over time. At the end, the computer instructed participants to return the tablet to staff.				
Walton, 2014[115]	IG1	Youth	BIs were conducted in a private room and could be paused to allow for medical care. The BIs integrated motivational interviewing (MI) spirit and techniques, emphasizing personal responsibility, supporting self efficacy, eliciting commitment talk for avoiding cannabis use and change talk for reducing alcohol, other drugs and delinquency. The BIs also included normative resetting and role-play scenarios. Cultural relevance to address the study population (~50% African American) was incorporated into the content based on feedback from focus testing, including providing diversity in language (key messages, scripts for CBI), item-listed checkboxes (e.g. goals, reasons to avoid using) and scenario topics. Therapists were trained in MI, including the use of rulers to increase self-efficacy and commitment talk for abstinence/reduction of other risk behaviors (average length = 38 minutes, standard deviation = 14). A computer displayed tailored feedback and prompt content. Fidelity was monitored by audio-taping and providing feedback via regular individual and group	0.14 wks; 1; sessions 38 min	Primary Care; Individual (in-person); Educator or Counselor NOS	Minimal	Participants were given a brochure containing warning signs of problems with cannabis and community resources (e.g. substance use, mental health and leisure activities).

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			supervision. Also given a brochure containing warning signs of problems with cannabis and community resources (e.g. substance use, mental health and leisure activities).				
	IG2	Youth	BIs were conducted in a private room and could be paused to allow for medical care. The BIs integrated motivational interviewing (MI) spirit and techniques, emphasizing personal responsibility, supporting self efficacy, eliciting commitment talk for avoiding cannabis use and change talk for reducing alcohol, other drugs and delinquency. The BIs also included normative resetting and role-play scenarios. Cultural relevance to address the study population (~50% African American) was incorporated into the content based on feedback from focus testing, including providing diversity in language (key messages, scripts for CBI), item-listed checkboxes (e.g. goals, reasons to avoid using) and scenario topics. Using touch-screens and headphones for audio, the CBI was an animated, interactive program (average length = 33 minutes, standard deviation = 13) delivered by a virtual therapist, who provided affirmations and	0.14 wks; 1; sessions 33 min	Primary Care; Computer-based; Self-Admin	Minimal	Given a brochure containing warning signs of problems with cannabis and community resources (e.g. substance use, mental health and leisure activities).

Appendix D Table 3. Intervention Descriptions

Author, year	IG	Intervention target	Detailed IG description	Intervention duration; No of sessions; Total min	Intervention setting; Intervention format; Intervention provider	CG category	Detailed CG description
			summaries. Guided by a buddy chosen by participants, the role-play scenarios showed characters in risky situations, with progression over time in various consequences, eliciting participant interaction and role-modeling positive choices. Also given a brochure containing warning signs of problems with cannabis and community resources (e.g. substance use, mental health and leisure activities).				

Abbreviations: BI = Brief Intervention; CBI = Computer brief intervention; CG = Control group; IG = Intervention group; IHS = Indian Health Service; MDCPS = Miami-Dade County Public School; MI = Motivational interviewing; NOS = Not otherwise specified; NR = Not reported; PCP = Primary care physician; PFI = Individual personalized feedback; PHAT = Promoting Health Among Teens.

Appendix D Table 4. Health, Social, and Legal Outcomes (KQ1)

Outcome	Author year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Depression symptoms	Barlow, 2006[835]	20-item self-report scored on a 4-point scale with a possible score from 0-60; 0-60 (Low)	NR	IG1 (Overall)	5	11.6 (10), 19†	15.2 (8), 22†	MeanDiff: -3.10 (-8.80 to 2.50)†	0.27
					9	8.4 (10), 19†	14.2 (11), 22†	MeanDiff: -6.10 (-13.00 to 0.85)†	0.08
	Barlow, 2013[83]	CES-D score; 0-60 (Low)	1 week	IG1 (Overall)	4	-.3 (.), 159	0 (.), 163	MeanDiff: -0.34 (-1.19 to 0.51)	0.44
					8	-.9 (.), 159	0 (.), 163	MeanDiff: -0.95 (-2.09 to 0.19)	0.10
					14	-1.8 (.), 159	0 (.), 163	MeanDiff: -1.89 (-3.80 to 0.06)	0.06
					38	-.9 (.), 159	.3 (.), 163	MeanDiff: -1.17 (-2.05 to -0.28)	0.01
	Fang, 2010[92]	Depression; 0-2 (Low)	2 weeks	IG1 (Overall)	6	-.1 (.8), 54	0 (.7), 50	CalcMeanDiffChg: -0.12 (-0.40 to 0.16)	0.045
					12	-.1 (.8), 54	.1 (.7), 50	CalcMeanDiffChg: -0.18 (-0.46 to 0.10)	0.315
					24	-.1 (.9), 50	0 (.6), 43	CalcMeanDiffChg: -0.14 (-0.44 to 0.16)	0.315
	Schinke, 2009a[107]	1-5 (Low)	NA	IG1 (Overall)	12	-.1 (.8), 205	.1 (.8), 327	TxtEffectEst: -0.18 (-0.32 to -0.04)	NR, NS
	Schinke, 2009b[108]	Adolescent-reported depression; 1-5 (Low)	2 weeks	IG1 (Overall)	12	0 (.8), 434	0 (.8), 430	CalcMeanDiffChg: 0.01 (-0.09 to 0.11)	NR, NS
					24	.1 (.8), 415	0 (.8), 413	CalcMeanDiffChg: 0.11 (0.00 to 0.22)	NR, NS
	Schwinn, 2018[111]	5-point Likert-scaled items that asks girls to rate the extent to which they were bothered (not at all = 0, All the time = 4) by various symptoms in the past month.; 0-20 (Low)	1 month	IG1 (Overall)	3	1.8 (1), 376†	1.9 (1), 380†	Bweight: -0.10 (-0.22 to 0.02)†	0.109
				IG1 (Overall)	15	1.8 (1), 370†	1.9 (1), 382†	Bweight: -0.14 (-0.28 to 0.00)†	0.051
	Walkup, 2009[113]	0-60 (Low)	NR	IG1 (Overall)	5	-2 (11.8), 54†	-3.3 (10.7), 71†	Beta: 0.05 (-3.99 to 4.09)†	NR, NS
					9	-4 (12.2), 47†	-4 (10.7), 68†	Beta: -0.58 (-4.71 to 3.55)†	NR, NS

Appendix D Table 4. Health, Social, and Legal Outcomes (KQ1)

Outcome	Author year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Anxiety symptoms	Schwinn, 2018[111]	5-point Likert-scaled items that asks girls to rate the extent to which they were bothered (not at all = 0, All the time = 4) by various symptoms in the past month.; 0-20 (Low)	1 month	IG1 (Overall)	3	1.5 (1), 376†	1.6 (1), 380†	Bweight: -0.06 (-0.20 to 0.08)†	0.436
					15	1.6 (1), 370†	1.7 (1), 382†	Bweight: -0.08 (-0.24 to 0.08)†	0.288
Other symptoms	Baldus, 2016[81]	Parent-reported problem behavior (SDQ subscale); NR (Low)	NR	IG1 (Overall)	8	-.4 (2.5), 147	-.3 (2.1), 145	MeanDiffinChange: 0.08 (-0.30 to 0.46)	0.550
					20	-.4 (2.2), 147	-.3 (2.8), 145	MeanDiffinChange: 0.17 (-0.21 to 0.57)	0.412
		Self-reported problem behavior (RAASI); NR (Low)	NR	IG1 (Overall)	8	.3 (3.7), 147	.4 (3.9), 145	MeanDiffinChange: 0.05 (-0.61 to 0.71)	0.748
					20	.5 (4.4), 147	.7 (4.9), 145	MeanDiffinChange: 0.23 (-0.43 to 0.89)	0.503
	Bannink, 2014[82]	Total difficulties score (SDQ); 0-40 (Low)	NR	IG1 (Overall)	4	-1.3 (5.1), 430	-.8 (5.4), 434	Beta: -0.60 (-1.17 to -0.04)	0.04
				IG2 (Overall)	4	-1.1 (5.4), 392	-.8 (5.4), 434	Beta: -0.24 (-0.78 to 0.29)	0.37
		Total emotional and behavior problems, youth report (Achenbach system); 0-210 (Low)	NR	IG1 (Overall)	4	31.6 (22.6), 430†	34.8 (25.3), 434†	Beta: -2.74 (-5.92 to 0.44)†	0.09
				IG2 (Overall)	4	33.9 (23), 392†	34.8 (25.3), 434†	Beta: -0.89 (-4.18 to 2.40)†	0.60
	Barlow, 2013[83]	Externalizing T-score (Achenbach system); 0-100 (Low)	NR	IG1 (Overall)	8	-1.9 (.), 159	-.7 (.), 163	MeanDiff: -1.37 (-3.12 to 0.39)	0.13
					14	-3.8 (.), 159	-1.5 (.), 163	MeanDiff: -2.50 (-4.89 to -0.12)	0.04
					38	-.6 (.), 159	.4 (.), 163	MeanDiff: -1.23 (-2.45 to -0.02)	<0.05
		Internalizing T-score (Achenbach system); 0-100 (Low)	NR	IG1 (Overall)	8	-2.3 (.), 159	-1.1 (.), 163	MeanDiff: -1.32 (-3.17 to 0.53)	0.16
	Barlow, 2013[83]		NR	IG1 (Overall)	14	-4.7 (.), 159	-2.3 (.), 163	MeanDiff: -2.51 (-5.12 to 0.09)	0.06

Appendix D Table 4. Health, Social, and Legal Outcomes (KQ1)

Outcome	Author year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
		Internalizing T-score (Achenbach system); 0-100 (Low)			38	-3.2 (.), 159	-2.5 (.), 163	MeanDiff: -0.83 (-2.17 to 0.50)	0.23
		Mental Health score (POSIT); NR (Low)	NR	IG1 (Overall)	4	-.1 (.), 159	-.1 (.), 163	MeanDiff: -0.33 (-0.77 to 0.11)	0.14
					8	-.3 (.), 159	-.4 (.), 163	MeanDiff: -0.25 (-0.73 to 0.23)	0.30
					14	-.5 (.), 159	-.8 (.), 163	MeanDiff: -0.14 (0.81 to 0.54)	0.70
		Total emotional and behavior problems T-score (Achenbach system); 0-100 (Low)	NR	IG1 (Overall)	8	-2.3 (.), 159	-1.3 (.), 163	MeanDiff: -1.38 (-3.22 to 0.45)	0.14
					14	-4.5 (.), 159	-2.6 (.), 163	MeanDiff: -2.36 (-4.90 to 0.19)	0.07
					38	-2 (.), 159	-1.6 (.), 163	MeanDiff: -0.86 (-2.10 to 0.39)	0.18
	Foxcroft, 2017[93]	Externalizing behaviors (SDQ subscale); 0-10 (Low)	NR	IG1 (Overall)	12	. (.), 233	. (.), 194	Mean Ratio: -0.10 (-0.23 to 0.03)	NR, NS
					24	. (.), 174	. (.), 154	Mean Ratio: -0.06 (-0.23 to 0.11)	NR, NS
	Jalling, 2016[95]	Externalizing score, youth report (Achenbach system); 0-64 (Low)	6 months	IG1 (Overall)	6	-.7 (10), 70	-.1 (9.6), 81	CalcMeanDiffChg: -0.56 (-3.70 to 2.58)	NR, NS
				IG2 (Overall)	6	0 (10.9), 86	-.1 (9.6), 81	CalcMeanDiffChg: 0.18 (-2.93 to 3.29)	NR, NS
		Internalizing + Externalizing, youth report (Achenbach system); NR (Low)	6 months	IG1 (Overall)	6	-1.3 (24.9), 70	-.3 (26.3), 81	CalcMeanDiffChg: -1.02 (-9.19 to 7.15)	NR, NS
				IG2 (Overall)	6	. (.), 86	-.3 (26.3), 81	--	NR, NS
		Psychosocial functioning, parent report (Y-OQ total score); -16-240 (Low)	NR	IG1 (Overall)	6	-9.5 (31.6), 71	-9.2 (30.3), 82	CalcMeanDiffChg: -0.21 (-10.07 to 9.65)	NR, NS
				IG2	6	-12.3 (27.1), 71	-14.2 (27.4), 82	CalcMeanDiffChg: 1.99 (-6.66 to 10.64)	
		Psychosocial functioning, parent report (Y-OQ total score); -16-240 (Low)	NR	IG2 (Overall)	6	-10.5 (29.5), 88	-9.2 (30.3), 82	CalcMeanDiffChg: -1.26 (-10.26 to 7.74)	NR, NS
				IG2	6	-16.7 (22.4), 88	-14.2 (27.4), 82	CalcMeanDiffChg: -2.42 (-9.98 to 5.14)	
		Psychosocial functioning, youth report (Y-OQ total score); -16-240 (Low)	NR	IG1 (Overall)	6	-3.6 (32.6), 70	-6.1 (32.3), 81	CalcMeanDiffChg: 2.45 (-7.93 to 12.83)	NR, NS

Appendix D Table 4. Health, Social, and Legal Outcomes (KQ1)

Outcome	Author year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Other symptoms	Jalling, 2016[95]	Psychosocial functioning, youth report (Y-OQ total score); -16-240 (Low)	NR	IG1	6	-12.5 (27.3), 70	-13.4 (29.5), 81	CalcMeanDiffChg: 0.87 (-8.19 to 9.93)	
				IG2 (Overall)	6	-4.1 (29.6), 86	-6.1 (32.3), 81	CalcMeanDiffChg: 2.01 (-7.40 to 11.42)	NR, NS
				IG2	6	-9.9 (26.5), 86	-13.4 (29.5), 81	CalcMeanDiffChg: 3.48 (-5.05 to 12.01)	
		Total emotional and behavioral problems score (Achenbach system); 0-210 (Low)	6 months	IG2 (Overall)	6	-20.9 (22.8), 88	-15.7 (24), 82	CalcMeanDiffChg: -5.24 (-12.29 to 1.81)	NR, NS
				IG1 (Overall)	6	-16.4 (27.1), 71	-15.7 (24), 82	CalcMeanDiffChg: -0.68 (-8.84 to 7.48)	NR, NS
	Kim, 2011[98]	Internalizing + Externalizing, youth report (Achenbach system); NR (Low)	NR	IG1 (Overall)	24	12.8 (8.5), 48†	12.5 (8.3), 52†	CohensD: 0.27 (-3.03 to 3.57)†	NS
	Sanci, 2015[106]	Emotional distress in last month	1 month	IG1 (Overall)	0	121/377 (32.1)	143/524 (27.4)	OR: 1.26 (0.83 to 1.91)	NSD
					3	67/377 (17.9)	91/524 (17.3)	OR: 1.00 (0.70 to 1.41)	0.99
					12	68/377 (18.1)	90/524 (17.1)	OR: 1.04 (0.70 to 1.57)	0.83
		Fear or abuse in relationships in last 12 months	1 year	IG1 (17+)	0	69/316 (21.8)	92/411 (22.4)	OR: 0.97 (0.58 to 1.62)	NSD
	Schwinn, 2018[111]	Perceived stress; girls rated degree to which their life situations were unpredictable, uncontrollable, and stressful during the past month (Never = 0, All the time = 3); 0-12 (Low)	1 month	IG1 (Overall)	3	1.5 (.8), 376†	1.6 (.8), 380†	Bweight: -0.06 (-0.16 to 0.04)†	0.244
					15	1.5 (.8), 370†	1.6 (.8), 382†	Bweight: -0.08 (-0.18 to 0.02)†	0.111
		Self-esteem; Ten, 4-point Likert-scaled items combined to form a self-esteem index with lower scores indicating higher self-esteem; 0-30 (Low)	NR	IG1 (Overall)	3	2.3 (.6), 376†	2.4 (.6), 380†	Bweight: -0.11 (-0.21 to -0.01)†	0.013
					15	2.3 (.6), 370†	2.4 (.6), 382†	Bweight: -0.08 (-0.18 to 0.02)†	0.074

Appendix D Table 4. Health, Social, and Legal Outcomes (KQ1)

Outcome	Author year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Global functioning	Bannink, 2014[82]	Health-related QOL (CHQ-CF-GH4 score); 0-100 (High)	NR	IG1 (Overall)	4	2.4 (18.5), 430	.1 (18), 434	Beta: 1.03 (-1.12 to 3.19)	0.35
				IG2 (Overall)	4	3.9 (17.3), 392	.1 (18), 434	Beta: 2.79 (0.72 to 4.87)	0.008
Family cohesion - adolescent report	Schinke, 2009a[107]	Communication, mother-daughter; 1-5 (High)	1 week	IG1 (Overall)	12	.1 (1.1), 205	-.2 (1.2), 327	TxtEffectEst: 0.32 (0.13 to 0.51)	<0.01
		Parental monitoring; 1-5 (High)	NA	IG1 (Overall)	12	.1 (.8), 205	-.2 (.9), 327	TxtEffectEst: 0.30 (0.16 to 0.44)	<0.05
	Schinke, 2009b[108]	Communication, mother-daughter; 1-5 (High)	1 week	IG1 (Overall)	12	.4 (2.4), 434	-.2 (2.2), 430	CalcMeanDiffChg: 0.62 (0.32 to 0.92)	<0.004
					24	0 (2.4), 415	-.2 (2.2), 413	CalcMeanDiffChg: 0.25 (-0.06 to 0.56)	<0.004
		Mother-daughter closeness; 1-5 (High)	NA	IG1 (Overall)	12	-.7 (1.4), 434	-1 (1.4), 430	CalcMeanDiffChg: 0.34 (0.15 to 0.53)	<0.002
					24	-.8 (1.4), 415	-1.1 (1.4), 413	CalcMeanDiffChg: 0.37 (0.18 to 0.56)	<0.002
		Parental monitoring ("I tell my mom what I plan to do with my friends."); 1-5 (High)	NA	IG1 (Overall)	12	.1 (.8), 434	-.1 (.9), 430	CalcMeanDiffChg: 0.22 (0.11 to 0.33)	<0.0001
					24	0 (.8), 415	-.2 (.9), 413	CalcMeanDiffChg: 0.29 (0.17 to 0.41)	<0.0001
Family cohesion - parent report	Estrada, 2018[90]	Communication, parent-adolescent (Barnes and Olson, 1985); "I can discuss my beliefs with my child without feeling restrained or embarrassed."; scale 1 (Strongly disagree) to 5 (Strongly agree); 1-5 (High)	NA	IG1 (Overall)	3	. (.), 84	. (.), 101	Beta: 1.65 (-0.45 to 3.84)	0.12
		Parental monitoring of peers (Pantin 1996); "How well do you personally know your child's friends?"; scale 1 (Not at all) to 5 (Extremely well); 1-5 (High)	NA	IG1 (Overall)	3	. (.), 84	. (.), 101	Beta: 0.85 (-0.09 to 1.81)	0.07

Appendix D Table 4. Health, Social, and Legal Outcomes (KQ1)

Outcome	Author year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Family cohesion - parent report	Estrada, 2018[90]	Positive parenting (Tolan et al., 1997); When your child has done something that you like or approve of, do you say something nice about it; praise or give approval?"; scale 0 (Never) to 4 (Always); 0-4 (High)	NA	IG1 (Overall)	3	. (.), 84	. (.), 101	Beta: 0.13 (-0.94 to 1.22)	0.80
	Foxcroft, 2017[93]	Communication, aggressive and hostile behavior and in interactions; 0-5 (Low)	NR	IG1 (Overall)	12	. (.), 233	. (.), 194	Mean Ratio: 0.02 (-0.06 to 0.11)	NR, NS
					24	. (.), 174	. (.), 154	Mean Ratio: 0.01 (-0.07 to 0.10)	NR, NS
Family cohesion - mother report	Fang, 2010[92]	Communication, mother-daughter; 1-5 (High)	1 week	IG1 (Overall)	6	.2 (2.1), 54	-.4 (2.1), 50	CalcMeanDiffChg: 0.55 (-0.25 to 1.35)	0.03
					12	.2 (2), 54	-.3 (2.1), 50	CalcMeanDiffChg: 0.52 (-0.28 to 1.32)	0.049
					24	.3 (2), 50	-.4 (2.2), 43	CalcMeanDiffChg: 0.63 (-0.23 to 1.49)	0.049
		Mother-daughter closeness; 1-5 (High)	NA	IG1 (Overall)	6	.4 (1), 54	-.2 (1.1), 50	CalcMeanDiffChg: 0.56 (0.15 to 0.97)	0.0001
					12	.4 (1), 54	-.2 (1.2), 50	CalcMeanDiffChg: 0.57 (0.16 to 0.98)	0.0002
					24	.3 (.9), 50	-.2 (1.1), 43	CalcMeanDiffChg: 0.53 (0.12 to 0.94)	0.0002
		Parental monitoring; 1-5 (High)	NA	IG1 (Overall)	6	.2 (.6), 54	-.2 (.9), 50	CalcMeanDiffChg: 0.35 (0.06 to 0.64)	0.0003
					12	.1 (.6), 54	-.2 (.9), 50	CalcMeanDiffChg: 0.33 (0.03 to 0.63)	0.019
					24	0 (.7), 50	-.2 (.9), 43	CalcMeanDiffChg: 0.25 (-0.08 to 0.58)	0.019
	Schinke, 2009a[107]	Communication; 1-5 (High)	1 week	IG1 (Overall)	12	0 (1.9), 205	-.3 (1.9), 327	TxtEffectEst: 0.33 (0.00 to 0.66)	<0.01
		Parental monitoring; 1-5 (High)	NA	IG1 (Overall)	12	-.4 (1), 205	-1.1 (1.1), 327	TxtEffectEst: 0.62 (0.44 to 0.80)	<0.0001
	Schinke, 2009b[108]	Communication, mother-daughter; 1-5 (High)	1 week	IG1 (Overall)	12	.3 (2.3), 434	.2 (2.2), 430	CalcMeanDiffChg: 0.03 (-0.26 to 0.32)	<0.0001

Appendix D Table 4. Health, Social, and Legal Outcomes (KQ1)

Outcome	Author year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	Schinke, 2009b[108]	Communication, mother-daughter; 1-5 (High)	1 week	IG1 (Overall)	24	0 (2.2), 415	-1 (1.9), 413	CalcMeanDiffChg: 0.99 (0.71 to 1.27)	<0.0001
		Mother-daughter closeness; 1-5 (High)	NA	IG1 (Overall)	12	-.2 (1.6), 434	-.2 (1.6), 430	CalcMeanDiffChg: 0.09 (-0.12 to 0.30)	<0.0001
					24	-.4 (1.6), 415	-2.2 (1.4), 413	CalcMeanDiffChg: 1.86 (1.66 to 2.06)	<0.0001
		Parental monitoring; 1-5 (High)	NA	IG1 (Overall)	12	0 (.6), 434	-.1 (.7), 430	CalcMeanDiffChg: 0.04 (-0.04 to 0.12)	<0.0001
					24	-.1 (.6), 415	-.7 (1.6), 413	CalcMeanDiffChg: 0.53 (0.37 to 0.69)	<0.0001
Other Delinquent Behavior	Dembo, 2016[88]	Official arrest charges	NA	IG1 (Overall)	4	--	--	TxtEffectEst: -0.08 (-0.21 to 0.05)	NR, NS
					7	--	--	TxtEffectEst: 0.07 (-0.05 to 0.20)	NR, NS
					13	--	--	TxtEffectEst: -0.02 (-0.17 to 0.14)	NR, NS
					19	--	--	TxtEffectEst: 0.09 (-0.07 to 0.24)	NR, NS
					25	--	--	TxtEffectEst: -0.08 (-0.19 to 0.03)	0.069
				IG2 (Overall)	4	--	--	TxtEffectEst: -0.08 (-0.19 to 0.03)	NR, NS
					7	--	--	TxtEffectEst: 0.00 (-0.11 to 0.11)	NR, NS
					13	--	--	TxtEffectEst: -0.06 (-0.21 to 0.08)	NR, NS
					19	--	--	TxtEffectEst: 0.10 (-0.05 to 0.25)	NR, NS
					25	--	--	TxtEffectEst: -0.23 (-0.36 to -0.11)	<0.001
		Self-reported delinquency; Range NR (Low)	NA	IG1 (Overall)	4	--	--	TxtEffectEst: -0.26 (-0.51 to -0.02)	NR, NS
					7	--	--	TxtEffectEst: 0.26 (0.02 to 0.51)	NR, NS
					13	--	--	TxtEffectEst: 0.16 (-0.07 to 0.39)	NR, NS
					19	--	--	TxtEffectEst: 0.09 (-0.17 to 0.35)	NR, NS

Appendix D Table 4. Health, Social, and Legal Outcomes (KQ1)

Outcome	Author year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	Dembo, 2016[88]	Self-reported delinquency; Range NR (Low)	NA	IG2 (Overall)	4	--	--	TxtEffectEst: -0.20 (-0.44 to 0.05)	NR, NS
					7	--	--	TxtEffectEst: 0.03 (-0.23 to 0.29)	NR, NS
					13	--	--	TxtEffectEst: -0.09 (-0.34 to 0.16)	NR, NS
					19	--	--	TxtEffectEst: 0.08 (-0.17 to 0.32)	NR, NS
	Foxcroft, 2017[93]	Index of aggressive and destructive conduct; 0-4 (Low)	NR	IG1 (Overall)	12	. (.), 233	. (.), 194	Mean Ratio: 0.00 (-0.09 to 0.09)	NR, NS
					24	. (.), 174	. (.), 154	Mean Ratio: 0.00 (-0.12 to 0.11)	NR, NS
	Jalling, 2016[95]	Total self-reported delinquency score (SRD); 0-360 (Low)	6 months	IG1 (Overall)	6	2.3 (36.1), 70	-2.1 (36.1), 81	CalcMeanDiffChg: 4.41 (-7.13 to 15.95)	NR, NS
		SRD, total score; 0-360 (Low)	6 months	IG2 (Overall)	6	2.2 (50.1), 86	-2.1 (36.1), 81	CalcMeanDiffChg: 4.31 (-8.89 to 17.51)	NR, NS
	Kim, 2011[98]	Self-reported delinquent behavior in past year; NR	1 year	IG1 (Overall)	36	.3 (.9), 48†	.9 (2.7), 52†	CohensD: -0.65 (-1.43 to 0.13)†	0.098
	Walton, 2014[115]	Ten items assessing frequency of violent and non-violent delinquency (e.g. physical fighting, stealing, selling drugs) were summed, range 0-10 where lower is better; 0-10 (Low)	3 months	IG1 (Overall)	3	. (.), 199	. (.), 216	IRRnegbin: 0.53 (0.36 to 0.79)	<0.01
					6	. (.), 200	. (.), 211	IRRnegbin: 0.81 (0.51 to 1.30)	NR, NS
					12	. (.), 201	. (.), 207	IRRnegbin: 1.03 (0.64 to 1.65)	NR, NS
				IG2 (Overall)	3	. (.), 220	. (.), 216	IRRnegbin: 0.90 (0.62 to 1.31)	NR, NS
					6	. (.), 218	. (.), 211	IRRnegbin: 0.94 (0.60 to 1.48)	NR, NS
					12	. (.), 220	. (.), 207	IRRnegbin: 0.85 (0.53 to 1.36)	NR, NS
Consequences of Drug Use	D'Amico, 2018[116]	Number of negative consequences experienced - marijuana	3 months	IG1 (Overall)	3	1.7 (5.2), 113†	1.9 (7.2), 86†	CalcMeanDiffChg: 0.06 (-1.33 to 1.45)†	0.93
	D'Amico, 2018[116]	Number of negative consequences experienced - marijuana	3 months	IG1 (Overall)	6	0.7 (1.5), 127†	1.5 (5.7), 111†	CalcMeanDiffChg: -0.72 (-1.72 to 0.28)†	0.16

Appendix D Table 4. Health, Social, and Legal Outcomes (KQ1)

Outcome	Author year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	D'Amico, 2018[116]	Number of negative consequences experienced - marijuana	3 months	IG1 (Overall)	12	0.9 (3.3), 122†	2.4 (9.3), 114†	CalcMeanDiffChg: -1.75 (-3.38 to -0.12)†	0.04
	D'Amico, 2018[116]	No. of negative consequences experienced - alcohol	3 months	IG1 (Overall)	3	2.2 (5.1), 113†	3.4 (9), 86†	CalcMeanDiffChg: -1.16 (-2.81 to 0.49)†	0.17
	D'Amico, 2018[116]	No. of negative consequences experienced - alcohol	3 months	IG1 (Overall)	6	2.2 (3.5), 127†	3.6 (8.5), 111†	CalcMeanDiffChg: -1.34 (-2.85 to 0.17)†	0.08
	D'Amico, 2018[116]	No. of negative consequences experienced - alcohol	3 months	IG1 (Overall)	12	2 (4.5), 122†	4.3 (12.4), 114†	CalcMeanDiffChg: -2.33 (-4.49 to -0.17)†	0.03
	Lee, 2010[100]	Rutgers Marijuana Problem Index. Respondents indicate how many times, from 0 (never) to 4 (more than 10 times), they experienced each of 18 negative consequences due to marijuana use in the past 3 months. Items include: "Not able to do your homework or study for a test" and "Missed out on other things because you spent too much money on marijuana." Items were summed to assess number of different problems experienced; 0-72 (Low)	3 months	IG1 (Overall)	3	.4 (3.4), 162	.1 (2.5), 162	CalcMeanDiffChg: 0.23 (-0.42 to 0.88)	NR, NS
					6	.5 (3.5), 160	.3 (2.7), 160	CalcMeanDiffChg: 0.15 (-0.53 to 0.83)	NR, NS
	Walton, 2013[114]	Cannabis related consequences in the past 3 months, consisting of 23 items	3 months	IG1 (Overall)	3	-1.7 (14.1), 101	-.4 (15.1), 96	TxtEffectEst: -0.18 (-0.42 to 0.06)	0.15
					6	-2.9 (14.3), 102	-3 (14.4), 97	TxtEffectEst: -0.08 (-0.37 to 0.21)	0.60

Appendix D Table 4. Health, Social, and Legal Outcomes (KQ1)

Outcome	Author year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
		adapted from the Rutgers Alcohol Problems Index and 5 items from the Severity of Dependence Scale (interpersonal, intrapersonal, and substance use disorder problems); NR (Low)			12	-3.1 (14.3), 104	-2.5 (14.7), 94	TxtEffectEst: -0.07 (-0.36 to 0.22)	0.62
				IG2 (Overall)	3	-2.8 (15.3), 82	-.4 (15.1), 96	TxtEffectEst: -0.24 (-0.48 to 0.00)	<0.05
					6	-3.8 (14.6), 79	-3 (14.4), 97	TxtEffectEst: -0.15 (-0.46 to 0.16)	0.37
					12	-1.6 (14.7), 77	-2.5 (14.7), 94	TxtEffectEst: 0.08 (-0.25 to 0.41)	0.62

*Author reported.
† Mean value at followup, rather than change from baseline.

Abbreviations: Beta = Beta coefficient; Bweight = Beta weight; CalcMeanDiffChg = Calculated Mean Difference in Change; CES-D = Center for Epidemiologic Studies Depression Scale; CG = Control group; CHQ-CF-GH4 = Child Health Questionnaire-Child Form-General Health; CohensD = Cohen's d; FU = Followup; IG = Intervention group; IRRnegbin = Incident rate ratio (negative binomial); MeanDiff = Mean Difference; MeanDiffinChange = Mean Difference in Change; NA = Not applicable; NR = Not reported; NS = Not significant; OR = Odds Ratio; POSIT = Problem Oriented Screening Instrument for Teenagers; RAASI = Reynolds Adolescent Adjustment Screening Inventory; SD = Standard deviation; SDQ = Strengths and Difficulties Questionnaire; TxtEffectEst = Treatment effect estimate; Y-OQ = Youth Outcome Questionnaire.

Appendix D. Table 5. Drug Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Cannabis abstinence	Harris, 2012[80]	Cessation of use	1 year	IG1 (Prague - Any BL cannabis use)	12	15/38 (39.5)	7/36 (19.4)	OR: 2.70 (0.94 to 7.73)	<0.05
				IG1 (New England - Any BL cannabis use)	12	28/95 (29.5)	27/101 (26.7)	OR: 1.15 (0.61 to 2.14)	NR, NS
Cannabis any use	Baldus, 2016[81]	Self-reported lifetime use	Lifetime	IG1 (Overall)	0	3/147 (2.1)	2/145 (1.4)	OR: 1.49 (0.25 to 9.05)	0.686
					20	13/126 (10.3)	14/121 (11.6)	OR: 0.86 (0.41 to 1.81)	0.696
		Self-reported past 30-day use	1 month	IG1 (Overall)	0	4/147 (2.8)	1/145 (0.7)	OR: 4.03 (0.44 to 36.48)	NSD
					8	5/147 (3.7)	3/145 (2.3)	OR: 0.93 (0.33 to 2.66)	0.897
					20	8/147 (5.6)	10/145 (6.7)	OR: 0.74 (0.28 to 1.96)	0.537
	Barlow, 2013[83]	Any marijuana use in past month	1 month	IG1 (Overall)	0	13/159 (8.2)	10/163 (6.1)	OR: 1.18 (0.49 to 2.83)	0.71
					4	33/159 (20.6)	34/163 (21.0)	OR: 0.87 (0.44 to 1.70)	0.68
					8	20/159 (12.4)	31/163 (18.8)	OR: 0.57 (0.29 to 1.11)	0.10
					14	30/159 (18.9)	32/163 (19.6)	OR: 0.83 (0.44 to 1.58)	0.57
					38	17/159 (10.7)	25/163 (15.6)	OR: 0.65 (0.48 to 0.89)	0.007
	Dembo, 2016[88]	Marijuana use; 0-6 (Low)	NR	IG1 (Overall)	7	. (.), 98	. (.), 101	TxtEffectEst: -0.03 (-0.71 to 0.65)	NR, NS
					13	. (.), 98	. (.), 101	TxtEffectEst: 0.05 (-0.59 to 0.70)	NR, NS
					19	. (.), 98	. (.), 101	TxtEffectEst: 0.01 (-0.75 to 0.78)	NR, NS
				IG1 (Female)	4	--	--	TxtEffectEst: -0.67 (NR)	NR, NS

Appendix D. Table 5. Drug Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Cannabis any use	Dembo, 2016[88]	Marijuana use; 0-6 (Low)	NR	IG1 (Male)	4	--	--	TxtEffectEst: 0.31 (NR)	NR, NS
				IG2 (Overall)	7	. (.), 101	. (.), 101	TxtEffectEst: 0.10 (-0.41 to 0.61)	NR. NS
				IG2 (Overall)	13	. (.), 101	. (.), 101	TxtEffectEst: -0.07 (-0.71 to 0.56)	NR, NS
				IG2 (Overall)	19	. (.), 101	. (.), 101	TxtEffectEst: -0.84 (-1.47 to -0.21)	<0.01
				IG2 (Female)	4	--	--	TxtEffectEst: -0.01 (NR)	NR, NS
				IG2 (Male)	4	--	--	TxtEffectEst: 0.00 (NR)	NR, NS
	Gmel, 2013[94]	6 months cannabis use	6 months	IG1 (Overall)	0	181/392 (46.2)	205/461 (44.5)	OR: 1.07 (0.82 to 1.40)	NSD
						97/288 (33.7)	148/384 (38.6)	OR: 0.81 (0.59 to 1.11)	0.013
		More than weekly use	6 months	IG1 (Overall)	0	54/392 (13.9)	87/461 (18.8)	OR: 0.69 (0.47 to 0.99)	<0.05
					6	42/288 (14.6)	76/384 (19.8)	OR: 0.69 (0.46 to 1.05)	0.493
	Harris, 2012[80]	Any past 12-month use	1 year	IG1 (New England)	0	95/765 (12.4)	101/758 (13.3)	OR: 0.92 (0.68 to 1.25)	NR, NS
				IG1 (Prague)	0	38/264 (14.4)	36/266 (13.6)	OR: 1.07 (0.66 to 1.76)	NR, NS
				IG1 (New England)	12	119/765 (15.6)	133/758 (17.5)	OR: 0.87 (0.66 to 1.13)	NR, NS
				IG1 (Prague)	12	45/264 (17.0)	76/266 (28.7)	OR: 0.51 (0.34 to 0.78)	<0.05
		Any past 90-day use	3 months	IG1 (New England)	3	56/761 (7.4)	72/755 (9.5)	OR: 0.75 (0.52 to 1.09)	NR, NS
				IG1 (Prague)	3	15/271 (5.5)	24/245 (9.8)	OR: 0.54 (0.28 to 1.05)	<0.05
		Initiation of marijuana use	1 year	IG1 (Prague - No BL cannabis use)	12	22/226 (9.7)	47/230 (20.4)	OR: 0.42 (0.24 to 0.72)	<0.05
				IG1 (New England - No BL cannabis use)	12	52/670 (7.8)	58/657 (8.8)	OR: 0.87 (0.59 to 1.28)	NR, NS

Appendix D. Table 5. Drug Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Cannabis any use	Kerr, 2013[97]	Lifetime marijuana use	Lifetime	IG1 (Overall)	12	./834 (.)	./820 (.)	Regression coefficient: 0.56	<0.001 (favors CG)
		Past month marijuana use; continuous measure to determine frequency of use	1 month	IG1 (Overall)	12	./834 (.)	./820 (.)	Regression coefficient: -0.18	NR, NS
	Knight, 2019[72]	Number with any cannabis use	12 months	IG1 (Overall)	3	140/626 (22.4)	69/243 (28.4)	OR: 0.73 (0.52 to 1.02)	NSD
	Knight, 2019[72]	Number with any cannabis use	12 months	IG1 (Overall)	6	172/626 (27.5)	82/243 (33.7)	OR: 0.74 (0.54 to 1.02)	NSD
	Knight, 2019[72]	Number with any cannabis use	12 months	IG1 (Overall)	9	201/626 (32.1)	91/243 (37.4)	OR: 0.79 (0.58 to 1.08)	NSD
	Knight, 2019[72]	Number with any cannabis use	12 months	IG1 (Overall)	12	232/626 (37.1)	101/243 (41.6)	OR: 0.83 (0.61 to 1.12)	NSD
	Knight, 2019[72]	Number with any cannabis use	12 months	IG1 (Alcohol or other drug use in past 12 months at baseline)	3	113/148 (76.4)	53/63 (84.1)	OR: 0.61 (0.28 to 1.32)	NSD
	Knight, 2019[72]	Number with any cannabis use	12 months	IG1 (No alcohol or other drug use in past 12 months at baseline)	3	27/478 (5.6)	16/180 (8.9)	OR: 0.61 (0.32 to 1.17)	NSD
	Knight, 2019[72]	Number with any cannabis use	12 months	IG1 (Alcohol or other drug use in past 12 months at baseline)	6	126/148 (85.1)	59/63 (93.7)	OR: 0.39 (0.13 to 1.18)	NSD
	Knight, 2019[72]	Number with any cannabis use	12 months	IG1 (No alcohol or other drug use in past 12 months at baseline)	6	46/478 (9.6)	23/180 (12.8)	OR: 0.73 (0.43 to 1.24)	NSD
	Knight, 2019[72]	Number with any cannabis use	12 months	IG1 (Alcohol or other	9	136/148 (91.9)	61/63 (96.8)	OR: 0.37 (0.08 to 1.71)	NSD

Appendix D. Table 5. Drug Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
				drug use in past 12 months at baseline)					
	Knight, 2019[72]	Number with any cannabis use	12 months	IG1 (No alcohol or other drug use in past 12 months at baseline)	9	65/478 (13.6)	30/180 (16.7)	OR: 0.79 (0.49 to 1.26)	NSD
	Knight, 2019[72]	Number with any cannabis use	12 months	IG1 (Alcohol or other drug use in past 12 months at baseline)	12	137/148 (92.6)	63/63 (100.0)	HR: 0.62 (0.41 to 0.94)	<0.05
	Knight, 2019[72]	Number with any cannabis use	12 months	IG1 (No alcohol or other drug use in past 12 months at baseline)	12	95/478 (19.9)	38/180 (21.1)	HR: 0.76 (0.44 to 1.32)	NR, NS
	Malmberg, 2014[102]	Lifetime use	Lifetime	IG1 (Overall)	0	29/1225 (2.4)	15/1191 (1.3)	OR: 2.46 (0.47 to 12.84)	NSD
					8	68/1114 (6.1)	58/1109 (5.2)	OR: 1.22 (0.49 to 3.03)	0.517
					20	122/1003 (12.2)	92/982 (9.4)	OR: 1.34 (0.66 to 2.73)	0.517
					32	150/825 (18.2)	109/692 (15.7)	OR: 1.15 (0.59 to 2.25)	0.517
	Walton, 2014[115]	Any cannabis use	3 months	IG1 (Overall)	3	13/199 (6.5)	17/216 (7.9)	OR: 0.82 (0.39 to 1.73)	NSD
				IG1 (Overall)	6	18/200 (9.0)	19/211 (9.0)	OR: 1.00 (0.51 to 1.96)	NSD
				IG2 (Overall)	3	11/220 (5.0)	17/216 (7.9)	OR: 0.62 (0.28 to 1.35)	NSD
				IG2 (Overall)	6	13/218 (6.0)	19/211 (9.0)	OR: 0.64 (0.31 to 1.33)	NSD
			12 months	IG1 (Overall)	12	22/201 (10.9)	29/207 (14.0)	OR: 0.75 (0.42 to 1.36)	NSD

Appendix D. Table 5. Drug Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
				IG1 (Overall)	12	42/201 (20.9)	50/207 (24.2)	OR: 0.83 (0.52 to 1.32)	NSD
				IG2 (Overall)	12	37/220 (16.8)	50/207 (24.2)	OR: 0.63 (0.39 to 1.02)	NSD
				IG2 (Overall)	12	24/220 (10.9)	29/207 (14.0)	OR: 0.75 (0.42 to 1.34)	NSD
Cannabis frequency/ quantity - times used	D'Amico, 2018[116]	Times used marijuana in past 90 days	3 months	IG1 (Overall)	3	6.4 (8.1), 113†	5.9 (7.6), 86†	CalcMeanDiff: 0.43 (-1.75 to 2.61)†	0.99
				IG1 (Overall)	6	6.1 (7.9), 127†	5.1 (6.8), 111†	CalcMeanDiff: 1.06 (-0.81 to 2.93)†	0.35
				IG1 (Overall)	12	6.8 (8.4), 127†	5.2 (7.3), 114†	CalcMeanDiff: 1.55 (-0.43 to 3.53)†	0.23
	Estrada, 2018[90]	Times used marijuana in past 90 days	3 months	IG1 (Overall)	3	-0.8 (7.9), 84	0.8 (6.4), 101	CalcMeanDiffChg: -1.57 (-3.68 to 0.54)	<0.01
					12	-0.8 (8), 82	2 (11.3), 98	EffectSize: -2.74 (-5.56 to 0.08)	<0.01
	Fang, 2010[92]	Past 30-day use occasions	3 months	IG1 (Overall)	6	-0.2 (1.3), 54	-0.5 (2.6), 50	CalcMeanDiffChg: 0.27 (-0.52 to 1.06)	0.009
					12	-0.2 (1.3), 54	-0.2 (2.3), 50	CalcMeanDiffChg: -0.06 (-0.78 to 0.66)	0.043
					24	-0.2 (1.3), 50	0 (2.3), 43	CalcMeanDiffChg: -0.21 (-0.98 to 0.56)	0.043
	Johnson, 2015[96]	Time used marijuana in the past 30 days	3 months	IG1 (Overall)	6	1.3 (21.5), 101	3.7 (34.7), 99	RRnegbin: 1.83 (1.17 to 2.85)	≤0.05
	Schinke, 2009a[107]	Reported use occasions in past 30 days	3 months	IG1 (Overall)	12	0.1 (.4), 205	0.4 (1.9), 327	TxtEffectEst: -0.30 (-0.51 to -0.09)	<0.01
	Schinke, 2009b[108]	Times smoked marijuana in past month	3 months	IG1 (Overall)	12	0 (0), 434	0.1 (.6), 430	CalcMeanDiffChg: -0.03 (-0.09 to 0.03)	<0.016
					24	0.1 (.3), 415	0.3 (2.1), 413	CalcMeanDiffChg: -0.27 (-0.47 to -0.07)	<0.016
	Schwinn, 2010[110]	Report how many times in the past month any drug was used	3 months	IG1 (Overall)	6	0.1 (3.1), 108†	1.3 (3.3), 118†	CalcMeanDiff: -1.14 (-1.97 to -0.31)†	0.02
	Schwinn, 2015[112]	30-day marijuana use	3 months	IG1 (Overall)	3	-0.3 (5.2), 97	-0.4 (5.9), 103	CalcMeanDiffChg: 0.15 (-1.39 to 1.69)	NR, NS
	Schwinn, 2018[111]	Times used in past month	3 months	IG1 (Overall)	3	-1.5 (14.7), 376	-0.9 (12.5), 380	Bweight: -0.60 (-2.25 to 1.05)	NR, NS
					15	0.8 (15.3), 370	-0.2 (12.5), 382	Bweight: 1.47 (-0.29 to 3.23)	NR, NS

Appendix D. Table 5. Drug Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Cannabis frequency/ quantity - days used	Gmel, 2013[94]	Number of days with cannabis use per month	3 months	IG1 (Overall)	6	0.1 (.), 288	0.2 (.), 384	Beta: -0.27 (-0.60 to 0.06)	0.113
		Number of days with cannabis use per month, consistent users	3 months	IG1 (Consistent users)	6	0.4 (.), .	0.7 (.), .	Beta: -0.45 (-1.38 to 0.48)	0.342
	Lee, 2010[100]	On how many days did you use any kind of marijuana or hashish?	3 months	IG1 (Overall)	3	-0.7 (15), 162	-0.8 (16), 162	CalcMeanDiffChg: 0.03 (-3.35 to 3.41)	NR, NS
					6	1.2 (17.5), 160	2.1 (17.9), 160	CalcMeanDiffChg: -0.94 (-4.82 to 2.94)	NR, NS
Cannabis frequency/ quantity - score	Kim, 2011[98]	Marijuana use in past year (1=never, 9=daily); 1-9 (Low)	1 year	IG1 (Overall)	36	1.3 (.8), 48†	2.3 (2.4), 52†	CohensD: -1.04 (-1.74 to -0.34)†	0.01
	Mason, 2015[103]	Participants were asked the number of days they have used marijuana within the last month, coded as 0= 0 days, 1= 1 or 2 days, 3= 3 to 5 days, 4=6 to 9 days, 5=10 to 19 days, 6=20 to 29 days, and 7=all 30 days.; 0-7 (Low)	1 month	IG1 (Overall)	6	. (.), 57	. (.), 60	TxtEffectEst: -0.08 (-0.18 to 0.02)	NR, NS
	Mason, 2015[103]	Participants were asked the number of days they have used marijuana within the last month, coded as 0= 0 days, 1= 1 or 2 days, 3= 3 to 5 days, 4=6 to 9 days, 5=10 to 19 days, 6=20 to 29 days, and 7=all 30 days.; 0-7 (Low)	1 month	IG1 (Female)	3	0 (.), 44	-0.3 (.), 40	--	NR, NS
				IG1 (Male)	3	-0.2 (.), 15	0.1 (.), 20	--	NR, NS
				IG1 (Female)	6	0.1 (.), 44	-0.5 (.), 40	--	NR, NS
				IG1 (Male)	6	-0.3 (.), 15	0.3 (.), 20	--	NR, NS
	Walton, 2013[114]	Past 3 month frequency of cannabis. Response choices were: never = 0; 1–2	3 months	IG1 (Overall)	3	-0.8 (2), 101	-1.2 (2), 96	TxtEffectEst: -0.18 (-0.43 to 0.07)	0.16
					6	-0.7 (2), 102	-1.2 (2), 97	TxtEffectEst: 0.25 (-0.02 to 0.52)	0.08

Appendix D. Table 5. Drug Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
		days = 1; once a month or less = 2; 2–3 days per month = 3; 1–2 days per week = 4; 3–5 days per week = 5; and every day or almost every day = 6.; 0-6 (Low)			12	-.5 (2.1), 104	-1.1 (2.1), 94	TxtEffectEst: 0.15 (-0.12 to 0.42)	0.28
				IG2 (Overall)	3	-1 (2.1), 82	-1.2 (2), 96	TxtEffectEst: -0.08 (-0.37 to 0.21)	0.57
					6	-1.1 (2), 79	-1.2 (2), 97	TxtEffectEst: 0.08 (-0.23 to 0.39)	0.62
					12	-1 (2.1), 77	-1.1 (2.1), 94	TxtEffectEst: -0.03 (-0.34 to 0.28)	0.85
	Walton, 2014[115]	Cannabis (e.g. marijuana, weed, pot) use frequency. Response choices were: never, 1–2 days, once a month or less, 2–3 days per month, 1–2 days per week, 3–5 days per week and every day or almost every day.; 0-6 (Low)	3 months	IG1 (Overall)	3	. (.), 199	. (.), 216	IRRnegbin: 0.84 (0.49 to 1.42)	NR, NS
	Walton, 2014[115]	Cannabis (e.g. marijuana, weed, pot) use frequency. Response choices were: never, 1–2 days, once a month or less, 2–3 days per month, 1–2 days per week, 3–5 days per week and every day or almost every day.; 0-6 (Low)	3 months	IG1 (Overall)	6	. (.), 200	. (.), 211	IRRnegbin: 0.66 (0.41 to 1.06)	NR, NS
					12	. (.), 201	. (.), 207	IRRnegbin: 0.94 (0.21 to 4.18)	NR, NS
				IG2 (Overall)	3	. (.), 220	. (.), 216	IRRnegbin: 0.53 (0.29 to 0.95)	<0.05
					6	. (.), 218	. (.), 211	IRRnegbin: 0.61 (0.37 to 0.99)	<0.05
	Walton, 2014[115]	Cannabis (e.g. marijuana, weed, pot) use frequency. Response choices were: never, 1–2 days, once a month or less, 2–3 days per month, 1–2 days per week, 3–5 days per week and every day or almost every day.; 0-6 (Low)	3 months	IG2 (Overall)	12	. (.), 220	. (.), 207	IRRnegbin: 0.86 (0.58 to 1.27)	NR, NS

Appendix D. Table 5. Drug Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Other drug any use	Estrada, 2018[90]	Proportion with prescription drug (mis)use use over time	NR	IG1 (Overall)	0	3/113 (2.7)	1/117 (0.1)	OR: 3.16 (0.32 to 30.87)	NSD
					3	3/84 (3.6)	4/101 (4.0)	OR: 0.90 (0.20 to 4.13)	NR, NS
					12	2/82 (2.4)	5/98 (5.1)	OR: 0.47 (0.09 to 2.46)	NR, NS
Other drug frequency/ quantity - times used	Estrada, 2018[90]	Times (mis)used prescription drugs in past 90 days	3 months	IG1 (Overall)	3	0.2 (1.2), 84	-0.1 (8.3), 101	CalcMeanDiffChg: 0.33 (-1.31 to 1.97)	<0.01
					12	0 (0.3), 82	0.1 (8.6), 98	EffectSize: -0.15 (-1.85 to 1.55)	<0.01
	Estrada, 2018[90]	Times used cocaine in past 90 days	3 months	IG1 (Overall)	3	-0.7 (8), 84	0.6 (6.5), 101	CalcMeanDiffChg: -1.31 (-3.43 to 0.81)	NR, NS
					12	-0.8 (8.4), 82	0.8 (7.3), 98	EffectSize: -1.57 (-3.90 to 0.76)	NR, NS
	Estrada, 2018[90]	Times used inhalants in past 90 days	3 months	IG1 (Overall)	3	-0.7 (8), 84	0.6 (6.5), 101	CalcMeanDiffChg: -1.35 (-3.47 to 0.77)	<0.001
	Estrada, 2018[90]	Times used inhalants in past 90 days	3 months	IG1 (Overall)	12	-0.8 (8.2), 82	0.8 (7.3), 98	EffectSize: -1.53 (-3.83 to 0.77)	<0.001
		Times used other (NOS) drug in past 90 days	3 months	IG1 (Overall)	3	-0.6 (7.9), 84	0.7 (6.9), 101	CalcMeanDiffChg: -1.34 (-3.50 to 0.82)	NR, NS
					12	-0.8 (8.4), 82	0.8 (7.7), 98	EffectSize: -1.64 (-4.01 to 0.73)	NR, NS
	Fang, 2010[92]	Past 30-day prescription drug use occasions	3 months	IG1 (Overall)	6	-1.9 (8.9), 54	-1 (4.3), 50	CalcMeanDiffChg: -0.93 (-3.59 to 1.73)	0.017
					12	-1.7 (8.5), 54	3.4 (19.5), 50	CalcMeanDiffChg: -5.13 (-10.98 to 0.72)	0.047
					24	-1.9 (8.9), 50	9.4 (36.8), 43	CalcMeanDiffChg: -11.34 (-22.60 to -0.08)	0.047
	Schinke, 2009a[107]	Reported prescription use occasions in past 30 days	3 months	IG1 (Overall)	12	-0.4 (2.5), 205	0.2 (4.2), 327	TxtEffectEst: -0.66 (-1.23 to -0.09)	<0.0001
	Schinke, 2009b[108]	Times used illicit prescriptions in past 30 days	3 months	IG1 (Overall)	12	-0.1 (.6), 434	0 (0.3), 430	CalcMeanDiffChg: -0.12 (-0.18 to -0.06)	<0.03
					24	-0.1 (.5), 415	0.1 (0.5), 413	CalcMeanDiffChg: -0.15 (-0.22 to -0.08)	<0.03
		Times used inhalants in past 30 days	3 months	IG1 (Overall)	12	-0.1 (.8), 434	0.1 (0.8), 430	CalcMeanDiffChg: -0.15 (-0.26 to -0.04)	<0.024
					24	-0.1 (0.8), 415	0.1 (0.5), 413	CalcMeanDiffChg: -0.12 (-0.21 to -0.03)	<0.024

Appendix D. Table 5. Drug Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	Schwinn, 2015[112]	30-day inhalants, club drugs, steroids, cocaine, methamphetamines, prescription drugs, and heroin use	3 months	IG1 (Overall)	3	-0.4 (1.1), 97	-0.4 (2.6), 103	CalcMeanDiffChg: 0.06 (-0.48 to 0.60)	<0.05
	Schwinn, 2018[111]	Times used club drugs, cocaine, ecstasy, hallucinogens, heroin, inhalants, methamphetamines, steroids, and prescription drugs in past month	3 months	IG1 (Overall)	3	-2.2 (14.3), 376	-1.8 (11), 380	Bweight: -1.47 (-3.00 to 0.06)	NR, NS
	Schwinn, 2018[111]	Times used club drugs, cocaine, ecstasy, hallucinogens, heroin, inhalants, methamphetamines, steroids, and prescription drugs in past month	3 months	IG1 (Overall)	15	-2.2 (14.3), 370	-2 (11), 382	Bweight: -1.08 (-2.79 to 0.63)	NR, NS
Other drug frequency/ quantity - score	Walton, 2013[114]	Past 3 month frequency of inhalants, cocaine, heroin, other hallucinogens, nonmedical use of painkillers/opioids, stimulants, and sedatives. Response choices were: never = 0; 1–2 days = 1; once a month or less = 2; 2–3 days per month = 3; 1–2 days per week; 0-6 (Low)	3 months	IG1 (Overall)	3	-0.2 (1.2), 101	0 (3.6), 96	TxtEffectEst: 0.61 (-0.15 to 1.37)	0.12
					6	-0.2 (1.2), 102	0 (4), 97	TxtEffectEst: -0.48 (-1.30 to 0.34)	0.255
					12	-0.1 (1.5), 104	-0.5 (2.5), 94	TxtEffectEst: 0.33 (-0.67 to 1.33)	0.52
				IG2 (Overall)	3	-0.7 (2.8), 82	0 (3.6), 96	TxtEffectEst: 1.82 (0.49 to 3.15)	<0.01
					6	-0.7 (2.8), 79	0 (4), 97	TxtEffectEst: -1.41 (-2.43 to -0.39)	<0.01
					12	-0.4 (2.7), 77	-0.5 (2.5), 94	TxtEffectEst: 0.21 (-0.73 to 1.15)	0.66

Appendix D. Table 5. Drug Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	Walton, 2014[115]	Illicit (inhalants, cocaine, heroin and other hallucinogens) and non-medical prescription drug use (painkillers/opiates, stimulants, and sedatives) (on your own without a doctor telling you to take them). Response options ranged from 0–6: never, 1–2 day; 0-42 (Low)	3 months	IG2 (Overall)	3	. (.), 220	. (.), 216	IRRnegbin: 0.52 (0.31 to 0.86)	<0.05
	Walton, 2014[115]	Illicit (inhalants, cocaine, heroin and other hallucinogens) and non-medical prescription drug use (painkillers/opiates, stimulants, and sedatives) (on your own without a doctor telling you to take them). Response options ranged from 0–6: never, 1–2 day; 0-42 (Low)	3 months	IG2 (Overall)	6	. (.), 218	. (.), 211	IRRnegbin: 0.97 (0.61 to 1.55)	NR, NS
					12	. (.), 220	. (.), 207	IRRnegbin: 0.78 (0.38 to 1.58)	NR, NS
		Illicit and non-medical prescription drug use (on your own without a doctor telling you to take them). Response options ranged from 0–6: never, 1–2 days, once a month or less, 2–3 days per month, 1–2 days per week, 3–5 days per week, every day.; 0-42 (Low)	3 months	IG1 (Overall)	3	. (.), 199	. (.), 216	IRRnegbin: 0.65 (0.39 to 1.08)	NR, NS
					6	. (.), 200	. (.), 211	IRRnegbin: 0.63 (0.37 to 1.07)	NR, NS
					12	. (.), 201	. (.), 207	IRRnegbin: 0.90 (0.39 to 2.04)	NR, NS

Appendix D. Table 5. Drug Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Any drug any use	Bannink, 2014[82]	Drug use in past 4 weeks	1 month	IG1 (Overall)	0	27/430 (6.3)	35/434 (8.1)	OR: 0.77 (0.37 to 1.59)	0.31
					4	44/430 (10.4)	36/434 (8.3)	OR: 1.54 (0.63 to 3.85)	0.34
				IG2 (Overall)	0	18/392 (4.6)	35/434 (8.1)	OR: 0.53 (0.23 to 1.22)	0.04
					4	23/392 (5.9)	36/434 (8.3)	OR: 0.94 (0.38 to 2.33)	0.90
	Barlow, 2013[83]	Any illegal drug use in past month	1 month	IG1 (Overall)	0	16/159 (10.1)	13/163 (8.0)	OR: 1.06 (0.48 to 2.35)	0.88
					4	36/159 (22.9)	36/163 (21.9)	OR: 1.03 (0.61 to 1.74)	0.84
					8	22/159 (13.8)	33/163 (20.2)	OR: 0.58 (0.31 to 1.10)	0.09
	Barlow, 2013[83]	Any illegal drug use in past month	1 month	IG1 (Overall)	14	34/159 (21.3)	36/163 (21.9)	OR: 0.83 (0.44 to 1.55)	0.55
					38	20/159 (12.3)	28/163 (17.3)	OR: 0.67 (0.50 to 0.91)	0.01
	Estrada, 2018[90]	Proportion of overall drug use over time	NR	IG1 (Overall)	0	6/113 (5.3)	4/117 (4.5)	OR: 1.58 (0.43 to 5.77)	NSD
					3	5/84 (6.0)	9/101 (8.9)	OR: 0.65 (0.21 to 2.01)	NSD
					12	6/82 (7.3)	14/98 (14.3)	OR: 0.47 (0.17 to 1.29)	NSD
	Foxcroft, 2017[93]	--	1 year	IG1 (Overall)	0	17/324 (5.3)	7/235 (3.0)	OR: 1.80 (0.74 to 4.42)	NSD
					12	14/222 (6.3)	6/193 (3.1)	OR: 1.25 (0.46 to 3.38)	NSD
					24	6/169 (3.6)	7/149 (4.7)	OR: 0.96 (0.40 to 2.24)	NSD
	Jalling, 2016[95]	Self-report of any drug use	6 months	IG1 (Overall)	0	5/70 (7.1)	17/81 (21.0)	OR: 0.29 (0.10 to 0.83)	<0.01
					6	12/70 (17.1)	9/81 (11.1)	OR: 3.23 (1.06 to 9.08)	<0.05
				IG2 (Overall)	0	18/85 (21.2)	17/81 (21.0)	OR: 1.01 (0.48 to 2.13)	NSD
					6	22/85 (25.9)	9/81 (11.1)	OR: 3.52 (1.23 to 10.10)	<0.05

Appendix D. Table 5. Drug Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	Sanci, 2015[106]	Any illicit drug use in last 12 months	1 year	IG1 (Overall)	0	95/377 (25.2)	144/524 (27.5)	OR: 0.90 (0.58 to 1.38)	NSD
					3	35/377 (9.3)	80/524 (15.3)	OR: 0.55 (0.33 to 0.90)	0.02
					12	38/377 (10.1)	82/524 (15.7)	OR: 0.61 (0.38 to 0.97)	0.04
	Walkup, 2009[113]	Illegal substance use in the past month	1 month	IG1 (Overall)	5	7/54 (13.0)	5/71 (7.0)	OR: 2.02 (0.51 to 7.92)	NR, NS
					9	3/47 (7.0)	2/68 (3.0)	OR: 2.57 (0.37 to 18.00)	NR, NS
Any drug severity	Barlow, 2013[83]	POSIT substance abuse score; 0-17 (Low)	NR	IG1 (Overall)	4	-0.1 (.), 159	0 (.), 163	MeanDiff: -0.05 (-0.37 to 0.27)	0.78
	Barlow, 2013[83]	POSIT substance abuse score; 0-17 (Low)	NR	IG1 (Overall)	8	-0.3 (.), 159	-0.1 (.), 163	MeanDiff: -0.16 (-0.48 to 0.17)	0.34
	Barlow, 2013[83]	POSIT substance abuse score; 0-17 (Low)	NR	IG1 (Overall)	38	-0.5 (.), 159	-0.2 (.), 163	MeanDiff: -0.32 (-0.80 to 0.16)	0.19
Any drug frequency/ quantity - times used	Estrada, 2018[90]	Assume # times used in past 90 days	3 months	IG1 (Overall)	3	-2.8 (31.7), 84	2.7 (26.2), 101	CalcMeanDiffChg: -5.54 (-14.04 to 2.96)	
	Estrada, 2018[90]	Assume # times used in past 90 days	3 months	IG1 (Overall)	12	-3.1 (33.1), 82	4.3 (30.7), 98	EffectSize: -7.47 (-16.86 to 1.92)	
	Rhee, 2008[105]	Number episodes of drug use in past year	3 months	IG1 (Overall)	2	-0.4 (2.2), 17	-0.7 (2.3), 18	CalcMeanDiffChg: 0.23 (-1.28 to 1.73)	NR, NS
	Rhee, 2008[105]	Number episodes of drug use in past year	3 months	IG1 (Overall)	4	-0.5 (2.3), 17	0 (2.5), 18	CalcMeanDiffChg: -0.47 (-2.05 to 1.11)	NR, NS
	Rhee, 2008[105]	Number episodes of drug use in past year	3 months	IG1 (Overall)	6	-0.4 (2.1), 17	-0.2 (2.5), 18	CalcMeanDiffChg: -0.18 (-1.73 to 1.36)	NR, NS
Any drug frequency/ quantity - score	Barlow, 2006[85]	Drug use, 8 self-reported items on a 4-point scale; 8-32 (NR)	NR	IG1 (Overall)	5	23.9 (8), 19†	22.5 (7), 22†	MeanDiff: 1.10 (-3.90 to 6.00)†	0.67
	Barlow, 2006[85]	Drug use, 8 self-reported items on a 4-point scale; 8-32 (NR)	NR	IG1 (Overall)	9	25.1 (6), 19†	22.4 (8), 22†	MeanDiff: 2.60 (-2.20 to 7.40)†	0.27

*Author reported.
†Mean value at followup, rather than change from baseline.

Appendix D. Table 5. Drug Use Outcomes (KQ2)

Abbreviations: Beta = Beta coefficient; BL = Baseline; Bweight = Beta weight; CalcMeanDiff = Calculated Mean Difference; CalcMeanDiffChg = Calculated Mean Difference in Change; CG = Control group; CohensD = Cohen's d; EffectSize = Effect size; FU = Followup; IG = Intervention group; IRRnegbin = Incident rate ratio (negative binomial); MeanDiff = Mean Difference; NR = Not reported; NS = Not significant; NSD = No significant difference; OR = Odds ratio; RRnegbin = Risk Ratio (negative binomial); SD = Standard deviation; TxtEffectEst = Treatment effect estimate.

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Composite any use	Barlow, 2013[83]	Any alcohol or illegal drug use in past month	1 month	IG1 (Overall)	0	20/159 (12.6)	17/163 (10.4)	OR: 0.93 (0.44 to 1.98)	0.86
	Barlow, 2013[83]	Any alcohol or illegal drug use in past month	1 month	IG1 (Overall)	4	52/159 (32.9)	47/163 (29.1)	OR: 1.04 (0.59 to 1.84)	0.89
	Barlow, 2013[83]	Any alcohol or illegal drug use in past month	1 month	IG1 (Overall)	8	44/159 (27.7)	50/163 (30.8)	OR: 0.76 (0.44 to 1.32)	0.33
	Barlow, 2013[83]	Any alcohol or illegal drug use in past month	1 month	IG1 (Overall)	14	62/159 (38.9)	56/163 (34.6)	OR: 1.07 (0.65 to 1.77)	0.79
Composite frequency/ quantity - times used	Kim, 2011[98]	Composite use (instances) in past year; 1-9 (Low)	3 months	IG1 (Overall)	36	0.4 (.2), 48†	0.5 (0.5), 52†	CohensD: -0.19 (-0.33 to -0.04)†	0.03
	Schwinn, 2010[110]	Report how many times in the past month any drug was used.; 0-7 (Low)	3 months	IG1 (Overall)	6	1 (2.5), 108†	2 (2.6), 118†	CalcMeanDiff: -1.05 (-1.72 to -0.38)†	0.01
Alcohol abstinence	Harris, 2012[80]	Cessation of use	1 year	IG1 (Prague - Any BL alcohol use)	12	5/153 (3.3)	9/163 (5.5)	OR: 0.58 (0.19 to 1.77)	NR, NS
	Harris, 2012[80]	Cessation of use	1 year	IG1 (New England - Any BL alcohol use)	12	38/194 (19.6)	48/240 (20.0)	OR: 0.97 (0.61 to 1.57)	NR, NS
Alcohol any use	Baldus, 2016[81]	Self-reported lifetime use	Lifetime	IG1 (Overall)	0	34/147 (23.3)	29/145 (20.4)	OR: 1.20 (0.69 to 2.11)	0.557
	Baldus, 2016[81]	Self-reported lifetime use	Lifetime	IG1 (Overall)	20	72/135 (53.3)	67/127 (52.8)	OR: 0.82 (0.45 to 1.52)	0.531
	Baldus, 2016[81]	Self-reported past 30-day use	1 month	IG1 (Overall)	0	10/147 (7.1)	9/145 (6.1)	OR: 1.10 (0.43 to 2.80)	NSD
	Baldus, 2016[81]	Self-reported past 30-day use	1 month	IG1 (Overall)	8	14/147 (9.6)	9/145 (6.2)	OR: 1.16 (0.44 to 3.09)	0.759
	Baldus, 2016[81]	Self-reported past 30-day use	1 month	IG1 (Overall)	20	30/147 (20.5)	26/145 (17.6)	OR: 1.07 (0.56 to 2.06)	0.41
	Barlow, 2013[83]	Any alcohol use in past month	1 month	IG1 (Overall)	0	7/159 (4.4)	5/163 (3.1)	OR: 0.77 (0.19 to 3.14)	0.71
	Barlow, 2013[83]	Any alcohol use in past month	1 month	IG1 (Overall)	4	28/159 (17.9)	29/163 (17.8)	OR: 0.80 (0.35 to 1.83)	0.60
	Barlow, 2013[83]	Any alcohol use in past month	1 month	IG1 (Overall)	8	27/159 (16.9)	33/163 (20.0)	OR: 0.71 (0.36 to 1.40)	0.33

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	Barlow, 2013[83]	Any alcohol use in past month	1 month	IG1 (Overall)	14	41/159 (25.8)	35/163 (21.6)	OR: 1.14 (0.63 to 2.05)	0.67
	Barlow, 2013[83]	Any alcohol use in past month	1 month	IG1 (Overall)	38	26/159 (16.5)	26/163 (15.7)	OR: 1.06 (0.80 to 1.41)	0.68
	Foxcroft, 2017[93]	Lifetime alcohol use, lifetime prevalence	Lifetime	IG1 (Overall)	0	86/338 (25.4)	48/241 (19.9)	OR: 1.37 (0.92 to 2.05)	NSD
	Foxcroft, 2017[93]	Lifetime alcohol use, lifetime prevalence	Lifetime	IG1 (Overall)	12	67/233 (28.8)	36/194 (18.6)	OR: 1.36 (0.77 to 2.44)	NSD
	Foxcroft, 2017[93]	Lifetime alcohol use, lifetime prevalence	Lifetime	IG1 (Overall)	24	61/174 (35.1)	45/154 (29.2)	OR: 0.93 (0.56 to 1.55)	NSD
	Foxcroft, 2017[93]	Past month alcohol use, 30-day prevalence	1 month	IG1 (Overall)	0	22/329 (6.7)	8/241 (3.3)	OR: 2.09 (0.91 to 4.77)	NSD
	Foxcroft, 2017[93]	Past month alcohol use, 30-day prevalence	1 month	IG1 (Overall)	12	16/225 (7.1)	12/192 (6.3)	OR: 0.98 (0.41 to 2.24)	NSD
	Foxcroft, 2017[93]	Past month alcohol use, 30-day prevalence	1 month	IG1 (Overall)	24	20/169 (11.8)	16/150 (10.7)	OR: 0.98 (0.50 to 1.93)	NSD
	Harris, 2012[80]	Alcohol initiation	1 year	IG1 (New England - No BL alcohol use)	12	68/571 (11.9)	92/518 (17.8)	OR: 0.63 (0.45 to 0.88)	<0.05
	Harris, 2012[80]	Alcohol initiation	1 year	IG1 (Prague - No BL alcohol use)	12	37/111 (33.3)	35/103 (43.7)	OR: 0.97 (0.55 to 1.71)	NR, NS
	Harris, 2012[80]	Any past-12-month use	1 year	IG1 (Prague)	0	153/264 (58.0)	163/266 (61.3)	OR: 0.87 (0.62 to 1.23)	NR, NS
	Harris, 2012[80]	Any past-12-month use	1 year	IG1 (New England)	0	194/765 (25.4)	240/758 (31.7)	OR: 0.73 (0.59 to 0.92)	NR, NS
	Harris, 2012[80]	Any past-12-month use	1 year	IG1 (Prague)	12	185/264 (70.1)	199/266 (74.8)	OR: 0.79 (0.54 to 1.16)	NR, NS
	Harris, 2012[80]	Any past-12-month use	1 year	IG1 (New England)	12	224/765 (29.3)	284/758 (37.5)	OR: 0.69 (0.56 to 0.86)	<0.05
	Harris, 2012[80]	Any past 90-day use	3 months	IG1 (New England)	3	118/761 (15.5)	173/755 (22.9)	OR: 0.62 (0.48 to 0.80)	<0.05
	Harris, 2012[80]	Any past 90-day use	3 months	IG1 (Prague)	3	126/271 (46.5)	127/245 (51.8)	OR: 0.81 (0.57 to 1.14)	NR, NS
	Kerr, 2013[97]	Lifetime alcohol	Lifetime	IG1 (Overall)	12	./834 (.)	./820 (.)	Regression coefficient: 0.00	NR, NS

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	Kerr, 2013[97]	Past month alcohol; continuous item asking the number of days the participant consumed alcohol	1 month	IG1 (Overall)	12	./834 (.)	./820 (.)	Regression coefficient: 0.03	NR, NS
	Knight, 2019[72]	Number with any alcohol use	1 year	IG1 (Overall)	3	115/626 (18.4)	70/243 (28.8)	70/243 (0.3)	<0.05
	Knight, 2019[72]	Number with any alcohol use	1 year	IG1 (Overall)	6	191/626 (30.5)	84/243 (34.6)	OR: 0.83 (0.61 to 1.14)	NSD
	Knight, 2019[72]	Number with any alcohol use	1 year	IG1 (Overall)	9	230/626 (36.7)	102/243 (42.0)	OR: 0.80 (0.59 to 1.09)	NSD
	Knight, 2019[72]	Number with any alcohol use	1 year	IG1 (Overall)	12	273/626 (43.6)	118/243 (48.6)	OR: 0.82 (0.61 to 1.10)	NSD
	Knight, 2019[72]	Number with any alcohol use	1 year	IG1 (Alcohol or other drug use in past 12 months at baseline)	3	84/148 (56.8)	47/63 (74.6)	OR: 0.45 (0.23 to 0.86)	<0.05
	Knight, 2019[72]	Number with any alcohol use	1 year	IG1 (No alcohol or other drug use in past 12 months at baseline)	3	31/478 (6.5)	23/180 (12.8)	OR: 0.47 (0.27 to 0.84)	<0.05
	Knight, 2019[72]	Number with any alcohol use	1 year	IG1 (Alcohol or other drug use in past 12 months at baseline)	6	116/148 (78.4)	53/63 (84.1)	OR: 0.68 (0.31 to 1.49)	NSD
	Knight, 2019[72]	Number with any alcohol use	1 year	IG1 (No alcohol or other drug use in past 12 months at baseline)	6	75/478 (15.7)	31/180 (17.2)	OR: 0.89 (0.57 to 1.42)	NSD

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	Knight, 2019[72]	Number with any alcohol use	1 year	IG1 (Alcohol or other drug use in past 12 months at baseline)	9	125/148 (84.5)	58/63 (92.1)	OR: 0.47 (0.17 to 1.29)	NSD
	Knight, 2019[72]	Number with any alcohol use	1 year	IG1 (No alcohol or other drug use in past 12 months at baseline)	9	105/478 (22.0)	44/180 (24.4)	OR: 0.87 (0.58 to 1.30)	NSD
	Knight, 2019[72]	Number with any alcohol use	1 year	IG1 (Alcohol or other drug use in past 12 months at baseline)	12	131/148 (88.5)	59/63 (93.7)	HR: 0.69 (0.47 to 1.02)	NSD
	Knight, 2019[72]	Number with any alcohol use	1 year	IG1 (No alcohol or other drug use in past 12 months at baseline)	12	142/478 (29.7)	59/180 (32.8)	HR: 0.87 (0.57 to 1.31)	NSD
	Malmberg, 2014[102]	Any alcohol use in the past month Positive response for "I drank alcohol 1-2 in the past month" or more use.	1 month	IG1 (Overall)	0	126/1225 (10.3)	119/1191 (10.0)	OR: 1.03 (0.53 to 1.99)	NSD
	Malmberg, 2014[102]	Any alcohol use in the past month Positive response for "I drank alcohol 1-2 in the	1 month	IG1 (Overall)	8	186/1114 (16.7)	171/1109 (15.4)	OR: 1.08 (0.61 to 1.89)	0.136

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
		past month" or more use.							
	Malmberg, 2014[102]	Any alcohol use in the past month Positive response for "I drank alcohol 1-2 in the past month" or more use.	1 month	IG1 (Overall)	20	315/1003 (31.4)	251/982 (25.6)	OR: 1.36 (0.83 to 2.21)	0.136
	Malmberg, 2014[102]	Any alcohol use in the past month Positive response for "I drank alcohol 1-2 in the past month" or more use.	1 month	IG1 (Overall)	32	491/825 (59.5)	365/692 (52.7)	OR: 1.31 (0.79 to 2.18)	0.136
	Malmberg, 2014[102]	Lifetime prevalence Ever consumed a glass of alcohol in their life	Lifetime	IG1 (Overall)	0	348/1225 (28.4)	303/1191 (25.4)	OR: 1.16 (0.74 to 1.81)	NSD
	Malmberg, 2014[102]	Lifetime prevalence Ever consumed a glass of alcohol in their life	Lifetime	IG1 (Overall)	8	430/1114 (38.6)	383/1109 (34.5)	OR: 1.18 (0.77 to 1.82)	0.236
	Malmberg, 2014[102]	Lifetime prevalence Ever consumed a glass of alcohol in their life	Lifetime	IG1 (Overall)	20	583/1003 (58.1)	487/982 (49.6)	OR: 1.40 (0.90 to 2.17)	0.236
	Malmberg, 2014[102]	Lifetime prevalence Ever consumed a glass of alcohol in their life	Lifetime	IG1 (Overall)	32	650/825 (78.8)	518/692 (74.9)	OR: 1.25 (0.69 to 2.27)	0.236
	Walkup, 2009[113]	Alcohol in last month	1 month	IG1 (Overall)	5	6/54 (11.0)	5/71 (7.0)	OR: 1.52 (0.42 to 5.46)	NR, NS
	Walkup, 2009[113]	Alcohol in last month	1 month	IG1 (Overall)	9	5/47 (12.0)	4/68 (6.0)	OR: 2.19 (0.55 to 8.78)	NR, NS
Alcohol risky use	D'Amico, 2018[116]	Heavy alcohol use in the past 90 days	3 months	IG1 (Overall)	3	2.8 (4.6), 113†	3 (4.8), 86†	CalcMeanDiff: -0.28 (-1.60 to 1.04)†	0.48
	D'Amico, 2018[116]	Heavy alcohol use in the past 90 days	3 months	IG1 (Overall)	6	2.7 (4.7), 127†	2.7 (4.7), 111†	CalcMeanDiff: 0.01 (-1.19 to 1.21)†	0.90

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	D'Amico, 2018[116]	Heavy alcohol use in the past 90 days	3 months	IG1 (Overall)	12	2.4 (4.6), 122†	2.8 (5.2), 114†	CalcMeanDiff: -0.41 (-1.66 to 0.84)†	0.28
	Bannink, 2014[82]	5 or more drinks on 1 or more occasions in past 4 weeks	1 month	IG1 (Overall)	0	157/430 (36.5)	140/434 (32.3)	OR: 1.21 (0.82 to 1.79)	0.20
	Bannink, 2014[82]	5 or more drinks on 1 or more occasions in past 4 weeks	1 month	IG1 (Overall)	4	145/430 (33.7)	157/434 (36.2)	OR: 0.90 (0.61 to 1.33)	0.35
	Bannink, 2014[82]	5 or more drinks on 1 or more occasions in past 4 weeks	1 month	IG2 (Overall)	0	137/392 (35.0)	140/434 (32.3)	OR: 1.14 (0.77 to 1.71)	0.48
	Bannink, 2014[82]	5 or more drinks on 1 or more occasions in past 4 weeks	1 month	IG2 (Overall)	4	160/392 (41.0)	157/434 (36.2)	OR: 1.11 (0.75 to 1.64)	0.62
	Foxcroft, 2017[93]	Past month binge drinking	1 month	IG1 (Overall)	0	13/328 (4.0)	8/239 (3.4)	OR: 1.19 (0.49 to 2.92)	NSD
	Foxcroft, 2017[93]	Past month binge drinking	1 month	IG1 (Overall)	12	13/225 (5.8)	9/193 (4.7)	OR: 0.88 (0.33 to 2.26)	NSD
	Foxcroft, 2017[93]	Past month binge drinking	1 month	IG1 (Overall)	24	12/170 (7.1)	10/151 (6.6)	OR: 0.89 (0.40 to 1.92)	NSD
	Gmel, 2013[94]	Heavy use (binge) episodes >1/mo	6 months	IG1 (Overall)	0	203/392 (51.7)	254/461 (55.2)	OR: 0.88 (0.67 to 1.15)	NSD
	Gmel, 2013[94]	Heavy use (binge) episodes >1/mo	6 months	IG1 (Overall)	6	140/288 (48.6)	189/384 (49.3)	OR: 0.98 (0.72 to 1.32)	0.559
	Gmel, 2013[94]	Risk volume, exceeds >21 drinks/week	6 months	IG1 (Overall)	0	37/392 (9.4)	./461 (.)	--	
	Gmel, 2013[94]	Risk volume, exceeds >21 drinks/week	6 months	IG1 (Overall)	6	23/288 (8.0)	33/384 (8.6)	OR: 0.92 (0.53 to 1.61)	0.784
	Knight, 2019[72]	Number with any heavy episodic drinking	1 year	IG1 (Alcohol or other drug use in past 12 months at baseline)	3	56/148 (37.8)	28/63 (44.4)	OR: 0.76 (0.42 to 1.38)	NSD
	Knight, 2019[72]	Number with any heavy episodic drinking	1 year	IG1 (Alcohol or other drug use in past 12	6	70/148 (47.3)	38/63 (60.3)	OR: 0.59 (0.32 to 1.07)	NSD

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
				months at baseline)					
	Knight, 2019[72]	Number with any heavy episodic drinking	1 year	IG1 (Alcohol or other drug use in past 12 months at baseline)	9	82/148 (55.4)	45/63 (71.4)	OR: 0.50 (0.26 to 0.94)	<0.05
	Knight, 2019[72]	Number with any heavy episodic drinking	1 year	IG1 (Alcohol or other drug use in past 12 months at baseline)	12	86/148 (58.1)	48/63 (76.2)	HR: 0.66 (0.40 to 1.10)	<0.05
	Malmberg, 2014[102]	Binge drinking (5 or more drinks on 1 occasion), in past 30 days.	1 month	IG1 (Overall)	0	85/1225 (6.9)	70/1191 (5.9)	OR: 1.25 (0.55 to 2.83)	NSD
	Malmberg, 2014[102]	Binge drinking (5 or more drinks on 1 occasion), in past 30 days.	1 month	IG1 (Overall)	8	118/1114 (10.6)	100/1109 (9.0)	OR: 1.20 (0.60 to 2.42)	0.350
	Malmberg, 2014[102]	Binge drinking (5 or more drinks on 1 occasion), in past 30 days.	1 month	IG1 (Overall)	20	264/1003 (26.3)	196/982 (20.0)	OR: 1.43 (0.85 to 2.42)	0.350
	Malmberg, 2014[102]	Binge drinking (5 or more drinks on 1 occasion), in past 30 days.	1 month	IG1 (Overall)	32	381/825 (46.2)	257/692 (37.1)	OR: 1.45 (0.86 to 2.42)	0.350
	Sanci, 2015[106]	≥ month use or any binge use (age 14-15); ≥ 3x/week or ≥ monthly binge use (age 16-24)	1 year	IG1 (Overall)	0	154/377 (42.4)	210/524 (41.8)	OR: 1.03 (0.70 to 1.53)	NSD
	Sanci, 2015[106]	≥ month use or any binge use (age 14-15); ≥ 3x/week or ≥ monthly binge use (age 16-24)	1 month	IG1 (Overall)	3	129/377 (34.1)	204/524 (39.0)	OR: 0.77 (0.55 to 1.06)	0.11

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	Sanci, 2015[106]	≥ month use or any binge use (age 14-15); ≥ 3x/week or ≥ monthly binge use (age 16-24)	1 month	IG1 (Overall)	12	121/377 (32.1)	182/524 (34.7)	OR: 0.84 (0.61 to 1.15)	0.28
Alcohol severity	Jalling, 2016[95]	AUDIT, total score; 0-44 (Low)	NR	IG1 (Overall)	6	-0.5 (7), 70	0.2 (6.5), 81	CalcMeanDiffChg: -0.71 (-2.88 to 1.46)	NR, NS
	Jalling, 2016[95]	AUDIT, total score; 0-40 (Low)	NR	IG2 (Overall)	6	1.4 (7), 86	0.2 (6.5), 81	CalcMeanDiffChg: 1.17 (-0.89 to 3.23)	0.06
	Walton, 2014[115]	Frequency, quantity, and heavy drinking; 0-13 (Low)	3 months	IG1 (Overall)	3	. (.), 199	. (.), 216	IRRnegbin: 1.38 (0.78 to 2.43)	NR, NS
	Walton, 2014[115]	Frequency, quantity, and heavy drinking; 0-13 (Low)	3 months	IG1 (Overall)	6	. (.), 200	. (.), 211	IRRnegbin: 0.57 (0.36 to 0.91)	<0.05
	Walton, 2014[115]	Frequency, quantity, and heavy drinking; 0-13 (Low)	3 months	IG1 (Overall)	12	. (.), 201	. (.), 207	IRRnegbin: 1.36 (0.84 to 2.23)	NR, NS
	Walton, 2014[115]	Frequency, quantity, and heavy drinking; 0-13 (Low)	3 months	IG2 (Overall)	3	. (.), 220	. (.), 216	IRRnegbin: 0.93 (0.52 to 1.68)	NR, NS
	Walton, 2014[115]	Frequency, quantity, and heavy drinking; 0-13 (Low)	3 months	IG2 (Overall)	6	. (.), 218	. (.), 211	IRRnegbin: 0.66 (0.42 to 1.04)	NR, NS
	Walton, 2014[115]	Frequency, quantity, and heavy drinking; 0-13 (Low)	3 months	IG2 (Overall)	12	. (.), 220	. (.), 207	IRRnegbin: 1.22 (0.75 to 1.99)	NR, NS
Alcohol frequency/ quantity - times used	D'Amico, 2018[116]	Times used alcohol in past 90 days	3 months	IG1 (Overall)	3	5.2 (5.6), 113†	5.6 (5.8), 86†	CalcMeanDiff: -0.46 (-2.07 to 1.15)†	0.22
	D'Amico, 2018[116]	Times used alcohol in past 90 days	3 months	IG1 (Overall)	6	4.7 (5.9), 127†	5.4 (6.4), 111†	CalcMeanDiff: -0.72 (-2.29 to 0.85)†	0.12
	D'Amico, 2018[116]	Times used alcohol in past 90 days	3 months	IG1 (Overall)	12	4.5 (5.7), 122†	5.1 (6.4), 114†	CalcMeanDiff: -0.55 (-2.10 to 1.00)†	0.15
	Estrada, 2018[90]	Times used alcohol in past 90 days	3 months	IG1 (Overall)	3	0.1 (1.4), 84	-0.1 (8.3), 101	CalcMeanDiffChg: 0.24 (-1.41 to 1.89)	0.623
	Estrada, 2018[90]	Times used alcohol in past 90 days	3 months	IG1 (Overall)	12	0.1 (1.5), 82	-0.6 (8.7), 98	EffectSize: 0.75 (-1.01 to 2.51)	0.623
	Fang, 2010[92]	Number of drinks in past 30-days	3 months	IG1 (Overall)	6	0.1 (.9), 54	1.4 (5), 50	CalcMeanDiffChg: -1.26 (-2.67 to 0.15)	0.016
	Fang, 2010[92]	Number of drinks in past 30-days	3 months	IG1 (Overall)	12	0 (0.6), 54	0.8 (3.9), 50	CalcMeanDiffChg: -0.75 (-1.85 to 0.35)	0.038

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	Fang, 2010[92]	Number of drinks in past 30-days	3 months	IG1 (Overall)	24	0 (0.8), 50	-0.6 (7.9), 43	CalcMeanDiffChg: 0.60 (-1.77 to 2.97)	0.038
	Gmel, 2013[94]	Number of drinks per week	3 months	IG1 (Overall)	6	-0.2 (.), 288	-0.1 (.), 384	Beta: -0.19 (-0.93 to 0.56)	0.627
	Johnson, 2015[96]	Times used in the past 30 days (if age less than 21)	3 months	IG1 (Overall)	6	-0.4 (5.2), 101	0.8 (8.5), 99	RRnegbin: 4.26 (2.58 to 7.08)	NR, NS
	Rhee, 2008[105]	Estimated total number of alcoholic drinks consumed in the past year	3 months	IG1 (Overall)	2	1 (7.5), 17	-2.8 (35), 18	CalcMeanDiffChg: 3.79 (-12.76 to 20.33)	NR, NS
	Rhee, 2008[105]	Estimated total number of alcoholic drinks consumed in the past year	3 months	IG1 (Overall)	4	2.8 (11.4), 17	-7 (36.2), 18	CalcMeanDiffChg: 9.82 (-7.75 to 27.40)	NR, NS
	Rhee, 2008[105]	Estimated total number of alcoholic drinks consumed in the past year	3 months	IG1 (Overall)	6	2.5 (9.7), 17	-8.6 (38), 18	CalcMeanDiffChg: 11.13 (-7.04 to 29.29)	NR, NS
	Schinke, 2009a[107]	Reported use occasions in past 30 days	3 months	IG1 (Overall)	12	0.3 (0.9), 205	0.7 (1.8), 327	TxtEffectEst: -0.42 (-0.65 to -0.19)	<0.05
	Schinke, 2009b[108]	Times used in past 30 days	3 months	IG1 (Overall)	12	0 (0.6), 434	0.2 (1.3), 430	CalcMeanDiffChg: -0.18 (-0.32 to -0.04)	<0.006
	Schinke, 2009b[108]	Times used in past 30 days	3 months	IG1 (Overall)	24	0.1 (0.8), 415	0.4 (1.8), 413	CalcMeanDiffChg: -0.36 (-0.55 to -0.17)	<0.006
	Schwinn, 2010[110]	Report how many times in the past month any drug was used.	3 months	IG1 (Overall)	6	1.3 (6.5), 108†	3.2 (6.8), 118†	CalcMeanDiff: -1.89 (-3.64 to -0.14)†	0.05
	Schwinn, 2015[112]	30-day alcohol use	3 months	IG1 (Overall)	3	0.5 (6.1), 97	1.1 (5.5), 103	CalcMeanDiffChg: -0.57 (-2.19 to 1.05)	NR, NS
	Schwinn, 2018[111]	Times used in past month	3 months	IG1 (Overall)	3	-1.3 (15.1), 376	-0.8 (12.9), 380	Bweight: -0.36 (-1.36 to 0.64)	NR, NS
	Schwinn, 2018[111]	Times used in past month	3 months	IG1 (Overall)	15	-0.6 (14.7), 370	0.5 (12.4), 382	Bweight: -0.84 (-1.78 to 0.10)	NR, NS
	Kim, 2011[98]	Alcohol use in past year (1=never, 9=daily); 1-9 (Low)	1 year	IG1 (Overall)	36	1.5 (0.9), 45†	1.8 (1.5), 52†	CohensD: -0.31 (-0.79 to 0.17)†	NS
Alcohol frequency/ quantity - score	Mason, 2015[103]	Participants were asked the number of days they have used alcohol within the last month,	1 month	IG1 (Overall)	6	. (.), 57	. (.), 60	TxtEffectEst: -0.20 (-0.42 to 0.02)	<0.10

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
		coded as 0= 0 days, 1= 1 or 2 days, 3= 3 to 5 days, 4=6 to 9 days, 5=10 to 19 days, 6=20 to 29 days, and 7=all 30 days.; 0-7 (Low)							
	Mason, 2015[103]	Participants were asked the number of days they have used alcohol within the last month, coded as 0= 0 days, 1= 1 or 2 days, 3= 3 to 5 days, 4=6 to 9 days, 5=10 to 19 days, 6=20 to 29 days, and 7=all 30 days.; 0-7 (Low)	1 month	IG1 (Male)	3	-0.1 (.), 15	0.1 (.), 20	--	0.08
	Mason, 2015[103]	Participants were asked the number of days they have used alcohol within the last month, coded as 0= 0 days, 1= 1 or 2 days, 3= 3 to 5 days, 4=6 to 9 days, 5=10 to 19 days, 6=20 to 29 days, and 7=all 30 days.; 0-7 (Low)	1 month	IG1 (Female)	3	0 (.), 44	-0.2 (.), 40	--	0.24
	Mason, 2015[103]	Participants were asked the number of days they have used alcohol within the last month, coded as 0= 0 days, 1= 1 or 2 days, 3= 3 to 5 days, 4=6 to 9 days, 5=10 to 19 days, 6=20 to 29 days, and 7=all 30 days.; 0-7 (Low)	1 month	IG1 (Male)	6	-0.3 (.), 15	0.3 (.), 20	--	0.08
	Mason, 2015[103]	Participants were asked the number of days they have used alcohol within the last month, coded as 0= 0 days, 1=	1 month	IG1 (Female)	6	0.1 (.), 44	-0.4 (.), 40	--	0.24

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
		1 or 2 days, 3= 3 to 5 days, 4=6 to 9 days, 5=10 to 19 days, 6=20 to 29 days, and 7=all 30 days.; 0-7 (Low)							
	Walton, 2013[114]	Past 3-month alcohol frequency.; 0-4 (Low)	3 months	IG1 (Overall)	3	0 (0.9), 101	-0.2 (1.1), 96	TxtEffectEst: 0.16 (-0.21 to 0.53)	0.39
	Walton, 2013[114]	Past 3-month alcohol frequency.; 0-4 (Low)	3 months	IG1 (Overall)	6	0 (0.9), 102	0 (1.2), 97	TxtEffectEst: -0.02 (-0.39 to 0.35)	0.94
	Walton, 2013[114]	Past 3-month alcohol frequency.; 0-4 (Low)	3 months	IG1 (Overall)	12	0.1 (1), 104	-0.2 (1), 94	TxtEffectEst: 0.37 (0.00 to 0.74)	0.05
	Walton, 2013[114]	Past 3-month alcohol frequency.; 0-4 (Low)	3 months	IG2 (Overall)	3	-0.3 (1), 82	-0.2 (1.1), 96	TxtEffectEst: -0.19 (-0.58 to 0.20)	0.34
	Walton, 2013[114]	Past 3-month alcohol frequency.; 0-4 (Low)	3 months	IG2 (Overall)	6	-0.2 (1), 79	0 (1.2), 97	TxtEffectEst: -0.25 (-0.64 to 0.14)	0.22
	Walton, 2013[114]	Past 3-month alcohol frequency.; 0-4 (Low)	3 months	IG2 (Overall)	12	-0.3 (1), 77	-0.2 (1), 94	TxtEffectEst: -0.16 (-0.55 to 0.23)	0.44
Tobacco any use	Baldus, 2016[81]	Self-reported lifetime use	Lifetime	IG1 (Overall)	0	23/147 (15.8)	24/145 (17.0)	OR: 0.94 (0.50 to 1.75)	0.772
	Baldus, 2016[81]	Self-reported lifetime use	Lifetime	IG1 (Overall)	20	46/132 (34.9)	56/129 (43.4)	OR: 0.63 (0.37 to 1.07)	0.085
	Baldus, 2016[81]	Self-reported past 30-day use	1 month	IG1 (Overall)	0	10/147 (7.0)	8/145 (5.7)	OR: 1.25 (0.48 to 3.26)	NSD
	Baldus, 2016[81]	Self-reported past 30-day use	1 month	IG1 (Overall)	8	14/147 (9.6)	13/145 (9.2)	OR: 1.09 (0.52 to 2.31)	0.820
	Baldus, 2016[81]	Self-reported past 30-day use	1 month	IG1 (Overall)	20	25/147 (16.7)	24/145 (16.5)	OR: 0.72 (0.37 to 1.39)	0.324
	Bannink, 2014[82]	Regular smokers, smoking anywhere from less than once a week to every day.	NR	IG1 (Overall)	0	77/430 (18.0)	80/434 (18.4)	OR: 0.98 (0.61 to 1.59)	0.92
	Bannink, 2014[82]	Regular smokers, smoking anywhere from less than once a week to every day.	NR	IG1 (Overall)	4	74/430 (17.2)	83/434 (19.1)	OR: 0.95 (0.58 to 1.57)	0.84
	Bannink, 2014[82]	Regular smokers, smoking anywhere from less than once a week to every day.	NR	IG2 (Overall)	0	63/392 (16.1)	80/434 (18.4)	OR: 0.84 (0.51 to 1.40)	0.39
	Bannink, 2014[82]	Regular smokers, smoking anywhere from	NR	IG2 (Overall)	4	67/392 (17.1)	83/434 (19.1)	OR: 0.97 (0.61 to 1.56)	0.90

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
		less than once a week to every day.							
	Foxcroft, 2017[93]	Past month cigarette use, prevalence	1 month	IG1 (Overall)	0	21/329 (6.4)	6/240 (2.5)	OR: 2.66 (1.06 to 6.69)	<0.05
	Foxcroft, 2017[93]	Past month cigarette use, prevalence	1 month	IG1 (Overall)	12	21/229 (9.2)	11/192 (5.7)	OR: 1.13 (0.47 to 2.77)	NR, NS
	Foxcroft, 2017[93]	Past month cigarette use, prevalence	1 month	IG1 (Overall)	24	22/173 (12.7)	9/154 (5.8)	OR: 1.31 (0.56 to 2.99)	NR, NS
	Gmel, 2013[94]	Past 6 months smoking	6 months	IG1 (Overall)	0	208/392 (53.1)	254/461 (55.2)	OR: 0.92 (0.70 to 1.21)	NSD
	Gmel, 2013[94]	Past 6 months smoking	6 months	IG1 (Overall)	6	142/288 (49.3)	203/384 (52.9)	OR: 0.87 (0.64 to 1.18)	0.486
	Kerr, 2013[97]	Lifetime tobacco	Lifetime	IG1 (Overall)	12	./834 (.)	./820 (.)	Regression coefficient: 0.01	NR, NS
	Kerr, 2013[97]	Past month tobacco; continuous item assessing number of days that the participant smoked	1 month	IG1 (Overall)	12	./834 (.)	./820 (.)	Regression coefficient: 0.06	NR, NS
	Malmberg, 2014[102]	Any lifetime use	Lifetime	IG1 (Overall)	0	277/1225 (22.6)	206/1191 (17.3)	OR: 1.42 (0.86 to 2.34)	NSD
	Malmberg, 2014[102]	Any lifetime use	Lifetime	IG1 (Overall)	8	342/1114 (30.7)	283/1109 (25.5)	OR: 1.28 (0.81 to 2.04)	0.842
	Malmberg, 2014[102]	Any lifetime use	Lifetime	IG1 (Overall)	20	392/1003 (39.1)	316/982 (32.2)	OR: 1.34 (0.84 to 2.11)	0.842
	Malmberg, 2014[102]	Any lifetime use	Lifetime	IG1 (Overall)	32	399/825 (48.4)	274/692 (39.6)	OR: 1.41 (0.85 to 2.35)	0.842
	Malmberg, 2014[102]	Regular tobacco users "I smoke occasionally, but not every day" and "I smoke at least once a day"	1 month	IG1 (Overall)	0	53/1225 (4.3)	46/1191 (3.9)	OR: 1.26 (0.46 to 3.45)	NSD
	Malmberg, 2014[102]	Regular tobacco users "I smoke occasionally, but not every day" and "I smoke at least once a day"	1 month	IG1 (Overall)	8	128/1114 (11.5)	82/1109 (7.4)	OR: 1.69 (0.82 to 3.48)	0.959
	Malmberg, 2014[102]	Regular tobacco users	1 month	IG1 (Overall)	20	155/1003 (15.5)	141/982 (14.4)	OR: 1.08 (0.58 to 1.99)	0.959

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
		"I smoke occasionally, but not every day" and "I smoke at least once a day"							
	Malmberg, 2014[102]	Regular tobacco users "I smoke occasionally, but not every day" and "I smoke at least once a day"	1 month	IG1 (Overall)	32	199/825 (24.1)	120/692 (17.3)	OR: 1.53 (0.81 to 2.89)	0.959
	Sanci, 2015[106]	Any use in last 12 months	1 year	IG1 (Overall)	0	140/377 (37.2)	210/524 (40.4)	OR: 0.88 (0.59 to 1.30)	NSD
	Sanci, 2015[106]	Tobacco smoking use in last month	1 month	IG1 (Overall)	3	89/377 (23.5)	135/524 (25.8)	OR: 0.90 (0.62 to 1.31)	0.60
	Sanci, 2015[106]	Tobacco smoking use in last month	1 month	IG1 (Overall)	12	82/377 (21.8)	142/524 (27.1)	OR: 0.78 (0.55 to 1.12)	0.18
	Walkup, 2009[113]	Cigarette use in last month	1 month	IG1 (Overall)	5	7/54 (13.0)	12/71 (17.0)	OR: 0.74 (0.24 to 2.30)	NR, NS
	Walkup, 2009[113]	Cigarette use in last month	1 month	IG1 (Overall)	9	9/47 (22.0)	8/68 (13.0)	OR: 2.06 (0.64 to 6.62)	NR, NS
Tobacco frequency/ quantity - times used	Estrada, 2018[90]	Times used tobacco in past 90 days	3 months	IG1 (Overall)	3	0.7 (9.4), 84	0.8 (10.8), 101	CalcMeanDiffChg: -0.16 (-3.07 to 2.75)	<0.01
	Estrada, 2018[90]	Times used tobacco in past 90 days	3 months	IG1 (Overall)	12	-0.5 (4.7), 82	-0.1 (8), 98	EffectSize: -0.47 (-2.35 to 1.41)	<0.01
	Fang, 2010[92]	Past 30-day use occasions	3 months	IG1 (Overall)	6	-0.2 (1.1), 54	5 (29.5), 50	CalcMeanDiffChg: -5.16 (-13.33 to 3.01)	0.06
	Fang, 2010[92]	Past 30-day use occasions	3 months	IG1 (Overall)	12	-0.2 (1.1), 54	0.8 (4.1), 50	CalcMeanDiffChg: -0.96 (-2.14 to 0.22)	0.171
	Fang, 2010[92]	Past 30-day use occasions	3 months	IG1 (Overall)	24	-0.2 (1.1), 50	5.3 (28.4), 43	CalcMeanDiffChg: -5.49 (-13.98 to 3.00)	0.171
	Rhee, 2008[105]	Average number of cigarettes per day in past 30 days	3 months	IG1 (Overall)	2	1.7 (13.1), 17	3.7 (17), 18	CalcMeanDiffChg: -2.04 (-12.06 to 7.98)	NR, NS
	Rhee, 2008[105]	Average number of cigarettes per day in past 30 days	3 months	IG1 (Overall)	4	-1.4 (8.3), 17	0.9 (12.2), 18	CalcMeanDiffChg: -2.28 (-9.17 to 4.61)	NR, NS
	Rhee, 2008[105]	Average number of cigarettes per day in past 30 days	3 months	IG1 (Overall)	6	0.7 (13.1), 17	1.3 (12.4), 18	CalcMeanDiffChg: -0.60 (-9.05 to 7.85)	NR, NS
	Schinke, 2009a[107]	30-day use occasions of cigarettes	3 months	IG1 (Overall)	12	0.1 (1.3), 205	0.2 (2.9), 327	TxtEffectEst: -0.18 (-0.54 to 0.18)	NR, NS

Appendix D. Table 6. Other Substance Use Outcomes (KQ2)

Outcome	Author, year	Outcome description; range (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	Schinke, 2009b[108]	Times used in past 30 days	3 months	IG1 (Overall)	12	2.6 (1), 434	2.9 (3.2), 430	CalcMeanDiffChg: -0.24 (-0.56 to 0.08)	NR, NS
	Schinke, 2009b[108]	Times used in past 30 days	3 months	IG1 (Overall)	24	2.7 (1.3), 415	3.6 (10.4), 413	CalcMeanDiffChg: -0.90 (-1.91 to 0.11)	NR, NS
	Schwinn, 2010[110]	Report how many times in the past month any drug was used.	3 months	IG1 (Overall)	6	4.7 (15.3), 108†	4.2 (16), 118†	CalcMeanDiff: 0.54 (-3.53 to 4.61)†	0.82
	Schwinn, 2015[112]	30-day cigarette use	3 months	IG1 (Overall)	3	-0.5 (6.3), 97	-0.1 (6.7), 103	CalcMeanDiffChg: -0.33 (-2.13 to 1.47)	NR, NS
	Schwinn, 2018[111]	Times used tobacco in past month	3 months	IG1 (Overall)	3	-2.2 (16.5), 376	-1.1 (14.7), 380	Bweight: -2.61 (-4.32 to -0.90)	<0.01
	Schwinn, 2018[111]	Times used tobacco in past month	3 months	IG1 (Overall)	15	-1.7 (15.7), 370	0.6 (15.5), 382	Bweight: -3.36 (-5.36 to -1.36)	<0.01
Tobacco frequency/ quantity - score	Kim, 2011[98]	Tobacco use in past year (1=never, 9=daily); 1-9 (Low)	1 year	IG1 (Overall)	36	1.5 (1.6), 48†	2.4 (2.5), 52†	CohensD: -0.87 (-1.69 to -0.05)†	0.04

*Author reported.
†Mean value at followup, rather than change from baseline.

Abbreviations: AUDIT = Alcohol Use Disorder Test; BL = Baseline; Bweight = Beta weight; CalcMeanDiff = Calculated Mean Difference; CalcMeanDiffChg = Calculated Mean Difference in Change; CG = Control group; CohensD = Cohen's d; EffectSize = Effect size; FU = Followup; IG = Intervention group; ; IRRnegbin = Incident rate ratio (negative binomial); NR = Not reported; NS = Not significant; NSD = No significant difference; OR = Odds ratio; RRnegbin = Risk Ratio (negative binomial); SD = Standard deviation; TxtEffectEst = Treatment effect estimate.

Appendix D. Table 7. Other Behavioral Outcomes (KQ2)

Outcome	Author, year	Outcome description (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Condom use	Bannink, 2014[82]	Always use a condom during intercourse	NR	IG1 (Overall)	0	68/130 (52.3)	49/96 (51.0)	OR: 1.05 (0.50 to 2.19)	0.55
	Bannink, 2014[82]	Always use a condom during intercourse	NR	IG1 (Overall)	4	66/151 (43.7)	43/106 (40.6)	OR: 1.36 (0.76 to 2.44)	0.31
	Bannink, 2014[82]	Always use a condom during intercourse	NR	IG2 (Overall)	0	52/98 (53.1)	49/96 (51.0)	OR: 1.08 (0.49 to 2.37)	0.50
	Bannink, 2014[82]	Always use a condom during intercourse	NR	IG2 (Overall)	4	62/119 (52.1)	43/106 (40.6)	OR: 2.09 (1.04 to 4.22)	0.04
	Estrada, 2018[90]	Condomless sex; items asked whether participants had oral, vaginal, or anal sex in the previous 90 days, and if they responded yes, then whether they used a condom during their last sexual encounter, measured on a 5-point scale. Frequency of condom use was rated on a scale from 0 (Never) - 4 (Always); 0-4 (High)	3 months	IG1 (Overall)	3	0 (0.6), 20	0 (0.6), 19	CalcMeanDiffChg: 0.01 (-0.38 to 0.40)	0.89
	Estrada, 2018[90]	Condomless sex; items asked whether participants had oral, vaginal, or anal sex in the previous 90 days, and if they responded yes, then whether they used a condom during their last sexual encounter, measured on a 5-point scale. Frequency of condom use was rated on a scale from 0 (Never) - 4 (Always); 0-4 (High)	3 months	IG1 (Overall)	12	0.2 (0.8), 21	0.1 (0.7), 18	EffectSize: 0.06 (-0.40 to 0.52)	0.89
	Sanci, 2015[106]	Risk of STI	NR	IG1 (Overall)	0	70/377 (18.7)	92/524 (17.7)	OR: 1.09 (0.66 to 1.78)	NSD
	Sanci, 2015[106]	Risk of STI in last 3 months	3 months	IG1 (Overall)	3	54/377 (14.3)	101/524 (19.2)	OR: 0.70 (0.48 to 1.03)	0.07
	Sanci, 2015[106]	Risk of STI in last 3 months	3 months	IG1 (Overall)	12	39/377 (10.3)	66/524 (12.6)	OR: 0.79 (0.51 to 1.24)	0.31

Appendix D. Table 7. Other Behavioral Outcomes (KQ2)

Outcome	Author, year	Outcome description (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
Other	Sanci, 2015[106]	Risk of unplanned pregnancy	NR	IG1 (Overall)	0	53/377 (14.2)	61/524 (11.9)	OR: 1.28 (0.73 to 2.26)	NSD
	Sanci, 2015[106]	Risk of unplanned pregnancy in last 3 months	3 months	IG1 (Overall)	3	26/377 (7.0)	43/524 (8.2)	OR: 0.85 (0.50 to 1.42)	0.53
	Sanci, 2015[106]	Risk of unplanned pregnancy in last 3 months	3 months	IG1 (Overall)	12	26/377 (6.9)	53/524 (10.2)	OR: 0.53 (0.30 to 0.94)	0.03
Other behavioral	Knight, 2019[72]	Number riding in the past 3 months with a driver who had been drinking or using other drugs	3 months	IG1 (Riding risk at baseline)	6	20/44 (45.5)	12/21 (57.1)	OR: 0.63 (0.22 to 1.78)	NSD
	Knight, 2019[72]	Number riding in the past 3 months with a driver who had been drinking or using other drugs	3 months	IG1 (No riding risk at baseline)	6	35/429 (8.2)	19/158 (12.0)	OR: 0.65 (0.36 to 1.17)	NSD
	Knight, 2019[72]	Number riding in the past 3 months with a driver who had been drinking or using other drugs	3 months	IG1 (Riding risk at baseline)	9	16/39 (41.0)	13/21 (61.9)	OR: 0.43 (0.14 to 1.27)	NSD
	Knight, 2019[72]	Number riding in the past 3 months with a driver who had been drinking or using other drugs	3 months	IG1 (No riding risk at baseline)	9	33/419 (7.9)	10/163 (6.1)	OR: 1.31 (0.63 to 2.72)	NSD
	Knight, 2019[72]	Number riding in the past 3 months with a driver who had been drinking or using other drugs	3 months	IG1 (Riding risk at baseline)	12	18/47 (38.3)	13/19 (68.4)	OR: 0.29 (0.09 to 0.89)	<0.05
	Knight, 2019[72]	Number riding in the past 3 months with a driver who had been drinking or using other drugs	3 months	IG1 (No riding risk at baseline)	12	28/452 (6.2)	11/168 (6.5)	OR: 0.94 (0.46 to 1.94)	NSD
	Sanci, 2015[106]	One or more road safety risks	NR	IG1 (Overall)	0	301/377 (79.8)	408/524 (78.0)	OR: 1.11 (0.70 to 1.78)	NSD
	Sanci, 2015[106]	One or more road safety risks	NR	IG1 (Overall)	3	274/377 (72.6)	372/524 (71.0)	OR: 1.08 (0.79 to 1.41)	0.99
	Sanci, 2015[106]	One or more road safety risks	NR	IG1 (Overall)	12	269/377 (71.4)	387/524 (73.9)	OR: 0.81 (0.59 to 1.11)	0.19
	Walton, 2013[114]	Driving under the influence of cannabis (cannabis DUI) in the past 3 months: never, 1-2 times, 3-5 times, 6-9 times, 10+ times; NR (Low)	3 months	IG2 (Overall)	3	-0.1 (1), 82	0.1 (0.8), 96	TxtEffectEst: -0.55 (-1.24 to 0.14)	0.11

Appendix D. Table 7. Other Behavioral Outcomes (KQ2)

Outcome	Author, year	Outcome description (direction of better outcome)	Recall period	Group	FU, mo	IG n/n (%) or Mean (SD), n	CG n/n (%) or Mean (SD), n	Effect	p*
	Walton, 2013[114]	Driving under the influence of cannabis (cannabis DUI) in the past 3 months: never, 1-2 times, 3-5 times, 6-9 times, 10+ times; NR (Low)	3 months	IG2 (Overall)	6	0 (1.1), 79	0.1 (0.8), 97	TxtEffectEst: -0.34 (-1.07 to 0.39)	0.36
	Walton, 2013[114]	Driving under the influence of cannabis (cannabis DUI) in the past 3 months: never, 1-2 times, 3-5 times, 6-9 times, 10+ times; NR (Low)	3 months	IG2 (Overall)	12	0 (1), 77	0 (0.8), 94	TxtEffectEst: -0.17 (-1.03 to 0.69)	0.70
	Walton, 2013[114]	Driving under the influence of cannabis (cannabis DUI) in the past 3 months: never, 1-2 times, 3-5 times, 6-9 times, 10+ times	3 months	IG1 (Overall)	3	-0.2 (0.8), 101	0.1 (0.8), 96	TxtEffectEst: -0.87 (-1.52 to -0.22)	<0.01
	Walton, 2013[114]	Driving under the influence of cannabis (cannabis DUI) in the past 3 months: never, 1-2 times, 3-5 times, 6-9 times, 10+ times	3 months	IG1 (Overall)	6	-0.1 (0.9), 102	0.1 (0.8), 97	TxtEffectEst: -0.68 (-1.48 to 0.12)	0.10
	Walton, 2013[114]	Driving under the influence of cannabis (cannabis DUI) in the past 3 months: never, 1-2 times, 3-5 times, 6-9 times, 10+ times	3 months	IG1 (Overall)	12	-0.1 (0.9), 104	0 (0.8), 94	TxtEffectEst: -0.32 (-1.12 to 0.48)	0.44

*Author reported.
†Mean value at followup, rather than change from baseline.

Abbreviations: CalcMeanDiffChg = Calculated Mean Difference in Change; CG = Control group; DUI = Driving Under the Influence; EffectSize = Effect size; FU = Followup; IG = Intervention group; NR = Not reported; NSD = No significant difference; OR = Odds ratio; SD = Standard deviation; STI = Sexually transmitted infection; TxtEffectEst: Treatment effect estimate.

Appendix E. List of Abbreviations

AA = Associate Degree
AAP = American Academy of Pediatrics
AHRQ = Agency for Healthcare Research and Quality
AI/AN = American Indian/Alaska Native
Alc = Alcohol; AUS = Australia
ARD = absolute risk difference
ASEBA = Achenbach System of Empirically Based Assessment
AUS = Australia
AUDIT = Alcohol Use Disorder Test
BA = Bachelor of Arts
BL = Baseline
CAN = Canada
CCT = Controlled clinical trial
CD = Children's Depression Inventory
CES-D = Center for Epidemiologic Studies Depression Scale
CG = Control group
CHE = Switzerland
CHQ-CF-GH4 = Child Health Questionnaire-Child Form-General Health
CI = Confidence interval
CZE = Czech Republic
DAWN = Drug Abuse Warning Network
DEU = Germany
DL = DerSimonian and Laird
DSM = Diagnostic and Statistical Manual of Mental Disorders
ED = Emergency department
EPC = Evidence-based Practice Center
Fam = Family functioning
FU = Follow up
GED = General Education Development
GRADE = Grading of Recommendations Assessment, Development and Evaluation
HDI = Human Development Index
HS = High School
IG = Intervention group
IQR = Interquartile range
KQ = Key Question
MD = Mean difference
MH = Mental health
NA = Not applicable
NLD = Netherlands
NR = Not reported
NS = Not significant
NSDUH = National Survey on Drug Use and Health
Obs. = Observations
OR = Odds ratio
Oth = Other health behavior
POL = Poland

Appendix E. List of Abbreviations

POSIT = Problem Oriented Screening Instrument for Teenagers
RAASI = Reynolds Adolescent Adjustment Screening Inventory
RCT = Randomized controlled trial
REML = Restricted maximum likelihood
RSex = Risky sexual behavior
SAMHSA = Substance Abuse and Mental Health Services Administration
SBIRT = Substance use, brief intervention, and/or referral to treatment
SD = Standard deviation
SDQ = Strengths and Difficulties Questionnaire
SES = Socioeconomic status
SFP = Strengthening Families Program
SMD = Standardized mean difference
SocLeg = Social-legal
SS = Secondary school
SWE = Sweden
THC = Tetrahydrocannabinol
Tob = Tobacco
USA = United States of America
USPSTF = U.S. Preventative Services Task Force
Y-OQ = Youth Outcome Questionnaire

Appendix F. Ongoing Studies

Trial identifier	Study name	Location	Estimated N and Age range	Interventions	Outcome Measures	Status
NCT02290938	Motivational Interviewing and Culture for Urban Native American Youth (MICUNAY)	USA	200 14 - 18 years	Motivational Interviewing and Culture for Urban Native American Youth vs. Community Wellness Gathering	Alcohol use | marijuana use | spirituality | Cultural identification | cultural identification	Recruiting Start date: July 2014 Est completion date: June 2018
NCT01813123	A Web-Based Intervention to Prevent Drug Abuse Among Adolescent Girls	USA	788 13 - 14 years	RealTeen vs. No Intervention	30-day alcohol and drug use	Active, not recruiting Start date: Mar 2013 Est completion date: Sept 2018
NCT01744951	ADAPT: Adoption-specific Treatment Prevention Pilot Trial	USA	60 5 - 14 years	Adoption-specific Treatment Prevention Pilot Trial vs. Care as Usual	Parent Weekly Report | Number of child participants whose internalizing and externalizing behaviors improve	Active, not recruiting Start date: Oct 2012 Est completion date: Dec 2018
NCT03051633	Substance Use Prevention Campaign for American Indian Youth	USA	548 11 - 14 years	Be Under Your Own Influence vs. No Intervention	Substance use survey | Attitudes survey	Active, not recruiting Start date: April 2014 Est completion date: Feb 2019
NCT03157700	Interactive Technology for Media Literacy Drug Prevention in Community Groups	USA	1200 13+ years (youth: 13 - 15 years; adults: 21+)	REAL media curriculum vs. Programming as usual	Change in 15-item Intentions to Use Substances Measure (3 mo) | Change in 15-item Intentions to Use Substances Measure (9 mo) | Change in 5-item Lifetime Substance Use Measure (3 mo) | Change in 5-item Lifetime Substance Use Measure (9 mo) | Change in 5-item Frequency of Substance Use	Recruiting Start date: Mar 2018 Est completion date: Feb 2019

Appendix F. Ongoing Studies

Trial identifier	Study name	Location	Estimated N and Age range	Interventions	Outcome Measures	Status
					Measure (3 mo) | Change in 5-item Frequency of Substance Use Measure (9 mo)	
NCT03142009	Family Listening Program: Multi-Tribal Implementation and Evaluation	USA	576 8 - 11 years	Intergenerational culturally adapted curriculum vs. No Intervention	Child substance abuse | Child well-being | Family well-being	Recruiting Start date: April 2014 Est completion date: Mar 2019
NCT02383225	Culturally Grounded Early Substance Use Prevention for American Indian Families	USA	832 10 - 85 years	Substance Use Resistance Skills vs. Facebook Supplement vs. Lakota Language enhancement vs. Lakota Language enhancement + Facebook + Supplement + Substance Use Resistance Skills	Youth lifetime alcohol use | Youth past-month alcohol use | Youth maximum alcohol use in past month | Youth age of first alcohol use | Youth lifetime cigarette use | Youth past-month cigarette use | Youth age of first cigarette use | Youth prevalence of smokeless tobacco use | Youth frequency of past-month smokeless tobacco use | Youth age of first smokeless tobacco use | Youth lifetime prevalence of e-cigarette use | Youth past-month e-cigarette use | Youth lifetime marijuana use | Youth past-month marijuana use | Youth age of first marijuana use | Youth lifetime prevalence of huffing glue/gas | Youth past-month huffing | Youth age of first huffing | Youth perceived consistency of parental discipline practices | Youth perceived parental standard setting | Youth perceived parental monitoring | Youth perceived parental positive affect | Youth perceived parental approval | Youth perceived parental negative affect | Youth perceived parent-child communication | Youth perceived parent-child communication about alcohol and drugs | Youth perceived enforcement of family rules | Youth perceived parental autonomy support | Parent-child shared activities - youth report | Family cohesion - youth report | Family conflict resolution - youth report | Family expressiveness - youth report | Lakota cultural socialization - youth report | Youth perceived parental disapproval of alcohol, tobacco, and marijuana | Descriptive norms for alcohol,	Active, not recruiting Start date: Mar 2015 Est completion date: Mar 2019

Appendix F. Ongoing Studies

Trial identifier	Study name	Location	Estimated N and Age range	Interventions	Outcome Measures	Status
					tobacco, and marijuana - youth report | Youth antisocial behavior | Youth prosocial behavior | Youth deviant peer influences | Youth prosocial peer influences | Youth peer resistance skills | Youth lifetime history of stressful life events | Youth stress management skills | Youth psychological well-being | Youth knowledge of Lakota kinship terminology | Youth self-esteem | General parent-child communication - parent/guardian report | Parent-child communication about family issues - parent/guardian report | Parent-child communication about alcohol and drugs - parent/guardian report | Parent/guardian report of youth behavior | Parent/guardian report parent-child shared activities | Parental monitoring - parent/guardian report | General family rules - parent/guardian report | Family rules about substance use - parent/guardian report | Parent discipline practices | Other household member discipline practices | Standard setting | Parent-child conflict, parent/guardian report | Parent support, parent/guardian report | Parental positive affect, parent/guardian report | Parental negative affect, parent/guardian report | Parental anger management, parent/guardian report | Parental self-efficacy | Family meetings, parent/guardian report | Family cohesion, parent/guardian report | Family conflict resolution, parent/guardian report | Family expressiveness, parent/guardian report | Lakota cultural socialization, parent/guardian report | Lakota parenting practices | Knowledge of Lakota kinship terminology | Parent lifetime alcohol use | Parent past month alcohol use | Parent past month alcohol use quantity | Parent past month alcohol use maximum quantity | Parent past month alcohol use usual quantity | Parent past month alcohol intoxication frequency | Parent first age of alcohol use | Parent first age of alcohol	

Appendix F. Ongoing Studies

Trial identifier	Study name	Location	Estimated N and Age range	Interventions	Outcome Measures	Status
					intoxication | Parent lifetime cigarette use | Parent past month cigarette use | Parent age of first cigarette use | Parent lifetime smokeless tobacco use | Parent past month smokeless tobacco use | Parent age of first smokeless tobacco use | Parent lifetime e-cigarette use | Parent frequency of past-month e-cigarette use | Parent lifetime marijuana use | Parent past-month marijuana use | Parent age of first marijuana use | Parent lifetime huffing | Parent past month huffing | Parent age of first huffing | Parent lifetime use of non-prescription painkillers | Parent past month non-prescription painkiller use | Parent lifetime stimulant use | Parent past month stimulant use | Parent lifetime sedative use | Parent past month sedative use | Parent lifetime heroin use | Parent past month heroin use | Parent lifetime methamphetamine use | Parent past month methamphetamine use | Parent lifetime hallucinogen use | Parent past month hallucinogen use | Parent lifetime club drug use | Parent past month club drug use | Parent lifetime cocaine/crack use | Parent past month cocaine/crack use | Parent HIV risk behavior | Parent psychological distress | Parent life satisfaction	
NCT02420990	CASALEAP IT2A: Integrated Treatment for Adolescents With ADHD	USA	140 12 - 18 years	Medication decision-making intervention vs. Family psycho-education, family-based motivation, and academic training	Conduct Problems | Substance Use Problems | ADHD Symptoms | Medication Uptake	Recruiting Start date: April 2015 Est completion date: Mar 2019
NCT02744118	Helping Eliminate Marijuana Use Through Pediatric Practice (HEMPP)	USA	1020 13 - 25 years	5A's Model vs. Healthy Internet Use Model	Change in Adolescent Marijuana Use | Health and Behavioral Outcomes Related to Adolescent Marijuana Use	Recruiting Start date: April 2016

Appendix F. Ongoing Studies

Trial identifier	Study name	Location	Estimated N and Age range	Interventions	Outcome Measures	Status
						Est completion date: Mar 2019
NCT03086434	Intertribal Talking Circle for the Prevention of Substance Abuse in Native Youth	USA	630 10 - 55 years	Culturally Tailored Intervention vs. Standard Substance Abuse Education	Substance Use | Native Self-Reliance	Enrolling by invitation Start date: May 2014 Est completion date: April 2019
NCT03074877	SKY: Substance Use Screening and Prevention for Adolescents in Pediatric Primary Care	USA	1000 9 - 13 years	Family Check-Up vs. Waitlist Group vs. No Intervention	Assessment of Liability and EXposure to Substance use and Antisocial behavior (ALEXSA) | Centers for Epidemiological Studies Depression Scale|Demographic Questionnaire (DEMO) | Dyadic Adjustment Scale|Financial Stress Questionnaire (FINCE) | Me and My Neighborhood Questionnaire (MMNQ) | Parent Substance Use Questionnaire (SUBST-PC)| Child Behavior Checklist (CBCL) | Extracurricular Activities (ECA) |Recent Activities Interview (RAI) | Screen for Child Anxiety-Related Emotional Disorders (SCR) | Self-Report of Delinquency (SHORT) (SRD) | Child Substance Use (TC Subst) | Youth Risk Behavior Survey (YRBS) | Adult Child Relationship scale (ACRS) | Experiences Microaggression Scale (MIC) | Child Daily Face-to-Face Racial Discrimination (CDIS) | Parental Involvement Scale (PI) |Parental Monitoring Interview - Parent Response, - Child Response (PMI-PR, PMI-CR) | Parenting Children and Adolescents measure (PARCA) | Parental Rating of Peers and Social Skills (PPRSK) | Parent Child Hot topics Discussion Task | Parent Child Hot Topics Questionnaire (PCHT) | Monitoring & Listening Discussion Task | Recognition Discussion Task | Family Culture Discussion Task	Recruiting Start date: June 2014 Est completion date: May 2019

Appendix F. Ongoing Studies

Trial identifier	Study name	Location	Estimated N and Age range	Interventions	Outcome Measures	Status
NCT02622451	Differential Sensitivity Markers in Youth Drug Abuse Prevention	USA	200 12 - 17 years	Teen Intervene vs. Everyday Parenting	Delayed Discounting Task | Iowa Gambling Task | Urinalysis | Peer Substance Use Test | Peer Delinquency Scale | Project Towards No Drug Abuse Survey | Alcohol Expectancy Questionnaire | Single-item self-efficacy Scale | Client Satisfaction Questionnaire | Highly Sensitive Person Scale | Parental Monitoring Instrument | Parenting Relationship Questionnaire (PRQ) | Family Problem Solving Communication Index | Parental Locus of Control Questionnaire | Family Assessment Measure - III | Conflict Behavior Questionnaire	Recruiting Start date: Dec 2015 Est completion date: May 2019
NCT03119415	Enlisting Peer Cooperation and Prosociality in the Service of Substance Use Prevention in Middle School (Prosocial)	USA	2064 Students in 7th grade (first year) or 8th grade (second year)	Cooperative Learning vs. Business as Usual	Substance use | Strengths and Difficulties Questionnaire | Engagement vs. Disaffection with Learning | Classroom Life Scale | University of Illinois Bully Scale	Active, not recruiting Start date: July 2016 Est completion date: June 2019
NCT02038231	PM: Parenting Mindfully Study	USA	100 12 - 16 years	Parenting Mindfully Program vs. Parent Education Program	Change in Substance Use | Change in Adolescent Sex Behaviors | Change in Parenting |Change in Adolescent Stress Responses	Active, not recruiting Start date: Feb 2014 Est completion date: July 2019
NCT02375516	Preventing Drug Abuse Among Hispanic Adolescents	USA	678 12 - 15 years	Prevention Program vs. Control group	Change in average number of drug abuse instances	Active, not recruiting Start date: Sept 2012 Est completion date: Aug 2019
NCT03125291	Bridges: Optimizing a Drug Abuse Prevention Program for Dissemination	USA	600 10 - 15 years	Bridges 4-week Program vs. Bridges Workshop	Substance Use Problems and Risky Behaviors | Mental Health | Academic Outcomes	Active, not recruiting Start date: July

Appendix F. Ongoing Studies

Trial identifier	Study name	Location	Estimated N and Age range	Interventions	Outcome Measures	Status
						2015 Est completion date: Sept 2019
NCT03060291	Prevention of Substance Use in At-Risk Students: A Family-Centered Web Program	USA	347 Youth: enrolled in 6th or 7th grade	Web/ Mobile-only vs. Web/mobile + coach vs. Wait list control	Youth Behavioral Control (parent report) | Youth Behavioral Control (youth report) | Youth Substance Use (parent report) | Youth Substance Use (youth report) | Youth Problem Behavior (parent report)|Youth Problem Behavior (youth report) | Family Conflict (parent report) | Family Conflict (youth report) | Positive Family Relationships (parent report) |Positive Family Relationships (youth report) | Positive Behavior Support (parent report) | Limit Setting (parent report) | Monitoring (parent report)| School Involvement (parent report)|Parenting Self-Efficacy (parent report)	Active, not recruiting Start date: Feb 2017 Est completion date: Sept 2019
ACTRN12612000026820	The CAP Study: Evaluating a comprehensive universal and targeted intervention designed to prevent substance use and related harms in Australian adolescents	Australia	1920 12 - 15 years	Climate Schools and Preventure (CAP) vs. Standard treatment vs. Climate Schools only vs. Preventure only	Uptake and harmful use of alcohol and illicit substance | Substance use related harms | Alcohol and cannabis knowledge and attitudes | Mental health comorbidity | Behavioural problems | Other drug use | Use of illicit drugs | Assess efficacy of intervention in reducing aggression | Peer problems	Active, not recruiting Start date: Jan 2012 Est completion date: Oct 2019
NCT02803567	Trial of a Novel Brief Intervention on Health Behaviors for Youth With Chronic Medical Conditions	USA	450 14 - 17 years	Brief psycho-educational intervention vs. Control	Frequency and quantity of alcohol use | Frequency of marijuana use | Perceived risk of harm of substance use | Medication Adherence	Recruiting Start date: April 2017 Est completion date: Dec 2019
NCT03157895	A Trial of Connecting to Promote Foster Teen Well-Being	USA	240 11 - 15 years	Connecting program vs. Children's Administration services as usual	Delay in drug use initiation | Substance use frequency | Non-violent delinquent behavior frequency | Violent delinquent behavior frequency | Delay in initiation of sexual activity | Residential placement stability | Growth in caregiver/youth bonding | Youth attitudes about HIV related risks | Youth attitudes favorable toward substance use	Recruiting Start date: Dec 2016 Est completion date: Jan 2020

Appendix F. Ongoing Studies

Trial identifier	Study name	Location	Estimated N and Age range	Interventions	Outcome Measures	Status
NCT03009539	eHealth Evidence-based Intervention (EBI) for Latino Youth in Primary Care	USA	456 12-16 years	eHealth Familias Unidas Primary Care vs. Treatment as usual	Change from baseline in past 90-day drug use as measured at 6, 12, 24 and 36 months post baseline | Change from baseline in unprotected sexual behavior | Change from baseline in sexually transmitted infection incidence (i.e., gonorrhea and chlamydia) | Change from baseline in family functioning	Recruiting Start date: April 2017 Est completion date: March 2020
NCT02502799	Intervention for Teens With ADHD and Substance Use	USA	300 12 - 16 years	Parent training and adolescent cognitive behavioral therapy (PT/ACBT) vs. PT/ACBT plus concurrent stimulant medication (PT/ACBT + MED) vs. Continued monitoring of substance use with no additional treatment	Past 90-day substance use | Evidence of illicit substances in urine screen | Parent-adolescent conflict | Disruptive Behaviors | Likelihood of future substance use | Youth impairment	Recruiting Start date: July 2015 Est completion date: Aug 2020
NCT03107117	JJMISCOPE: Computer-Assisted Brief Intervention	USA	90 14 - 17 years	Computer Counseling vs. Standard Care	Time Line Follow Back Interview (TLFB) | Marijuana and alcohol problems	Not yet recruiting Start date: Sept 2017 Est completion date: Aug 2020
NCT02553616	An Intervention to Promote Healthy Behaviors in Homeless Youth	USA	600 18 - 23 years	Intervention to Promote Healthy Behaviors vs. No Intervention	Substance use | Condom use most recent sex | life satisfaction | condom use intention | substance use refusal self-efficacy	Recruiting
NCT02700035	BZDDD: A Family-Centered Ojibwe Substance Abuse Prevention	USA	1500 8 - 100 years	Bii-Zin-Da-De-Dah (Listening to One Another) vs. BZDDD Prevention Program Control	Change in Cigarette Use | Change in Alcohol Use | Change in Illicit Drug Use	Enrolling by invitation Start date: Jan 2017

Appendix F. Ongoing Studies

Trial identifier	Study name	Location	Estimated N and Age range	Interventions	Outcome Measures	Status
						Est completion date: April 2021
NCT03642106	The Together We Can Against Alcohol Tobacco and Drug Use: A Feasibility Trial With Latino Immigrant Youth (TWC)	USA	400 12 to 17	Unidos Se Puede vs. Attention placebo control	Change in past 30-day ATOD use (alcohol, tobacco, marijuana) | Change in Allostatic Load	Recruiting Start date: Jan 2017 Est completion date: June 2021
NCT03409328	Understanding and Reducing HIV Risk Behavior and Substance Use Among Self-identified Bisexual Adolescent Men	USA	60 14- 17 years	HIV and substance use prevention vs. Waitlist	Feasibility | Acceptability | HIV knowledge | STI knowledge | Preventive behavior intentions | Condom use self-efficacy | Bisexual stigma and pride | Condom use | Past-month alcohol and drug use | Alcohol and drug use before/during sex	Not yet recruiting Est start date: Sept 2020 Est completion date: Aug 2021
NCT03710720	Trauma Informed Prevention for Substance Use and Risky Sex (TIPS)	USA	40 13 - 18 years	Trauma Focused-Cognitive Behavioral Therapy plus TIPS app vs. Trauma Focused-Cognitive Behavioral Therapy	Risky Sexual Behaviors Scale | Family Environment Scale | Bad Friends Subscale of the Pittsburgh Youth Study | Alabama Parenting Questionnaire | UCLA PTSD Index DSM-V | Children's Depression Inventory | Timeline Follow Back | CRAFFT Screening Tool for Adolescent Substance Abuse	Not yet recruiting Est start date: Nov 2018 Est completion date: Aug 2021
NCT03227809	First Years Away From Home: Letting Go and Staying Connected (FYAH:LGSC)	USA	900 17 - 22 years	Handbook condition vs. Handbook plus condition vs. Control	Change over time in 30-day alcohol use | Cumulative grade point average | Continuous matriculation at university during first two years | Past 30-day frequency of risky sexual behavior | Lifetime alcohol use | Past 30-day frequency of marijuana use | Past 30-day frequency of prescription drug misuse | Past 30-day frequency of illicit drug use | Lifetime marijuana use | Lifetime prescription drug misuse | Lifetime illicit drug use | Lifetime risky sexual behaviors | Past two-week heavy episodic drinking episodes | Rutgers Alcohol Problem Index | Marijuana Consequences Index | Sexual Consequences Index | Reinforcement of positive behaviors by	Recruiting Start date: April 2017 Est completion date: Sept 2021

Appendix F. Ongoing Studies

Trial identifier	Study name	Location	Estimated N and Age range	Interventions	Outcome Measures	Status
					parents | Peer rewards for antisocial behaviors | Parental attitudes favorable to drug use | Student attitudes favorable to drug use | Sense of belonging | Parent-Student Communication about Alcohol Scale | Parental Monitoring and Consequences | Perception of Parents Scale | Emotional closeness between parent and student | Frequency of parent-student communication | Modality of parent-student communication | Content of parent-student communication | Emotional tone of parent-student communication	
ACTRN12613000723785	The CSC intervention: A comprehensive universal internet-based intervention to prevent anxiety, depression, substance use, and related harms in Australian adolescents aged 13 to 16 years.	Australia	8400 13 - 14 years	Climate Schools-Substance Use (CS-SU) vs. Climate Schools-Mental Health (CS-MH) vs. The Climate Schools Combined (CSC) vs. Control	Use and harmful use of alcohol and cannabis | Overall anxiety/depression levels | Anxiety, depression and substance use knowledge | Alcohol use related harms | Peer alcohol use | Self-efficacy to resist peer pressure | General disability | Truancy | Link between personality and substance use | Moderators of the primary outcomes | Suicide risk | Psychotic experiences | Emotion regulation | Peer networks | Cost effectiveness	Active, not recruiting Start date: Jan 2013 Est completion date: Dec 2021
NCT03735784	Intervention for Substance Use and Sexual Risk Behavior in Homeless Youth	USA	400 18 - 25 years	AWARE curriculum vs. Standard Care	Substance use | Unprotected sex	Not yet recruiting Est start date: Nov 2018 Est completion date: Mar 2022
NCT03458299	Strategies: Motivational Interviewing/Psychoeducation	USA	300 13 - 20	Motivational Interviewing vs. Psychoeducation	Drinking QF | Binge drinking/being drunk Frequency | Commercial Tobacco and Other Drug Use days | DUI/RWDD days | Negative consequences of drinking or using drugs composite	Enrolling by invitation Start date: Jan 2018 Est completion date: Mar 2022
NCT03219190	A High School Program for Preventing Prescription Drug Abuse	USA	3000	LST High School Online vs. Treatment as Usual	Change in any prescription drug use in the past year	Active, not recruiting

Appendix F. Ongoing Studies

Trial identifier	Study name	Location	Estimated N and Age range	Interventions	Outcome Measures	Status
			11 - 14 years			Start date: May 2017 Est completion date: April 2022
NCT03489434	Technology-Based Prevention for Adolescents in Primary Care	USA	48 14 - 18 years	Preliminary prevention program component content based on evidence-based prevention programs for substance use, sexual assault, and sexual risk behaviors vs. No Intervention	Substance use	Recruiting Est start date: Feb 2018 Est completion date: June 2022
NCT03517111	The Impact of a Parenting Intervention on Latino Youth Health Behaviors (FPNG+)	USA	2988 12 + years (youth: 12 - 14 years; adults: 18+ years)	Nutrition/substance use prevention vs. Substance use prevention only vs. Academic success program	Recent use of substances | Drug resistance strategies | Nutrition outcomes | Overall family functioning | Parents' social support | Acculturation | Food Insecurity | Resilience | Self-efficacy for Parenting Index | Parent self-agency | Parent-child communication | Child Feeding Questionnaire | Multidimensional Acculturative Stress Inventory | Body weight | Height | Body mass index | Systolic blood pressure | Diastolic blood pressure | Total cholesterol | Glycosylated hemoglobin (HbA1c) | Diet of adolescents | Diet of the parents | Home food environment	Not yet recruiting Est start date: Aug 2018 Est completion date: Sept 2022