JAMA | US Preventive Services Task Force | EVIDENCE REPORT

Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults

Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

Elizabeth O'Connor, PhD; Rachel Thomas, MPH; Caitlyn A. Senger, MPH; Leslie Perdue, MPH; Shannon Robalino, MSLS; Carrie Patnode, PhD, MPH

IMPORTANCE Illicit and nonmedical (use in ways other than instructed) drug use is common in adolescents and young adults and increases the risk of harmful outcomes such as injuries, violence, and poorer academic performance.

OBJECTIVE To review the benefits and harms of interventions to prevent illicit and nonmedical drug use in children, adolescents, and young adults to inform the US Preventive Services Task Force.

DATA SOURCES MEDLINE, PubMED, PsycINFO, and the Cochrane Central Register of Controlled Trials (January 1, 2013, to January 31, 2019 [children and adolescents]; January 1, 1992, to January 31, 2019 [young adults <25 years]); surveillance through March 20, 2020.

STUDY SELECTION Clinical trials of behavioral counseling interventions to prevent initiation of illicit and nonmedical drug use among young people.

DATA EXTRACTION AND SYNTHESIS Critical appraisal was completed independently by 2 investigators. Data were extracted by 1 reviewer and checked by a second. Random-effects meta-analysis was used to estimate the effect sizes associated with the interventions.

MAIN OUTCOMES AND MEASURES Number of times illicit drugs were used; any illicit drug or any cannabis use.

RESULTS Twenty-nine trials (N = 18 353) met inclusion criteria. Health, social, or legal outcomes such as mental health symptoms, family functioning, consequences of drug use, and arrests were reported in 19 trials and most showed no group differences. The effects on illicit drug use in 26 trials among nonpregnant youth (n = 17 811) were highly variable; the pooled result did not show a clinically important or statistically significant association with illicit drug use (standardized mean difference, −0.08 [95% CI, −0.16 to 0.001]; 24 effects [from 23 studies]; n = 12 801; I^2 = 57.0%). The percentage of participants using illicit drugs ranged from 2.3% to 38.6% in the control groups and 2.4% to 33.7% in the intervention groups at 3 to 32 months' follow-up. The median absolute risk difference between groups was −2.8%, favoring the intervention group (range, −11.5% to 14.8%). The remaining 3 trials provided a perinatal home-visiting intervention to pregnant Native American youth. One trial (n=322) found a reduction in illicit drug use at 38 months (eg, cannabis use in the previous month, 10.7% in the intervention group and 15.6% in the control group) but not at earlier follow-up assessments. Across all 29 trials, only 1 trial reported on harms and found no statistically significant group differences.

CONCLUSIONS AND RELEVANCE The evidence for behavioral counseling interventions to prevent initiation of illicit and nonmedical drug use among adolescents and young adults was inconsistent and imprecise, with some interventions associated with reduction in use and others associated with no benefit or increased use. Health, social, and legal outcomes were sparsely reported, and few showed improvements.

Author Audio Interview

Related article page 2060 and JAMA Patient Page page 2104

Supplemental content

Author Affiliations: Kaiser Permanente Evidence-based Practice Center, Center for Health Research, Kaiser Permanente, Portland, Oregon (O'Connor, Thomas, Senger, Perdue, Patnode); Center for Evidence-based Policy, Oregon Health & Science University, Portland (Robalino).

Corresponding Author: Elizabeth O'Connor, PhD, Kaiser Permanente Evidence-based Practice Center, Center for Health Research, Kaiser Permanente Northwest, 3800 N Interstate Ave, Portland, OR 97227 (Elizabeth.OConnor@kpchr.org).

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In 2017, 5455 adolescents and young adults aged 15 to 24 years died of an illicit or prescription drug overdose—a 50% increase from 2007 to 2017.[1] Illicit and nonmedical drug use (use of medications in ways other than instructed; hereafter, illicit and nonmedical drug use are collectively referred to as "illicit drug use") is associated with additional negative consequences in young people, including an increased risk of motor vehicle crashes,[2,3] violence,[4] suicidal behavior,[5] and lower educational achievement.[6,7] Some long-term negative effects have been associated specifically with heavy cannabis use in adolescence, including anxiety in midlife[7]; impaired development of emotional resiliency[8]; impairments in abstract thinking, attention, learning, and psychomotor functioning[9,10]; and increased risk of psychosis.[11,12]

Illicit drug use is common in adolescents and young adults. The 2018 Monitoring the Future report on adolescent drug use estimated that 47.8% of 12th-graders in the US had ever used an illicit drug, including cannabis, which was the most frequently reported drug, as well as inhalants, hallucinogens, amphetamines, prescription drugs, and heroin.[13] Based on the 2016 National Survey of Drug Use and Health results, it was estimated that young adults aged 18 to 25 years had the highest rate of illicit and nonmedical drug use, with 23.2% reporting use in the past month.[14]

In 2014, the US Preventive Services Task Force (USPSTF) concluded that 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).[15] The current review was undertaken to help the USPSTF update its recommendation on this topic.

Methods

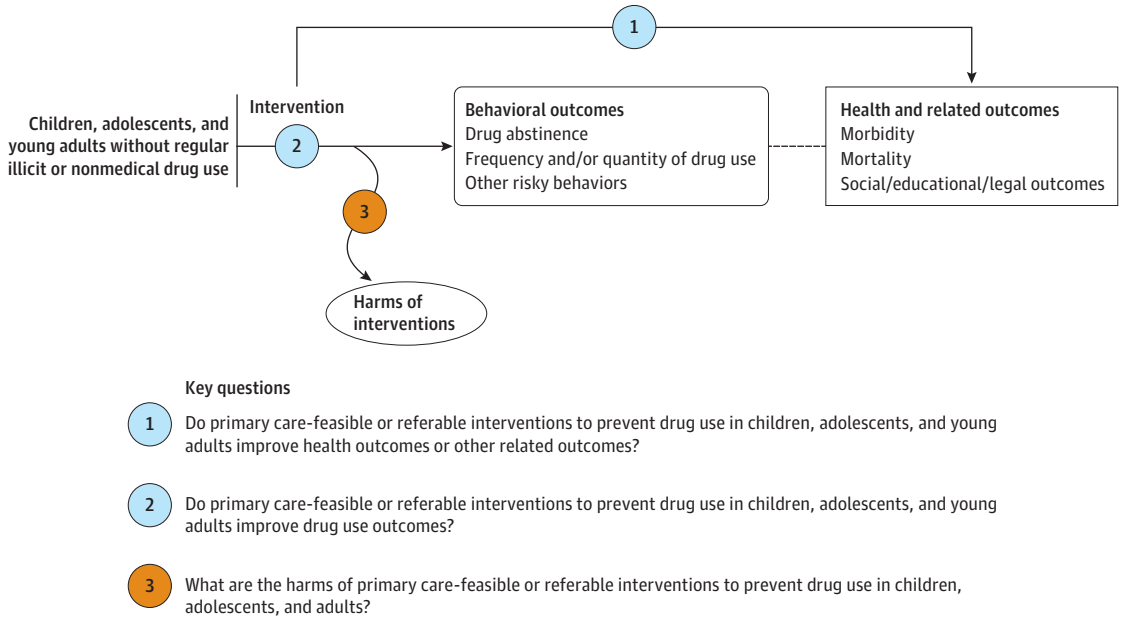
Scope of Review

This review addressed 3 key questions, shown in **Figure 1**. A draft of the analytic framework, review questions, and inclusion and exclusion criteria was posted on the USPSTF website from May 10 to June 7, 2018, for the purpose of gathering public input. Detailed methods (eg, more detailed information about quality rating criteria, data elements abstracted, study and intervention characteristics examined in meta-regression or subgroup analyses, methods for grading the strength of evidence for key questions, expert review and public comment process) are available in the full evidence report at https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/illicit-and-nonmedical-prescription-drug-use-in-children-and-adolescents-primary-care-interventions.

Data Sources and Searches

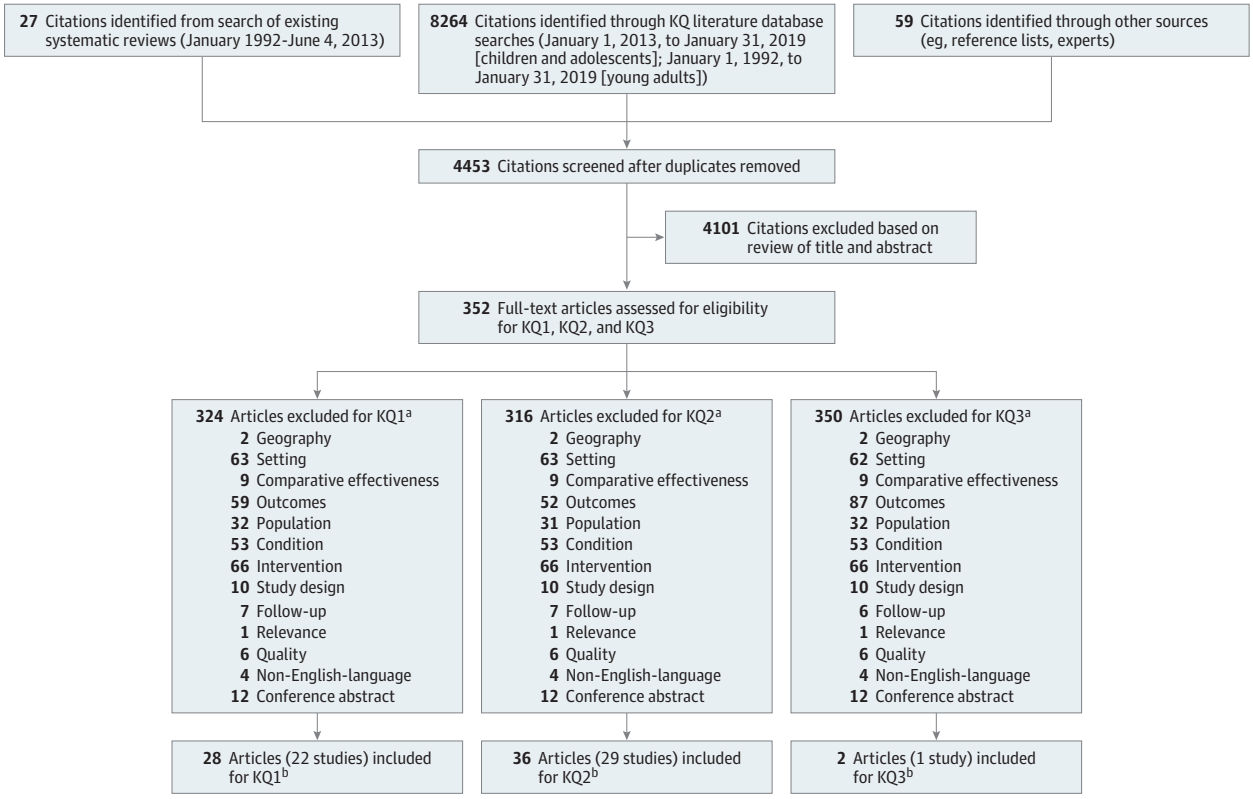
In addition to evaluating all trials included in the previous review[17] and references excluded from the previous review that would be eligible because of expanded inclusion criteria, MEDLINE, PubMed (for publisher-supplied records only), PsycINFO, and the Cochrane Central Register of Controlled Trials were searched for relevant English-language literature published beginning January 1, 2013, for children and adolescents or January 1, 1992, for young adults up to age 25 years and ending January 31, 2019 (eMethods in the Supplement). The database searches were supplemented with bibliographies of other relevant reviews, suggestions from experts, and monitoring of news and table-of-contents alerts.

Figure 1. Analytic Framework: Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults



Evidence reviews for the US Preventive Services Task Force (USPSTF) use an analytic framework to visually display the key questions that the review will address to allow the USPSTF to evaluate the effectiveness and safety of a preventive service. The questions are depicted by linkages that relate interventions and outcomes. A dashed line indicates a health outcome that immediately follows an intermediate outcome. Refer to the USPSTF Procedure Manual for interpretation of the analytic framework.[16]

Figure 2. Literature Search Flow Diagram: Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults



KQ indicates key question.

[a] Reason for Exclusion: Geography: Not a country with a very high Human Development Index ranking. Setting: Excluded on the basis of setting alone (eg, substance abuse treatment centers, school classrooms, work sites, inpatient/residential, other institutions [eg, juvenile detention facilities]). Comparative effectiveness: Control group received active intervention. Outcomes: No relevant outcomes. Population: Does not target youth or young adults, or average age of study sample older than 22 years; targets youth with health conditions that limit generalizability (schizophrenia/psychosis, HIV), individuals in juvenile justice system, court-mandated. Condition: Nonpsychoactive drugs, or more than 50% with regular drug use (weekly use, injection use, positive screener), harmful/hazardous use, or diagnosable disorder. Intervention: Not a primary care–relevant behavioral counseling intervention, or drug misuse is not a primary target of the intervention. Study design: Not a randomized clinical trial or controlled clinical trial. Follow-up: Less than 3 months (12 weeks) of follow-up after baseline (does not apply to harms). Relevance: Study aim not relevant. Quality: Study was poor quality. Non–English-language: Publication not in English. Conference abstract: Study abstract from conference only.

[b] Studies may be included for more than 1 key question.

Ongoing surveillance was conducted after January 2019 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.[18]

Study Selection

Two reviewers independently reviewed abstracts and full-text articles against prespecified inclusion criteria (**Figure 2**). Discrepancies were resolved via discussion and consultation with another reviewer as needed. Randomized clinical trials (RCTs), including cluster randomized trials, and nonrandomized controlled intervention studies were included if they were published in the English language and assessed behavioral counseling interventions designed to prevent or reduce illicit and nonmedical drug use in children, adolescents, and young adults (aged ≤25 years), including pregnant females, who did not regularly use illicit drugs or medications for nonmedical psychoactive effects. Interventions could target other risk behaviors in addition to illicit drug use (eg, alcohol use, tobacco use, risky sexual behavior) but were included only if there was some intervention content that directly addressed illicit drug use and the study reported a drug use outcome. A minimum of 3 months' follow-up was required. Interventions that used components that could not be replicated in a health care setting, such as broad public health, media, or policy interventions, were excluded.

Trials in countries rated as having "very high" human development according to the United Nations[19] were included if they were conducted in health care settings or other settings judged to be generalizable to primary care, including research, community, virtual, and school health clinics. Studies conducted in most other school settings were excluded because of concerns that generalizability to primary care may be limited. Studies were, however, included if they used schools only for recruitment purposes, as long as they recruited from multiple schools and most participants were not attending sessions at their own schools, or if they studied interventions that were conducted entirely online and did

not involve interactions among students at the same school or between students and teachers.

RCTs and nonrandomized controlled intervention studies that did not have a true control group (ie, comparative effectiveness trials) were excluded, and allowable control groups included no intervention (eg, usual care, wait list), a minimal intervention (eg, pamphlets, links to preexisting internet resources, or no more than a single brief contact per year), and attention controls (similar format and intensity but a different content area).

Data Extraction and Quality Assessment

Two reviewers applied USPSTF design-specific criteria (eTable 1 in the Supplement)[16] to assess the methodological quality of all eligible studies and assigned each study a quality rating of "good," "fair," or "poor" (eTable 1 in the Supplement). Discordant quality ratings were resolved through discussion or consultation with another reviewer. Studies were rated as poor quality and excluded from the review if they had a major flaw, such as very high attrition (generally >40%); differential attrition between intervention groups (generally >20%); substantial lack of baseline comparability between groups without adjustment; or major concerns about the trial conduct, analysis, or reporting of results. One reviewer extracted key elements of included studies into standardized forms in DistillerSR (Evidence Partners). A second reviewer checked the data for accuracy. Study design details were abstracted, along with population characteristics, intervention characteristics, and results.

Data Synthesis and Analysis

Summary tables were created for all KQs showing study, population, intervention characteristics, and outcomes. Three trials provided very intensive prenatal and postnatal home visits to pregnant American Indian youth. Because these trials (the Family Spirit trials) were substantially different from the other included trials, both because of the population of interest and the nature of the intervention, their results will be discussed separately from results from the remaining trials, which are referred to as the "general prevention" trials.

Illicit drug use was selected as the primary outcome for meta-analysis. Nineteen trials reported a continuous measure, most commonly the number of times illicit drugs were used over a specified period, and 13 trials reported the dichotomous outcomes of any illicit drug use or any cannabis use. Continuous measures were converted to Hedges g values, which is a standardized mean difference (SMD), based on either change from baseline or mean posttest scores, after converting all "times used" variables to the same time window of the previous 3 months. For dichotomous outcomes, log odds ratios (ORs) were converted to Cohen d and then to Hedges g values using standard formulae.[20] Hedges g can be interpreted as a Cohen d, for which a small effect is typically considered to be 0.20 to 0.50.[21] 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.

Pooled analyses of the general prevention trials were conducted using random-effects meta-analyses on SMDs for 3 categories of substances: illicit drugs, alcohol, and tobacco. Where multiple intervention groups or follow-up time points were provided, the intervention group with the most intensive or comprehensive drug prevention component was selected, reported at 6 to 12 months or the closest to that time frame. Dichotomous measures were selected over continuous measures, 1-month time frames were selected over longer observation windows, and outcomes assessing the use of any illicit drug over the use of a single drug (eg, cannabis) were selected when multiple outcomes were reported for the same study. In addition, ORs and between-group mean differences were pooled separately to better understand effects in the native units. Additionally, analyses of cannabis-specific results in native units are provided.

The DerSimonian and Laird model was used to calculate the pooled effect estimate across studies. In addition, because the DerSimonian and Laird method is prone to insufficient coverage of the full 95% CIs when the number of studies is small and statistical heterogeneity is high (I^2 values were typically near or above 50% in this review), restricted maximum likelihood models with the Knapp-Hartung correction for small samples were also run when pooling fewer than 10 trials. Funnel plots were generated and the Egger test was run to explore small-study effects, which can be related to publication bias.[22] Additionally, for the primary drug use outcome, meta-regression and subgroup analyses were conducted to explore study and intervention characteristics associated with effect size.

Stata version 15.1 (StataCorp) was used for all analyses. All significance testing was 2-sided, and $P \leq .05$ was considered statistically significant.

Results

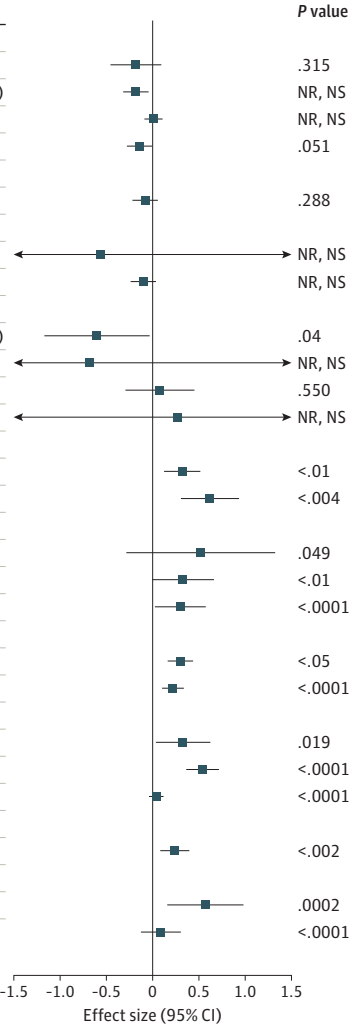
Twenty-nine studies (N = 18 353) were identified that met inclusion criteria, including 28 RCTs and 1 nonrandomized controlled trial,[23] reported in 38 publications.[18,23-58] Across all trials most participants were between the ages of 10 and 18 years, although 2 trials focused on young adults[37,43] and others covered a wide range, including young people up to age 20 to 24 years.[39,48,49,56] See eTable 2 in the Supplement for a list of all included studies and eTable 3 and eTable 4 in the Supplement for summaries of the study and population characteristics.

Twenty (69%) of the included studies addressed broad populations for universal prevention of drug use, but some focused on selected groups at increased risk of substance use or harms from substance use, such as pregnant American Indian youth,[26,28,56] girls in foster care,[41] sexual minority teens (self-identifying as lesbian, gay, bisexual, transgender, or questioning),[55] youth with asthma,[48] youth who were truant[31] or who had other school-related behavior problems,[33] or youth who had some early signs of risky substance use.[46] Planned intervention dose was variable, with a median of 3 sessions (interquartile range, 1-10 sessions) but a range of 1 to 46 sessions. Duration ranged from 1 day to more than 3 years, with a median of 6 weeks (interquartile range, 1 day to 26 weeks). Interventions for 12 of the trials were delivered exclusively through a computer.[25,33,35,43,45,50,51,53-55,57,58] Seven trials (with 9 intervention groups) took place in primary care settings.[18,23,39,49,57-59]

Only 4 trials appeared to focus on illicit drugs without explicit discussion of other substances or behaviors.[43,53-55] Nine trials focused broadly on substance use in their intervention messages, including alcohol or alcohol and tobacco in addition to illicit drug use.[18,23,37,45,46,48,57-59] The remaining used even more broadly targeted interventions that addressed additional behaviors

Figure 3. 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 Time Point Only

Source	Planned follow-up, mo	Scale range	Intervention		Control		Effect size (95% CI)	Study-reported *P* value
			No. of participants	Change, mean (SD)	No. of participants	Change, mean (SD)		
Depression symptoms								
Fang et al,[35] 2010	12	0-2	54	-0.1 (0.8)	50	0.1 (0.7)	-0.18 (-0.45 to 0.09)	.315
Schinke et al,[50] 2009	12	1-5	205	-0.1 (0.8)	327	0.1 (0.8)	-0.18 (-0.32 to -0.04)	NR, NS
Schinke et al,[51] 2009	12	1-5	434	0 (0.8)	430	0 (0.8)	0.01 (-0.09 to 0.11)	NR, NS
Schwinn et al,[54] 2018	15	0-20	370[a]	1.8 (1.0)	382[a]	1.9 (1.0)	-0.14 (-0.28 to 0.00)	.051
Anxiety symptoms								
Schwinn et al,[54] 2018	15	0-20	370[a]	1.6 (1.0)	382[a]	1.7 (1.0)	-0.08 (-0.22 to 0.06)	.288
Externalizing								
Jalling et al,[38] 2016	6	0-64	70	-0.7 (10)	81	-0.1 (9.6)	-0.56 (-3.70 to 2.58)	NR, NS
Foxcroft et al,[36] 2017	12	0-10	233	NR (NR)	194	NR (NR)	-0.10 (-0.24 to 0.04)	NR, NS
Global mental health functioning								
Bannink et al,[25] 2014	4	0-40	430	-1.3 (5.1)	434	-0.8 (5.4)	-0.60 (-1.17 to -0.03)	.04
Jalling et al,[38] 2016	6	0-210	71	-16.4 (27.1)	82	-15.7 (24)	-0.68 (-8.83 to 7.47)	NR, NS
Baldus et al,[24] 2016	8	NR	147	-0.4 (2.5)	145	-0.3 (2.1)	0.08 (-0.29 to 0.45)	.550
Kim and Leve,[41] 2011	24	NR	48[a]	12.8 (8.5)	52[a]	12.5 (8.3)	0.27 (-3.02 to 3.56)	NR, NS
Family communication, adolescent report								
Schinke et al,[50] 2009	12	1-5	205	0.1 (1.1)	327	-0.2 (1.2)	0.32 (0.12 to 0.52)	<.01
Schinke et al,[51] 2009	12	1-5	434	0.4 (2.4)	430	-0.2 (2.2)	0.62 (0.31 to 0.93)	<.004
Family communication, mother report								
Fang et al,[35] 2010	12	1-5	54	0.2 (2.0)	50	-0.3 (2.1)	0.52 (-0.28 to 1.32)	.049
Schinke et al,[50] 2009	12	1-5	205	0 (1.9)	327	-0.3 (1.9)	0.33 (0.00 to 0.66)	<.01
Schinke et al,[51] 2009	12	1-5	434	0 (2.1)	430	-0.3 (2.1)	0.30 (0.03 to 0.57)	<.0001
Parental monitoring, adolescent report								
Schinke et al,[50] 2009	12	1-5	205	0.1 (0.8)	327	-0.2 (0.9)	0.30 (0.16 to 0.44)	<.05
Schinke et al,[51] 2009	12	1-5	434	0.1 (0.8)	430	-0.1 (0.9)	0.22 (0.10 to 0.34)	<.0001
Parental monitoring, mother report								
Fang et al,[35] 2010	12	1-5	54	0.1 (0.6)	50	-0.2 (0.9)	0.33 (0.04 to 0.62)	.019
Schinke et al,[50] 2009	12	1-5	205	0.1 (1.0)	327	-0.5 (1.2)	0.54 (0.36 to 0.72)	<.0001
Schinke et al,[51] 2009	12	1-5	434	0 (0.6)	430	-0.1 (0.7)	0.04 (-0.04 to 0.12)	<.0001
Maternal closeness, adolescent report								
Schinke et al,[51] 2009	12	1-5	434	0.2 (1.1)	430	-0.1 (1.2)	0.24 (0.08 to 0.40)	<.002
Maternal closeness, mother report								
Fang et al,[35] 2010	12	1-5	54	0.4 (1.0)	50	-0.2 (1.2)	0.57 (0.16 to 0.98)	.0002
Schinke et al,[51] 2009	12	1-5	434	-0.2 (1.6)	430	-0.2 (1.6)	0.09 (-0.13 to 0.31)	<.0001



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 follow-up, regression parameter estimates (eg, β-weights, B-weights), Cohen d.KQ indicates key question; NR, not reported; NS, not significant.

[a] Mean value at follow-up, rather than change from baseline.

such as family functioning,[24,33,35,36,38,41,50,51] risky sexual behavior,[25,33,39,41,49] mental health and emotional well-being (including social skills training),[25,35,41,49-51] truancy and delinquent behaviors,[31] and breastfeeding and infant care.[26,28,56] Three trials examined a home-visiting intervention for pregnant American Indian adolescents and young adults recruited through the Indian Health Service, covering a range of preventive health topics.[26,28,56]

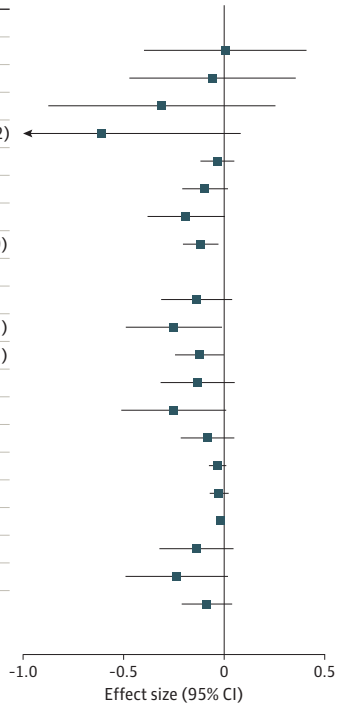
Benefits of Interventions

Key Question 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?

Health, social, or legal outcomes were reported in 16 of the general prevention trials[24,25,31,33,35,36,38,41,43,49-51,54,57-59] and all 3 Family Spirit trials.[26,28,56] No single outcome was widely reported. Mental health outcomes, such as depression, anxiety, and externalizing symptoms, and family functioning were the most commonly reported health outcomes, reported by 9 of the general prevention trials[24,25,35,36,38,41,50,51,54] and all 3 Family Spirit trials.[26,28,56] Most general prevention trials found no group differences on mental health symptom scales after 3 to 24 months (**Figure 3**), and results were mixed in the Family Spirit trials. Measures of family functioning were reported in 5 of the general prevention trials.[33,35,36,50,51] Improvement in several family functioning outcomes (family communication, parental monitoring, and maternal closeness) were found in 3 trials of computer-based interventions targeting middle school–aged females and their mothers[35,50,51] (**Figure 4**). Across all time points (up to 24 months), differences in change between groups in

Figure 4. Mental Health Outcomes Summary (KQ1) Among the Family Spirit Trials: Mean Difference Between Intervention and Control Groups, by Outcome

Source	Scale range	Planned follow-up, mo	Outcome	Intervention		Control		Effect size (95% CI)	Study-reported *P* value
				No. of participants	Change, mean (SD)	No. of participants	Change, mean (SD)		
Depression symptoms									
Walkup et al,[56] 2009	0-60	5	CES-D	54[a]	-2.0 (11.8)	71[a]	-3.3 (10.7)	0.05 (-3.99 to 4.09)	NR, NS
		9		47[a]	-4.0 (12.2)	68[a]	-4.0 (10.7)	-0.58 (-4.72 to 3.56)	NR, NS
Barlow et al,[28] 2006	0-60	5	CES-D	19[a]	11.6 (10)	22[a]	15.2 (8.0)	-3.10 (-8.74 to 2.54)	.27
		9		19[a]	8.4 (10)	22[a]	14.2 (11)	-6.10 (-13.02 to 0.82)	.08
Barlow et al,[26] 2013	0-60	4	CES-D	159	-0.3 (NR)	163	0 (NR)	-0.34 (-1.18 to 0.50)	.44
		8		159	-0.9 (NR)	163	0 (NR)	-0.95 (-2.09 to 0.19)	.10
		14		159	-1.8 (NR)	163	0 (NR)	-1.89 (-3.81 to 0.03)	.06
		38		159	-0.9 (NR)	163	0.3 (NR)	-1.17 (-2.05 to -0.29)	.01
Other symptoms									
Barlow et al,[26] 2013	0-100	8	Externalizing	159	-1.9 (NR)	163	-0.7 (NR)	-1.37 (-3.13 to 0.39)	.13
		14		159	-3.8 (NR)	163	-1.5 (NR)	-2.50 (-4.89 to -0.11)	.04
		38		159	-0.6 (NR)	163	0.4 (NR)	-1.23 (-2.45 to -0.01)	<.05
Barlow et al,[26] 2013	0-100	8	Internalizing	159	-2.3 (NR)	163	-1.1 (NR)	-1.32 (-3.16 to 0.52)	.16
		14		159	-4.7 (NR)	163	-2.3 (NR)	-2.51 (-5.12 to 0.10)	.06
		38		159	-3.2 (NR)	163	-2.5 (NR)	-0.83 (-2.16 to 0.50)	.23
Barlow et al,[26] 2013	0-100	4	Mental health score (POSIT)	159	-0.1 (NR)	163	-0.1 (NR)	-0.33 (-0.76 to 0.10)	.14
		8		159	-0.3 (NR)	163	-0.4 (NR)	-0.25 (-0.72 to 0.22)	.30
		14		159	-0.5 (NR)	163	-0.8 (NR)	-0.14 (-0.28 to 0.00)	.70
Barlow et al,[26] 2013		8	Total emotional/behavior problem score	159	-2.3 (NR)	163	-1.3 (NR)	-1.38 (-3.22 to 0.46)	.14
		14		159	-4.5 (NR)	163	-2.6 (NR)	-2.36 (-4.91 to 0.19)	.07
		38		159	-2.0 (NR)	163	-1.6 (NR)	-0.86 (-2.11 to 0.39)	.18

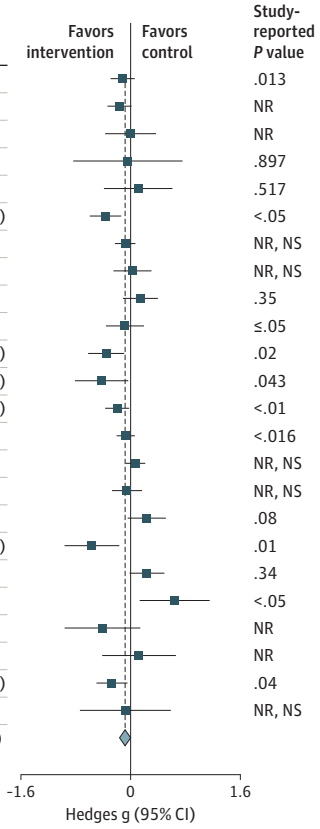


Weights are from random-effects analysis. Effect sizes are study-reported mean differences at follow-up (Barlow et al[28]; Barlow et al[26]) and beta-weight (Walkup et al[56]). CES-D indicates Center for Epidemiologic Studies Depression Scale; KQ, key question; NR, not reported; NS, not significant; POSIT, Problem Oriented Screening Instrument for Teenagers.

[a] Mean value at follow-up, rather than change from baseline.

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

Source	Outcome	Planned follow-up, mo	No./total (%) or change, mean (SD) [No.]		Hedges g (95% CI)	Study-reported *P* value
			Intervention	Control		
Gmel et al,[37] 2013	Cannabis any use	6	97/288 (33.7)	148/384 (38.6)	-0.12 (-0.29 to 0.06)	.013
Knight et al,[18], 2019	Cannabis any use	6	172/626 (0.3)	82/243 (0.3)	-0.16 (-0.34 to 0.01)	NR
Walton et al,[58] 2014	Cannabis any use	6	18/200 (9.0)	19/211 (9.0)	0.00 (-0.37 to 0.37)	NR
Baldus et al,[24] 2016	Cannabis any use	8	5/147 (3.7)	3/145 (2.3)	-0.04 (-0.84 to 0.76)	.897
Malmberg et al,[45] 2014	Cannabis any use	8	68/1114 (6.1)	58/1109 (5.2)	0.11 (-0.39 to 0.61)	.517
Harris et al,[23] 2012(CZ)	Cannabis any use	12	45/264 (17.0)	76/266 (28.7)	-0.37 (-0.60 to -0.14)	<.05
Harris et al,[23] 2012(US)	Cannabis any use	12	119/765 (15.6)	133/758 (17.5)	-0.08 (-0.23 to 0.07)	NR, NS
Schwinn et al,[55] 2015	Cannabis times used	3	-0.3 (5.2) [97]	-0.4 (5.9) [103]	0.03 (-0.25 to 0.30)	NR, NS
D'Amico et al,[59] 2018	Cannabis times used	6	6.1 (7.9) [127][a]	5.1 (6.8) [111][a]	0.14 (-0.11 to 0.40)	.35
Lindstrom Johnson et al,[39] 2015	Cannabis times used	6	1.3 (21.5) [101]	3.7 (34.7) [99]	-0.08 (-0.36 to 0.20)	≤.05
Schwinn et al,[53] 2010	Cannabis times used	6	0.1 (3.1) [108][a]	1.3 (3.3) [118][a]	-0.36 (-0.62 to -0.09)	.02
Fang et al,[35] 2010	Cannabis times used	12	0 (0.4) [54]	0.2 (0.8) [50]	-0.42 (-0.81 to -0.03)	.043
Schinke et al,[50] 2009	Cannabis times used	12	0.1 (0.4) [205]	0.4 (1.9) [327]	-0.20 (-0.37 to -0.02)	<.01
Schinke et al,[51] 2009	Cannabis times used	12	0 (0) [434]	0.1 (0.6) [430]	-0.07 (-0.20 to 0.06)	<.016
Schwinn et al,[54] 2018	Cannabis times used	15	0.8 (15.3) [370]	-0.2 (12.5) [382]	0.07 (-0.07 to 0.21)	NR, NS
Lee et al,[43] 2010	Cannabis days used	6	1.2 (17.5) [160]	2.1 (17.9) [160]	-0.05 (-0.27 to 0.17)	NR, NS
Walton et al,[57] 2013	Cannabis use score	6	-0.7 (2) [102]	-1.2 (2) [97]	0.24 (-0.04 to 0.51)	.08
Kim and Leve,[41] 2011	Cannabis use score	36	1.3 (0.8) [48][a]	2.3 (2.4) [52][a]	-0.56 (-0.96 to -0.16)	.01
Bannink et al,[25] 2014	Any drug any use	4	44/430 [10.4]	36/434 (8.3)	0.24 (-0.02 to 0.49)	.34
Jalling et al,[38] 2016	Any drug any use	6	12/70 (17.1)	9/81 (11.1)	0.64 (0.13 to 1.15)	<.05
Estrada et al,[33] 2019	Any drug any use	12	6/82 (7.3)	14/98 (14.3)	-0.41 (-0.96 to 0.14)	NR
Foxcroft et al,[36] 2017	Any drug any use	12	14/222 (6.3)	6/193 (3.1)	0.12 (-0.41 to 0.66)	NR
Sanci et al,[49] 2015	Any drug any use	12	38/377 (10.1)	82/524 (15.7)	-0.27 (-0.50 to -0.05)	.04
Rhee et al,[48] 2008	Any drug times used	6	-0.4 (2.1) [17]	-0.2 (2.5) [18]	-0.08 (-0.74 to 0.59)	NR, NS
Overall (I^2 = 57.0%, *P* <.001)					-0.08 (-0.16 to 0.00)	



Vertical dashed line indicates the overall measure of effect. NR indicates not reported; NS, not significant.

[a] Mean value at follow-up, rather than change from baseline

these trials most commonly fell between 0.3 and 0.6 on a 5-point scale. The other 2 trials did not find group differences on measures of communication,[33,36] parental monitoring,[33] or positive parenting, although data needed to include these results on the forest plot were not provided.[33]

Key Question 2. Do primary care–feasible or referable interventions to prevent drug use in children, adolescents, and young adults improve drug use outcomes?

The effects of the general prevention interventions on illicit and nonmedical drug use were wide ranging, and the result of the pooled analysis was not statistically significant and was unlikely to be clinically important (pooled SMD, −0.08 [95% CI, −0.16 to 0.001]; 24 effects [from 23 studies]; n = 12 801; I^2 = 57.0%) (**Figure 5**, **Table 1**). The pooled OR for any illicit drug use or any cannabis use was 0.82 (95% CI, 0.67 to 1.04; 12 effects [11 studies]; n = 9031; I^2 = 38.2% (Table 1). The percent using illicit drugs at follow-up ranged from 2.3% to 38.6% in the control groups and 2.4% to 33.7% in the intervention groups. The median absolute risk difference between groups was -2.8%, favoring the intervention group (range, -11.5% to 14.8%). Results were very similar when limited to cannabis outcomes only, except that the pooled result was statistically significant for the proportion reporting any cannabis use (OR, 0.78 [95% CI, 0.64 to 0.95]; 7 effects [6 studies]; n = 6520; I^2 = 1.3%) (Table 1). When examining numbers of times used in the previous 3 months, the pooled mean difference between groups was −0.21 times (95% CI, −0.44 to 0.02; 11 studies; n = 3651; I^2 = 51.0%) (Table 1).

Only 4 trials reported the effect of their interventions on misuse of prescription medications specifically. All 4 were computer-based interventions, and all broadly targeted substance use and other non–substance-related outcomes.[33,35,50,51] All 4 reported greater reductions in misuse of prescription medications with the intervention, ranging from 0.1 (95% CI not reported)[33] to 11.3 (95% CI, −22.6 to −0.08)[35] fewer times used over the previous 3 months, at up to 24 months' follow-up.

Despite the small pooled result, some interventions did show statistically significant reductions in illicit drug use at 1 or more follow-up time points.[23,33,35,39,49-51,53,57,58] Among the general prevention interventions, these included the computer-based interventions targeting young female adolescents,[35,50,51,53] the computer-based version of the Familias Unidas intervention (which has been widely studied in school settings) targeting eighth-graders with behavior problems,[33] a primary care clinician training intervention,[49] and the 46-session intervention for eighth-grade girls in foster care and their foster parents.[41] For example, one of the largest effects was found with the Familias Unidas intervention.

Table 1. Summary of Meta-Analysis Results for Substance Use Outcomes for General Prevention Trials (KQ2)

	No. of studies	Type of effect	Pooled result (95% CI)	No. of studies (No. of effects)	I^2, %	Tau^2	N	Range of effects[a]	Effects, median (IQR)[a]
Drug outcomes									
Primary drug outcome	26	SMD	−0.08 (−0.16 to 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 to 1.04)	11 (12)	38.2	0.041	9031	0.42 to 3.52	0.80 (0.64 to 0.95)
		ARD	NA	NA	NA	NA	NA	−11.5 to 14.8	−2.8 (−5.0 to 0.2)
Any cannabis use, %	6	OR	0.78 (0.64 to 0.95)[b]	6 (7)	1.3	0.0	6520	0.51 to 1.34	0.77 (0.71 to 0.86)
		ARD	NA	NA	NA	NA	NA	−11.5 to 2.8	−3.0 (−5.0 to −1.3)
Times used in previous 3 mo	12	MD	−0.21 (−0.44 to 0.02)	11 (11)	51.0	0.037	3651	ΔΔ: −7.5 to 1.0	ΔΔ: −0.3 (−1.6 to 0.0)
								Δ: −1.1 to 1.5	Δ: 0.7 (−0.4 to 1.3)
Times used cannabis in previous 3 mo	10	MD	−0.23 (−0.48 to 0.01)	10 (10)	58.1	0.045	3616	ΔΔ: −2.7 to 1.0	ΔΔ: −0.3 (−0.9 to 0.0)
								Δ: −1.1 to 1.6	Δ: 0.7 (−0.4 to 1.3)
Alcohol outcomes									
Primary alcohol outcome	24[c]	SMD	−0.11 (−0.16 to −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 to 0.96)[b]	5 (6)	0	0.009	5854	0.56 to 1.40	0.98 (0.81 to 1.18)
	5	ARD	NA	NA	NA	NA	NA	−10.4 to 10.2	1.0 (−5.0 to 4.0)
Risky alcohol use, %	5	OR	0.92 (0.72 to 1.17)[b]	5 (5)	0	0.0	5078	0.77 to 1.45	0.94 (0.88 to 1.20)
		ARD	NA	NA	NA	NA	NA	−4.7 to 8.9	0.8 (−2.4 to 4.6)
Times used alcohol in previous 3 mo	8	MD	-0.29 (-0.53 to -0.05)[b]	8 (8)	20.7	0.014	3192	ΔΔ: −1.2 to 0.8	ΔΔ: −0.2 (−0.4 to 0.2)
								Δ: −1.9 to −0.5	Δ: −0.6 (−1.3 to −0.5)
Total drinks in previous 3 mo[d]	3	MD	NA	NA	NA	NA	NA	ΔΔ: −3.8 to 2.8	ΔΔ: 1.4 (−2.2 to 2.5)
								Δ: NA (0 trials)	Δ: NA (0 trials)
Tobacco outcomes									
Primary tobacco outcome	16[c]	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)[b]	6 (6)	0	0.0	5373	0.63 to 1.69	1.08 (0.88 to 1.32)
		ARD	NA	NA	NA	NA	NA	−8.6 to 8.5	0.8 (−2.1 to 5.8)
Times used tobacco in previous 3 mo	8	MD	−0.30 (−0.58 to 0.02)[b]	8 (8)	0	0.0	2893	ΔΔ: −5.5 to −0.2	ΔΔ: −1.0 (−2.2 to −0.3)
								Δ: 0.54	Δ: NA (1 trial)

Abbreviations: ARD, absolute risk difference; IQR, interquartile range; MD, mean difference between groups; NA, not applicable; OR, odds ratio; SMD, standardized mean difference (Hedges g).

[a] Range of effects for all study groups and time points, ie, not limited to records in the meta-analysis. Δ indicates difference between groups at follow-up; ΔΔ, difference between groups in change from baseline.

[b] Effect based on restricted maximum likelihood model. Remaining effects based on DerSimonian and Laird model. Δ indicates difference between groups at follow-up; ΔΔ, difference between groups in change from baseline.

[c] 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.

[d] "Drink" not defined.

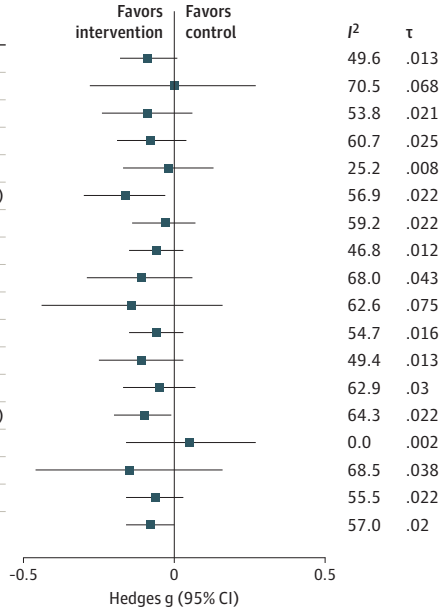
At 12 months' follow-up, it found that participants had used cannabis an average of 2.7 fewer times (95% CI, −3.7 to 0.5; $P < .01$) over the previous 3 months, had misused prescription medications 0.2 fewer times (95% CI, −1.8 to 1.6; $P < .01$), and had used inhalants 1.4 fewer times (95% CI, −3.5 to 0.77; $P < .001$). Effects were generally maintained through 12 months or beyond in these trials. Most of these interventions involved 9 or more intervention sessions, all but 1[53] included components for parents or caregivers as well as the youth, and all addressed a broad range of skills and topics. Other interventions demonstrated beneficial effects only for some patient subgroups, including 2 primary care–based interventions that used a computer-based assessment and intervention along with brief 1-time clinician counseling.[18,23] These trials found reduced drug illicit use among youth at their site in the Czech Republic but not in the US[23] and found reduced drug use among youth with a baseline history of substance use but not youth with no substance use the previous year.[18]

However, many interventions showed no clear evidence of benefit, and 2 reported increased illicit drug use in youth participating in the interventions for at least 1 drug-related outcome.[38,40] Ten trials had less than 12 months' follow-up, which may have been insufficient to find differences in younger adolescents with low use levels. None of the potential effect modifiers examined (study, population, intervention, and control characteristics) appeared to explain variability in effect sizes (**Figure 6**), and there was no evidence of a small-studies effect.

Pooled effects for alcohol and tobacco use both showed statistically significant, but very small, pooled results (alcohol pooled SMD, −0.11 [95% CI, −0.16 to −0.07]; 23 effects [from 22 studies]; n = 12 307; I^2 = 4.9% and tobacco pooled SMD, −0.09 [95% CI, −0.15 to −0.03]; 15 studies; n = 8366; I^2 = 35.0%) (Table 1). Other behavioral outcomes were sparsely reported, with most trials finding no differences between groups or finding differences only among some participant subgroups and not overall.

Figure 6. 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

Analysis	Model	No. of effects (studies)	No. analyzed	Hedges g (95% CI)	I^2	τ
US	DL	16 (16)	6753	-0.09 (-0.18 to 0.01)	49.6	.013
Non-US	REML	8 (8)	6048	0.00 (-0.28 to 0.27)	70.5	.068
Health care setting	REML	9 (8)	4906	-0.09 (-0.24 to 0.06)	53.8	.021
Non-health care setting	DL	15 (15)	7895	-0.08 (-0.19 to 0.04)	60.7	.025
US health care setting	REML	7 (7)	3475	-0.02 (-0.17 to 0.13)	25.2	.008
Middle school age	DL	10 (10)	5688	-0.16 (-0.30 to -0.03)	56.9	.022
Non-middle school age	DL	14 (13)	7113	-0.03 (-0.14 to 0.07)	59.2	.022
Targets substances only	DL	14 (13)	8398	-0.06 (-0.15 to 0.03)	46.8	.012
Also targets other outcomes	DL	10 (10)	4403	-0.11 (-0.29 to 0.06)	68.0	.043
Parent component	REML	8 (8)	2638	-0.14 (-0.44 to 0.16)	62.6	.075
Youth only	DL	16 (15)	10 163	-0.06 (-0.15 to 0.03)	54.7	.016
Computer only	REML	9 (9)	5401	-0.11 (-0.25 to 0.03)	49.4	.013
In-person/telephone	DL	15 (14)	7400	-0.05 (-0.17 to 0.07)	62.9	.03
Usual care control	DL	18 (17)	11 249	-0.10 (-0.20 to -0.01)	64.3	.022
Minimal intervention/attention control	REML	6 (6)	1552	0.05 (-0.16 to 0.27)	0.0	.002
Good quality	REML	5 (5)	2140	-0.15 (-0.46 to 0.16)	68.5	.038
Fair quality	DL	19 (18)	10 661	-0.06 (-0.16 to 0.03)	55.5	.022
All general prevention trials	DL	24 (23)	12 801	-0.08 (-0.16 to 0.00)	57.0	.02



DL indicates DerSimonian and Laird; KQ, key question; REML, restricted maximum likelihood.

Harms of Interventions

Key Question 3. What are the harms of primary care–feasible or referable interventions to prevent drug use in children, adolescents, and adults?

Only 1 of the included trials (a Family Spirit trial) directly reported on harms.[26] 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 they did not provide detailed data.[26] As mentioned above, 2 general prevention trials reported increased illicit drug use in intervention groups over the control groups.[38,40] Additionally, 7 other trials reported increases in illicit drug, alcohol, or tobacco use that were not statistically significant, with point estimates for the SMD larger than 0.20 or an OR of 2.0 or greater.[25,28,36,45,48,56,57]

Discussion

This evidence review included 29 studies, with findings that were inconsistent for illicit and nonmedical drug use, and effects ranging from clearly beneficial to possibly harmful (**Table 2**). While some interventions were associated with reduced illicit and nonmedical drug use, they tended to either target a relatively narrow population (eg, 10- to 14-year-old Asian American girls, truant youth, eighth-grade girls in foster care) with limited generalizability to other populations, or to not have 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 1-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.[18,23,57-59]

The previous USPSTF review on this topic[17] concluded that there was inadequate evidence to determine whether preventive interventions were effective in reducing the likelihood of illicit drug use, based on 6 trials, all of which were also included in the current review.[23,35,48,50,51,57] The current review added newly published literature, including 23 additional studies, and expanded the scope of this topic to include trials deemed feasible for implementation in a health care system (ie, clinicians and related staff in the primary care setting could have the skills necessary to deliver the intervention or could refer to others in the health system with the necessary skills), even if the study was conducted in the community or other non–health care settings. Despite this expansion of scope, the strength of evidence was low that primary care–relevant interventions could prevent illicit and nonmedical drug use in children, adolescents, and young adults. This was because of the inconsistency in effects, the relatively narrow target populations for most of the interventions that showed a benefit, and the lack of benefit among studies conducted in US-based primary care settings, which were primarily limited to low-dose interventions.[18]

Most of the studies of interventions to prevent illicit and nonmedical drug use have been conducted in school classrooms or afterschool settings, and other reviews have found these school-based prevention programs effective in reducing illicit drug use, including some approaches that would likely be feasible to implement in a health care setting.[60] Two interventions included in this review that have been primarily studied in school settings are Familias Unidas and the Strengthening Families Program: For Parents and Youth 10-14 (SFP 10-14). Familias Unidas[61] 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

Table 2. Summary of Evidence Among All 28 Included Trials (n = 17 482) of Interventions to Prevent Illicit and Nonmedical Drug Use in Children, Adolescents, and Young Adults, by Key Question

No. of studies (No. of observations)	Summary of findings	Consistency/ precision	Other limitations	Strength of evidence	Applicability
KQ1: Benefits of interventions—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 girls 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 narrow demographic or risk groups	Low evidence of small to no benefit	14 conducted in the US, 8 limited to females, including 3 that were limited to pregnant American Indian females recruited through the Indian Health Service; 4 additional trials conducted in US primary care settings
KQ2: Benefits of interventions—drug use and 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]; 24 effects [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]; 23 effects [from 22 studies]; n = 12 307; I^2 = 4.9%) and tobacco use (SMD, −0.09 [95% CI, −0.15 to −0.03]; 15 studies; n = 8366; I^2 = 35.0%) Of the 3 Family Spirit intervention trials among pregnant Native American adolescents, only the largest and best-quality trial found reductions in drug use and only at long-term (38-mo) follow-up	Inconsistent, imprecise	Heterogeneity in outcomes reported; only 6 rated as good quality; 10 trials had less than 12 mo of follow-up, which may be insufficient to find differences among 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 US, 15 of which included >50% racial or ethnic minority participants; primarily targeted adolescents (vs young adults); only 12 trials conducted in or recruited from health care settings, including 3 limited to pregnant Native American youth recruited through the Indian Health Service
KQ3: Harms of interventions					
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; raw proportions and details of how contact time was adjusted for were not provided	Insufficient	Trial directly reporting harms limited to pregnant Native American persons; trials showing statistically significant harmful drug outcomes conducted in Sweden and the US

Abbreviations: EPC, Evidence-based Practice Center; KQ, key question; NA, not applicable; SMD, standardized mean difference.

from middle schools, and sessions occurred outside of school hours. The intervention generally included 8 group sessions for parents and 4 family visits that included the adolescents.[62] The intervention has shown reductions in illicit drug, alcohol, and cigarette use, as well as improvements in family functioning.[63,64] The online version of Familias Unidas tested in this review reported lower frequency of illicit drug use in the intervention group and a between-group difference in the proportion using illicit drugs that was similar in magnitude to that seen in school-based studies.[33]

In contrast, the 3 trials in this review that either directly implemented or were based on the SFP 10-14 did not prove to be effective outside of school settings.[24,36,38] The Strengthening Families Program is a widely studied intervention designed for high-risk families; several versions exist for different age groups (eg, preschool, elementary, early teens, and high school).[65] 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 (eg, schools, community centers, drug courts); and has been adapted to be culturally sensitive.[65] A 10-year follow-up (n = 446 families) of an RCT originally conducted in Iowa in 1993 found a long-term reduction in substance use (27.5% of participants in the SFP 10-14 group had initiated illicit substance use by age 21 years, vs 38.3% in the control group [β = −0.14, P < .001]).[66,67] The beneficial effects of this program appear to have emerged between the 18- and 30-month assessments in most studies, and since the studies of SFP 10-14 included in this review followed up participants for a maximum of 24 months, the lack of benefit could have been attributable to insufficient follow-up rather than the setting. 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.

There are important limitations in the research that should be considered. First, reporting of health, social, and legal outcomes was sparse and heterogeneous, limiting the conclusions for these important outcomes. In addition, drug use outcomes were very heterogeneous, making it difficult to draw overall conclusions. Second, no evidence was found that included children younger than 10 years, likely because a very long follow-up window would be needed to determine the effect on illicit drug use. Additionally, very limited evidence on young adults was found, since this literature primarily focused on the reduction of use in those who were regular users, hazardous users, or who had a likely substance use disorder, which was excluded from the review. These types of secondary prevention trials are included in the USPSTF review on screening and interventions for drug misuse.[68]

Third, most of the interventions were studied by the teams who developed the intervention and have not been replicated by independent researchers. This may be especially important in this field, in which outcomes are measured by self-report and are subject to social desirability effects. In general, studies are needed that replicate in a health care context and that further refine and broadly implement some of the effective interventions described in this review. These include the clinician training and quality improvement intervention,[49] the computer-based Familias Unidas intervention,[33] and some of the computer-based interventions for adolescent girls.[50,51,53] Several of the primary care–based interventions showed a benefit for some outcomes for some subgroups, suggesting that the combination of a clinician interview and an electronic-based intervention has potential. However, the relatively small overall evidence base and inconsistencies across studies indicate a need for further study of these interventions. It would also be valuable to conduct a trial in a health care setting of the full in-person version of the Familias Unidas intervention and other interventions proven to be effective in schools. It is important to continue to explore the influence of context and mechanisms of change.

Limitations

This review has several limitations. First, trials that did not report a drug use outcome were excluded, so studies that only included intermediate outcomes such as child development or school functioning were excluded, even if substance abuse prevention might have been a long-term aim. Second, interventions that did not explicitly address prevention of illicit and nonmedical drug use were excluded, although some broad prevention or resilience interventions may be effective in preventing illicit drug use. Third, since trials targeting alcohol and tobacco use (without targeting illicit drug use) were not comprehensively included, the results for the alcohol and tobacco outcomes do not represent all available evidence on these topics.

Conclusions

The evidence for behavioral counseling interventions to prevent initiation of illicit and nonmedical drug use among adolescents and young adults was inconsistent and imprecise, with some interventions associated with reduction in use and others associated with no benefit or increased use. Health, social, and legal outcomes were sparsely reported, and few showed improvements.

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Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: O'Connor, Robalino, Patnode.
Critical revision of the manuscript for important intellectual content: Thomas, Senger, Perdue, Robalino, Patnode.
Statistical analysis: O'Connor, Patnode.
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