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Screening for Unhealthy Drug Use: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

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Screening for Unhealthy Drug Use
Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

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IMPORTANCE Illicit drug use is among the most common causes of preventable morbidity and mortality in the US.

OBJECTIVE To systematically review the literature on screening and interventions for drug use to inform the US Preventive Services Task Force.

DATA SOURCES MEDLINE, PubMed, PsycINFO, Embase, and Cochrane Central Register of Controlled Trials through September 18, 2018; literature surveillance through September 21, 2019.

STUDY SELECTION Test accuracy studies to detect drug misuse and randomized clinical trials of screening and interventions to reduce drug use.

DATA EXTRACTION AND SYNTHESIS Critical appraisal and data abstraction by 2 reviewers and random-effects meta-analyses.

MAIN OUTCOMES AND MEASURES Sensitivity, specificity, drug use and other health, social, and legal outcomes.

RESULTS Ninety-nine studies (N = 84 206) were included. Twenty-eight studies (n = 65 720) addressed drug screening accuracy. Among adults, sensitivity and specificity of screening tools for detecting unhealthy drug use ranged from 0.71 to 0.94 and 0.87 to 0.97, respectively. Interventions to reduce drug use were evaluated in 52 trials (n = 15 659) of psychosocial interventions, 7 trials (n = 1109) of opioid agonist therapy, and 13 trials (n = 1718) of naltrexone. Psychosocial interventions were associated with increased likelihood of drug use abstinence (15 trials, n = 3636; relative risk [RR], 1.60 [95% CI, 1.24 to 2.13]; absolute risk difference [ARD], 9% [95% CI, 5% to 15%]) and reduced number of drug use days (19 trials, n = 5085; mean difference, −0.49 day in the last 7 days [95% CI, −0.85 to −0.13]) vs no psychosocial intervention at 3- to 4-month follow-up. In treatment-seeking populations, opioid agonist therapy and naltrexone were associated with decreased risk of drug use relapse (4 trials, n = 567; RR, 0.75 [95% CI, 0.59 to 0.82]; ARD, −35% [95% CI, −67% to −3%] and 12 trials, n = 1599; RR, 0.73 [95% CI, 0.62 to 0.85]; ARD, −18% [95% CI, −26% to −10%], respectively) vs placebo or no medication. While evidence on harms was limited, it indicated no increased risk of serious adverse events.

CONCLUSIONS AND RELEVANCE Several screening instruments with acceptable sensitivity and specificity are available to screen for drug use, although there is no direct evidence on the benefits or harms of screening. Pharmacotherapy and psychosocial interventions are effective at improving drug use outcomes, but evidence of effectiveness remains primarily derived from trials conducted in treatment-seeking populations.

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Illicit drug use is among the most common causes of preventable morbidity and mortality in the US and a leading cause of years lived in disability.[1,2] In 2018, an estimated 11.7% of US residents 12 years or older were current illicit drug users (hereafter "drug use" and generally defined as use of illegal drugs and the nonmedical use of prescription medications).[3] This estimate largely represented use of marijuana (10.1%; estimated 27.7 million current users) and nonmedical prescription psychotherapeutic drugs (2.0%; estimated 5.4 million current users), particularly pain relievers (1.0%; estimated 2.9 million current users).[3] It was estimated that nearly 84% of those who needed treatment for a drug use disorder did not receive specialty treatment during the past year.[3] As such, screening for drug use is important, as it may allow clinicians to counsel patients and, when indicated, refer them to treatment.

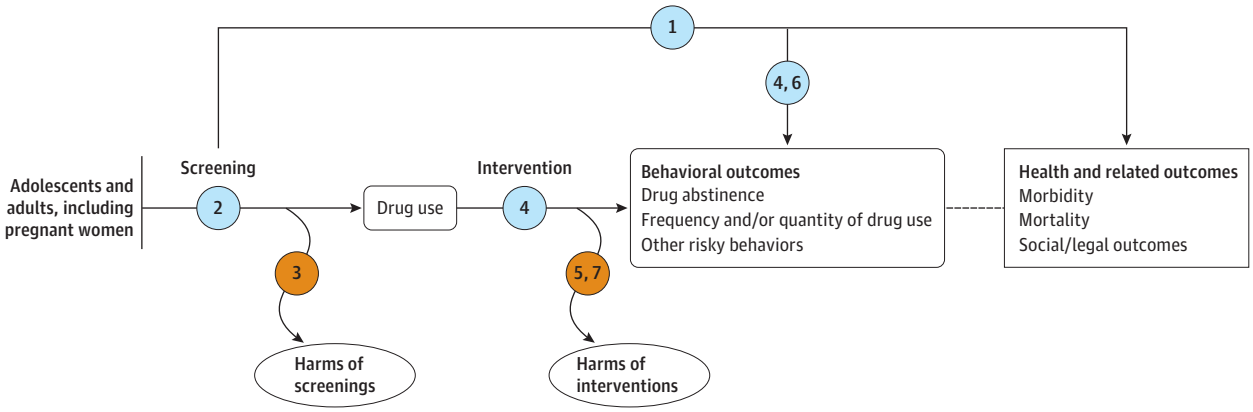
In 2008, the US Preventive Services Task Force (USPSTF) concluded that there was insufficient evidence to recommend for or against screening adolescents and adults, including pregnant women, for illicit drug use (I statement).[4] The objective of this review was to inform an updated recommendation by the USPSTF.

Methods

Scope of Review

This is an update of a systematic review[5] and supplemental report[6] that served as the basis for the 2008 recommendation. An analytic framework was developed with 7 key questions (KQs) (**Figure 1**) on the benefits (KQ1) and harms (KQ3) of screening for drug use,

Figure 1. Analytic Framework: Screening for Illicit Drug Use, Including Nonmedical Use of Prescription Drugs



Key questions

1. a. Does primary care screening[a] for drug use[b] in adolescents and adults, including pregnant women, reduce drug use or improve other risky behaviors?
   b. Does primary care screening[a] for drug use[b] in adolescents and adults, including pregnant women, reduce morbidity or improve other health, social, or legal outcomes?
2. What is the accuracy of drug use screening instruments?
3. What are the harms of primary care screening[a] for drug use[b] in adolescents and adults, including pregnant women?
4. a. Do interventions to reduce drug use[b] reduce drug use or improve other risky behaviors?
   b. Do interventions to reduce drug use[b] reduce morbidity or mortality or improve other health, social, or legal outcomes?
5. What are the harms of interventions to reduce drug use[b]?
6. Does naloxone reduce morbidity or mortality, or improve other health outcomes in persons with opioid use disorder or misuse?
7. What are the harms of naloxone in persons with opioid use disorder or misuse?

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.

[a] Screening refers to screening methods that pose questions about drug use or drug-related risks, not laboratory testing of biologic samples for the presence of drugs.

[b] Includes illicit drug use and nonmedical pharmaceutical drug use.

screening test accuracy (KQ2), benefits (KQ4) and harms (KQ5) of interventions to reduce drug use, and the benefits (KQ6) and harms (KQ7) of preemptively prescribed naloxone in persons with opioid use disorder or misuse. This article summarizes data from 2 reports: one focused on screening for drug use and interventions in screen-detected populations[7] and the other addressing interventions among patients with known drug use or seeking treatment ("treatment-seeking").[8] Both full reports are available at https://uspreventiveservicestaskforce.org/uspstf/recommendation/drug-use-illicit-screening. All results presented in the full reports are also presented in this article; more detailed methods and all forest plots are included in the full reports.

Data Sources and Searches

MEDLINE, PubMed, PsycINFO, the Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews, and EMBASE were searched for relevant English-language literature (eMethods in the Supplement). Searches encompassed literature published between January 1, 1998, and June 7, 2018, for KQs 1-3 and from database inception to September 18, 2018, for KQs 4-7. The reference lists of relevant studies and expert suggestions supplemented the electronic searches. ClinicalTrials.gov (https://ClinicalTrials.gov/) and the WHO International Clinical Trials Registry Platform (https://www.who.int/ictrp) were searched for ongoing trials. Active surveillance was conducted through September 21, 2019, through article alerts, targeted journal searches, and public comment to identify major studies that might affect the conclusions or understanding of the evidence. Four new test accuracy studies were identified to detect drug use disorder among adults and drug use among pregnant women.[9-12] Additionally, 1 new trial[13] of a psychosocial intervention among adolescents identified through screening was identified. These studies would not substantively change the findings or conclusions of this review and are not included in the results of this study.

Study Selection

At least 2 reviewers independently reviewed all identified titles and abstracts and relevant full-text articles to ensure consistency with predetermined inclusion and exclusion criteria (eTable 1 in the Supplement). For all KQs, studies among adolescents (defined as persons aged 12 to 17 years) and adults were included, including pregnant adolescents and adults. Studies screening for any illicit psychoactive or nonmedical pharmaceutical drug use were included, as were interventions targeting use of opioids, stimulants (eg, cocaine, methamphetamines), cannabis, or mixed drug use. For KQ1 and KQ3, randomized clinical trials or nonrandomized controlled intervention studies that compared individuals who received screening with those who received no screening or usual care were included. For KQ2, studies reporting sensitivity and specificity (or data to calculate) of a screening instrument to detect unhealthy drug use (including any drug use and drug use disorders) compared with a structured or semistructured clinical interview or biological samples were included.

Case-control studies were excluded. Eligible screening instruments included brief standardized instruments or a set of questions that screened directly for drug use or drug use risk or those that indirectly screened for drug use with questions regarding alcohol use or other risky behaviors. Studies evaluating the accuracy of biological drug screening tests (eg, urine samples) were not included. Given the variability in target conditions presented across the studies, conditions were collapsed into 3 groups: any use, unhealthy use (variably defined in the studies), or use disorder (*Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) [*DSM-IV*] abuse or dependence, *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) [*DSM-5*] use disorder). The target condition of "unhealthy use" included conditions such as the full spectrum of unhealthy use (eg, problem use or a use disorder), meeting any *DSM* criterion for a use disorder, heavy use (eg, using a substance twice or more per day) or negative consequences or problems related to drug use.

For evaluation of drug use interventions (KQs 4-7), eligible trials could enroll screen-detected patients or those seeking substance-use treatment or with signs and symptoms of drug use, regardless of drug use severity. Eligible psychosocial interventions used 1 or more of the following techniques: cognitive behavioral therapy (CBT), motivational interventions, contingency management, 12-step facilitation therapy, family interventions, and adaptations of these methods.[14] Interventions could be delivered in-person or using other modalities (eg, telephone, internet, or computer) and were categorized as brief (1 or 2 sessions, each less than 1 hour in duration) or intensive (not brief). Comparators included no intervention, usual care, or a brief intervention.

For pharmacotherapy, inclusion was restricted to US Food and Drug Administration (FDA)–approved medications for drug use disorders. As of September 2018, this included medications for treatment of opioid use disorder: buprenorphine (sublingual, buccal, or extended-release injection or implant), buprenorphine/naloxone (sublingual or buccal), methadone, and naltrexone (oral or extended-release injection). While implantable naltrexone is not FDA-approved, it was also included because evidence on injectable naltrexone was limited. Comparators included no intervention, usual care, or placebo. Trials of methadone or buprenorphine detoxification (withdrawal management) were excluded. For KQ6 and KQ7, studies of preemptive naloxone prescribed in clinical settings as a rescue medication for acute overdose events were included.

Outcomes were drug use (ie, abstinence, frequency and/or quantity of drug use, severity of drug use disorder), clinical outcomes (ie, all-cause mortality, drug-related mortality and morbidity, obstetrical/perinatal/neonatal outcomes, quality of life), other drug-related consequences (ie, legal problems, social and family relations, employment, school/educational outcomes), and harms, including serious adverse events such as death and adverse events resulting in hospitalizations or study withdrawal reported at least 3 months after baseline measurement. Retention in substance use treatment was also an outcome for pharmacological therapy.

Data Extraction and Quality Assessment

Two reviewers independently assessed the methodological quality of eligible studies. Disagreements were resolved by consensus and, if needed, consultation with a third reviewer. Each study was assigned a quality rating of "good," "fair," or "poor" according to the USPSTF study design–specific criteria (eTable 2 in the Supplement).[15] In accordance with the USPSTF Procedure Manual, studies rated as poor quality because of serious methodological shortcomings were excluded.[15] One reviewer abstracted descriptive and outcome data from fair- and good-quality studies into standardized evidence tables and a second checked for accuracy and completeness.

Data Synthesis and Analysis

Summary tables of study, population, screening, and intervention characteristics, as well as outcomes for each KQ, were created according to the type of screening instrument or intervention. The data for screening accuracy did not allow for quantitative pooling given the heterogeneity in instruments, reference conditions, and cutoffs included, so synthesis was qualitative. Screening instruments were categorized as (1) frequency-based (addressing any use, frequency of use, or both), (2) risk assessment (addressing the consequences of drug use, typically indicators of a use disorder and often with drug use frequency), or (3) indirect (did not screen for drug use directly but assessed correlates of drug use, such as alcohol or tobacco use, partner substance use, and other social factors).

For intervention effectiveness, data were analyzed separately for psychosocial interventions, opioid agonists (methadone and buprenorphine), and naltrexone. Meta-analyses were conducted using a random-effects profile likelihood model on abstinence (or relapse), drug use days, retention in treatment, drug use severity, and harms. Results were analyzed separately for outcomes assessed at 3 or 4 months and at 6 to 12 months. Drug use days were standardized to the number of days of drug use during the past 7 days. Drug use severity was analyzed as a standardized mean difference, given heterogeneity in measurement scales. Stratified analyses were conducted according to whether the population was screen-detected or treatment-seeking, the main type of drug measured (cannabis, stimulant, opioid, or mixed drugs), age group (adolescent [12-17 years], young adult [18-25 years], or adult [>25 years]), study quality, and pregnancy or postpartum status. For pharmacotherapies, stratified analyses were also conducted by route of administration, naltrexone dose, timing of outcome assessment, and intensity of the interventions. For psychosocial interventions, analyses were also conducted according to intervention intensity (brief vs intensive) and mode of delivery (face-to-face or other).

Heterogeneity between studies was evaluated by the χ^2 test and I^2 statistics. Analyses were conducted using Stata version 13.1 (StataCorp). All significance testing was 2-sided, and $P \leq .05$ was considered statistically significant.

The aggregate strength of evidence was assessed for each KQ using the approach described in the Agency for Healthcare Research and Quality methods guidance, based on the number, quality, and size of studies and the consistency and precision of results between studies.[16]

Results

A total of 28 012 titles and abstracts and 1398 articles were reviewed for eligibility; of these, 99 studies (N = 84 206) reported in 124 publications were included (**Figure 2**). Twenty-eight studies (n = 65 720) addressed the accuracy of drug use screening instruments, and 71 trials evaluated psychosocial interventions (52 trials, n = 15 659), opioid agonist therapy (7 trials, n = 1109), or naltrexone (13 trials, n = 1718) to reduce drug use.

Benefits of Screening

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

No eligible studies were identified.

Screening Accuracy

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

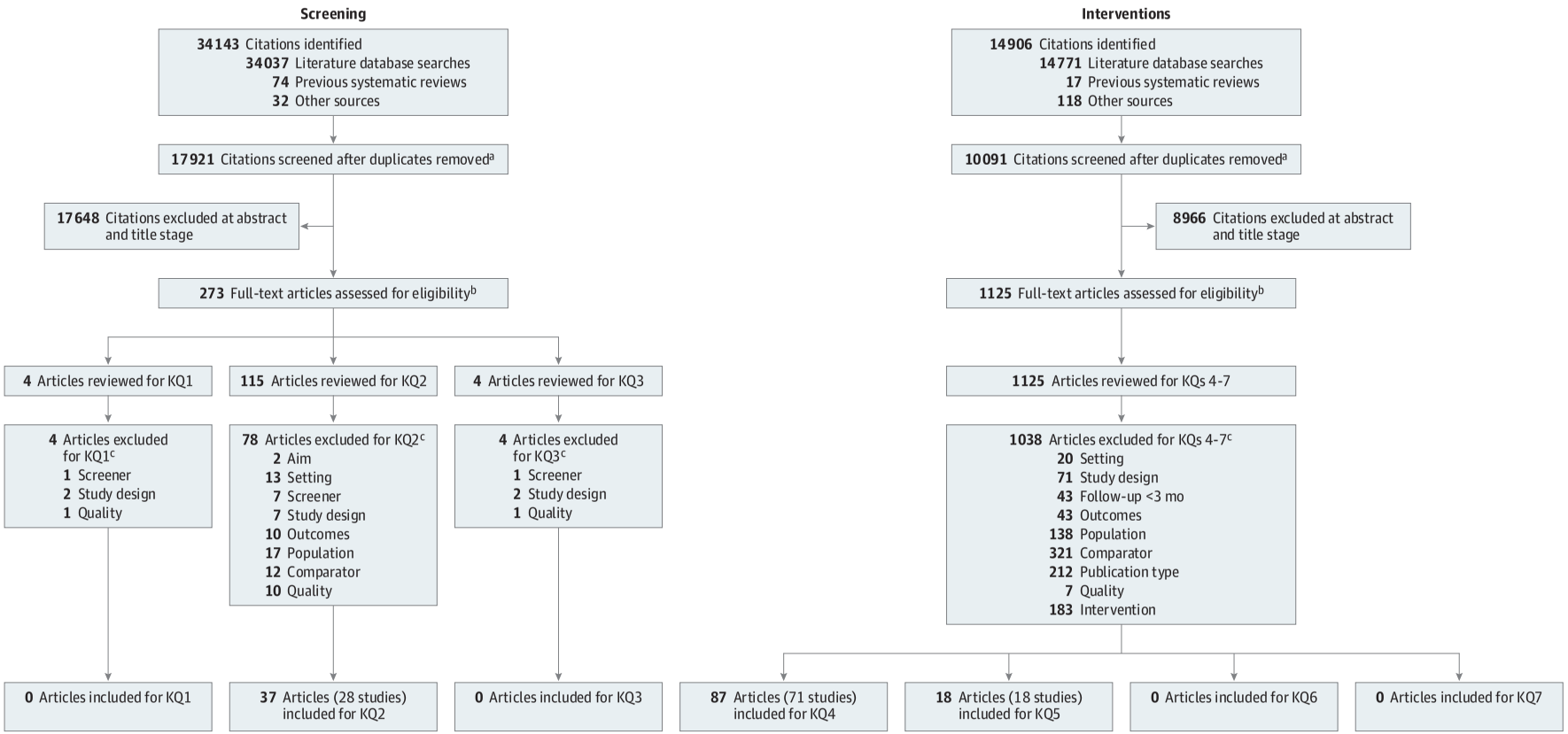
Twenty-eight studies[17-44] (reported in 37 publications[17-52]) with 65 720 participants addressed the accuracy of drug use screening instruments. Considerable heterogeneity among studies was present in the populations (eTable 3 in the Supplement), screening instruments (eTable 4 in the Supplement), substances addressed, reference standards, and target conditions. Specific screening instruments were generally not examined in more than 1 or 2 studies. Eleven studies recruited adolescents, 12 studies recruited adults, and 5 studies recruited pregnant or postpartum people (eTable 3 in the Supplement). Twenty-one of 28 studies were conducted in the US, and 17 of 28 recruited patients from primary care. The number screened ranged from 100 to 42 923, with the majority (20/28 studies) screening fewer than 1000 participants.

Most studies used a structured diagnostic interview as the substance use reference standard, sometimes in combination with other screening instruments (eg, ASSIST [Alcohol, Smoking and Substance Involvement Screening Test]), a timeline follow-back method,[53] or biologic confirmation. Seventeen of 28 studies were fair quality, with methodological shortcomings including not reporting enough information regarding the order and timing of the reference standard and screening instrument; not clearly reporting whether the researchers had knowledge of the screening instrument results during the administration and interpretation of the reference standard; not presenting a range of screening instrument cutoff values and selecting only the optimal cutoff; and unclear reporting of whether participant recruitment was random or consecutive.

Thirty screening instruments were evaluated. The screening instruments varied in the number of questions (range, 1-31), administration time, administration method (eg, in-person, telephone, electronic), and the substances addressed. Most of the screening instruments addressed the use of any drug (with or without addressing alcohol and tobacco use). Among these, the majority included an assessment of nonmedical use of prescription drugs, either through a specific question or by including it in the definition of drug use in the prescreening instructions.

Among adults, frequency- and risk-based screening tools showed sensitivity for detecting unhealthy use of any drug ranging from 0.71 to 0.94 (95% CI range, 0.62 to 0.97) and specificity ranging from 0.87 to 0.97 (95% CI range, 0.83 to 0.98) (3 studies, n = 1512) (**Table 1**; eTable 5 in the Supplement). For identifying drug use disorders among adults, sensitivity for frequency-based and risk assessment tools ranged from 0.85 to 1.00 (95% CI range, 0.67 to 1.00) and specificity ranged from 0.67 to 0.93 (95% CI, 0.58 to 0.95) (4 studies, n = 1651). In studies that examined unhealthy use of specific drugs, the ranges of sensitivity were lower and less precise for detecting unhealthy use or use disorders for prescription opioids and prescription sedatives (sensitivity ranged from 0.38 to 0.89 [95% CI range, 0.29 to 0.94]), compared with other classes of drugs. Confidence intervals, however, generally overlapped. Specificity for detecting unhealthy use or use disorders due to prescription misuse was comparable and ranged from 0.79 to 0.99 [95% CI range, 0.71 to 0.99]).

Figure 2. Literature Search Flow Diagram: Screening for Illicit Drug Use, Including Nonmedical Use of Prescription Drugs



[a] Number of citations screened after duplicates removed also reflects studies reviewed for key questions (KQs) 4 and 5 (efficacy and harms of psychosocial interventions in screen-detected populations) in the Screening for Drug Use Report.

[b] Counts of full-text articles reviewed are not mutually exclusive; some articles were reviewed for both reports.

[c] Reasons for exclusion: Aim: Not applicable/relevant to key question. Setting: Not conducted in a very high Human Development Index country or screening and/or intervention was not conducted in, recruited from, or feasible for primary care. Screener: Assessment for drug use does not include a brief standardized instrument or set of questions conducted in person or via telephone, mail, or electronically. Study design: Not a randomized clinical trial or case-crossover trial (KQs 1, 3, 4, 5); not a large cohort or case-control study (KQ2). Follow-up <3 mo: Less than 3 months' follow-up after baseline assessment. Outcomes: No measure of drug use reported (KQs 1, 3, 4, 5); no measure related to sensitivity and specificity reported for screening accuracy (KQ2). Population: Children younger than 12 years or populations otherwise out of scope (eg, psychotic disorder, receiving chronic opioid therapy, court-mandated drug treatment, or incarcerated). Comparator: Not an included comparator (eg, screening results given to control clinicians [KQs 1 and 3], no reference standard [KQ2], active intervention [KQs 4 and 5]). Publication type: Conference abstract, non–English-language publication, main results published prior to review start date (1992). Quality: Study was poor quality.

Table 1. Summary of Test Accuracy Ranges for Key Question 2

		Adolescents (11 studies)				Adults (12 studies)				Pregnant and postpartum persons (5 studies)			
		No. analyzed		Range		No. analyzed		Range		No. analyzed		Range	
Substance	Condition	Studies[a]	Participants	Sensitivity	Specificity	Studies[a]	Participants	Sensitivity	Specificity	Studies[a]	Participants	Sensitivity	Specificity
Any drug	Use	0				2	745	0.73-0.93	0.86-0.96	3	1456	0.37-0.76	0.68-0.83
	Unhealthy use	0				3	1512	0.71-0.94	0.87-0.97	0			
	Use disorder	0				4[b]	1651	0.85-1.0	0.67-0.93	1	745	0.89	0.74
Cannabis	Use	2	1703	0.68-0.79	0.92-1.0	1	399	0.95	0.82	1	274	0.53	0.82
	Unhealthy use	2	2092	0.84-0.98	0.82-0.91	1	1997	0.79-0.82	0.93	0			
	Use disorder	6	5735	0.71-0.98	0.79-0.95	3	2946	0.71-0.83	0.75-0.95	0			
Prescription drug[c]	Use	0				0				0			
	Unhealthy use	0				3	2693	0.44-0.71	0.79-0.99	0			
	Use disorder	0				3	2693	0.38-0.89	0.81-1.0	0			
Heroin	Use	0				0				0			
	Unhealthy use	0				1	1995	0.77-0.78	1.0	0			
	Use disorder	0				1	1995	0.66	1.0	0			
Cocaine and methamphetamines[d]	Use	0				1	399	0.86	0.84	0			
	Unhealthy use	0				1	1996	0.68-0.73	0.99	0			
	Use disorder	0				2	2395	0.57-0.90	0.87-0.99	0			

[a] A single study could use different methodologies for instrument administration or different screening instruments. Although all variations are captured in the ranges (eg, interviewer vs self-administered), the study is counted only once.

[b] Excluding Lane et al[38] (sensitivity, 0.29; specificity, 0.95). This study used a different outcome (abuse only), the Parental Screening Questionnaire as a screening tool, and is an outlier from the rest of the group.

[c] Includes any prescription drug, prescription opioids, and prescription sedatives.

[d] Includes cocaine alone and cocaine combined with methamphetamines.

Table 2. Summary of Pooled Findings: Psychosocial Interventions (Key Question 4)

Outcome, Timing	Study characteristics	Group analyzed	No. of trials	Effect size (95% CI)	I^2, %	*P* value
Abstinence						
3-4 mo	All trials	All participants	15	RR, 1.60 (1.24 to 2.13)	61	
	Type of drug use	Cannabis	7	RR, 2.08 (1.51 to 3.07)	28	.10
		Mixed drugs	7	RR, 1.24 (0.92 to 1.80)	60	
		Prescription drugs	1	RR, 2.08 (0.81 to 5.38)		
	Population	Screen-detected population	8	RR, 1.28 (0.97 to 1.84)	57	.05
		Treatment-seeking population	7	RR, 2.08 (1.51 to 3.07)	28	
	Type of intervention	Brief interventions	10	RR, 1.46 (1.11 to 2.09)	56	.34
		Other (more intensive) interventions	6	RR, 2.01 (1.17 to 3.58)	70	
	Age group	Adolescent/young adult	2	RR, 1.54 (0.78 to 5.22)	61	.77
		Adult	13	RR, 1.58 (1.20 to 2.16)	64	
	Pregnancy status[a]	Pregnant or postpartum	5	RR, 1.24 (0.99 to 1.89)	41	
		Not pregnant or postpartum	8	RR, 1.77 (1.17 to 2.80)	71	
	Mode of delivery	Face-to-face	7	RR, 1.77 (1.13 to 3.02)	76	.61
		Other (web, computer, telephone)	8	RR, 1.43 (1.10 to 2.04)	35	
	Study quality	Good	1	RR, 4.34 (1.75 to 10.72)		.10
		Fair	14	RR, 1.50 (1.18 to 1.98)	56	
6-12 mo	All trials	All participants	14	RR, 1.25 (1.11 to 1.52)	38	
	Type of drug use	Cannabis	4	RR, 1.58 (1.17 to 2.73)	36	.43
		Stimulants	4	RR, 1.45 (0.86 to 2.56)	65	
		Mixed drugs	5	RR, 1.12 (0.92 to 1.36)	0	
		Prescription drugs	1	RR, 1.25 (0.65 to 2.40)		
	Population	Screen-detected population	7	RR, 1.17 (0.99 to 1.41)	2	.26
		Treatment-seeking population	7	RR, 1.51 (1.14 to 2.37)	57	
	Type of intervention	Brief interventions	11	RR, 1.22 (1.08 to 1.42)	14	.22
		Other (more intensive) interventions	3	RR, 1.99 (0.55 to 7.80)	71	
	Age group	Adolescent/young adult	5	RR, 1.25 (1.04 to 1.64)	14	.52
		Adult	9	RR, 1.30 (1.05 to 1.80)	51	
	Postpartum status[a]	Postpartum	2	RR, 1.07 (0.76 to 1.71)	0	
		Not postpartum	7	RR, 1.41 (1.04 to 2.16)	57	
	Mode of delivery	Face-to-face	11	RR, 1.31 (1.13 to 1.69)	43	.23
		Other (web, computer, telephone)	3	RR, 1.04 (0.73 to 1.45)	0	
	Study quality	Good	2	RR, 1.11 (0.58 to 1.51)	58	.21
		Fair	12	RR, 1.35 (1.15 to 1.73)	35	
Drug use days[b]						
3-4 mo	All trials	All participants	19	MD, −0.49 (−0.85 to −0.13)	89	
	Type of drug use	Cannabis	14	MD, −0.68 (−1.14 to −0.23)	89	.11
		Any drug use	5	MD, −0.05 (−0.39 to 0.31)	58	
	Population	Screen-detected population	9	MD, −0.10 (−0.31 to 0.12)	46	.02
		Treatment-seeking population	10	MD, −0.91 (−1.52 to −0.31)	86	
	Type of intervention	Brief interventions	9	MD, −0.13 (−0.36 to 0.12)	42	.03
		Other (more intensive) interventions	10	MD, −0.88 (−1.50 to −0.28)	91	
	Age group	Adolescent	1	MD, −1.47 (−2.99 to 0.06)		.38
		Young adult or adolescent/young adult	8	MD, −0.15 (−0.37 to 0.03)	0	
		Adult	10	MD, −0.63 (−1.22 to −0.03)	93	
	Mode of delivery	Face-to-face	14	MD, −0.54 (−1.01 to −0.08)	90	.66
		Other (web, computer, telephone)	5	MD, −0.27 (−0.82 to 0.13)	49	
	Study quality	Good	5	MD, −0.42 (−1.30 to 0.48)	93	.82
		Fair	14	MD, −0.51 (−0.93 to −0.11)	86	

(continued)

Table 2. Summary of Pooled Findings: Psychosocial Interventions (Key Question 4) (continued)

Outcome, Timing	Study characteristics	Group analyzed	No. of trials	Effect size (95% CI)	I^2, %	*P* value
6-12 mo	All trials	All participants	15	MD, −0.08 (−0.30 to 0.11)	45	
	Type of drug use	Cannabis	7	MD, −0.21 (−0.65 to 0.16)	41	.42
		Stimulants	1	MD, −0.47 (−1.17 to 0.24)		
		Any drug use	7	MD, 0.04 (−0.22 to 0.28)	43	
	Population	Screen-detected population	10	MD, 0.00 (−0.24 to 0.22)	42	.22
		Treatment-seeking population	5	MD, −0.29 (−0.69 to 0.09)	12	
	Type of intervention	Brief interventions	11	MD, −0.06 (−0.24 to 0.11)	0	.90
		Other (more intensive) interventions	4	MD, −0.16 (−0.88 to 0.46)	79	
	Age group	Young adult or adolescent/ young adult	7	MD, −0.09 (−0.34 to 0.12)	0	.80
		Adult	8	MD, −0.07 (−0.40 to 0.22)	66	
	Mode of delivery	Face-to-face	13	MD, −0.10 (−0.36 to 0.12)	53	.80
		Other (web, computer, telephone)	2	MD, −0.05 (−0.42 to 0.38)	0	
	Study quality	Good	6	MD, −0.12 (−0.46 to 0.16)	36	.70
		Fair	9	MD, −0.04 (−0.38 to 0.23)	45	
Drug use severity						
6-12 mo	All trials	All participants	13	SMD, −0.10 (−0.24 to 0.02)	65	
	Type of drug use	Amphetamine use	1	SMD, 0.10 (−0.35 to 0.54)		.57
		Cannabis use	8	SMD, −0.16 (−0.37 to 0.03)	72	
		Mixed substance use	4	SMD, −0.001 (−0.18 to 0.12)	42	
	Population	Screen-detected population	9	SMD, −0.03 (−0.15 to 0.06)	40	.27
		Treatment-seeking population	4	SMD, −0.23 (−0.62 to 0.17)	82	
	Type of intervention	Brief interventions	10	SMD, −0.02 (−0.13 to 0.06)	35	.03
		Other (more intensive) interventions	3	SMD, −0.36 (−0.80 to 0.14)	71	
	Age group	Adolescent	2	SMD, −0.10 (−0.37 to 0.18)	44	.56
		Young adult	5	SMD, 0.02 (−0.16 to 0.15)	26	
		Adult	6	SMD, −0.18 (−0.44 to 0.04)	80	
	Mode of delivery	Face-to-face	9	SMD, −0.11 (−0.28 to 0.03)	70	.63
		Other (web, computer, telephone)	5	SMD, −0.03 (−0.28 to 0.16)	44	
	Study quality	Good	3	SMD, −0.02 (−0.41 to 0.22)	72	.69
		Fair	10	SMD, −0.12 (−0.27 to 0.03)	62	

Abbreviations: MD, mean difference; RR, risk ratio; SMD, standardized mean difference.

[a] Test of difference not conducted.

[b] Standardized to drug use in the past 7 days.

Sensitivity and specificity for detecting any prenatal drug use reported by pregnant or postpartum persons were generally lower than the estimates for nonpregnant persons and ranged from 0.37 to 0.76 (95% CI range, 0.24 to 0.86) and 0.68 to 0.83 (95% CI range, 0.55 to 0.91), respectively (3 studies, n = 1456). All studies used hair and urine analyses to validate drug use (Table 1; eTable 6 in the Supplement). The 4P's Plus, an indirect screening instrument, had a sensitivity of 0.87 (95% CI, 0.71 to 0.95) and specificity of 0.76 (95% CI, 0.70 to 0.82) for detecting any prenatal alcohol or drug use when compared with a diagnostic interview (n = 228) (eTable 6 in the Supplement).

For adolescents, most studies focused on cannabis use. Sensitivity of frequency- and risk-based instruments for any cannabis use or unhealthy cannabis use ranged from 0.68 to 0.98 (95% CI range, 0.64 to 0.99) and specificity ranged from 0.82 to 1.00 (95% CI range, 0.80 to 1.00) (Table 1; eTable 7 in the Supplement) (3 studies, n = 2228). Sensitivity and specificity for identifying a cannabis use disorder for frequency- and risk-based instruments ranged from 0.71 to 0.98 (95% CI range, 0.41 to 0.99) and 0.79 to 0.95 (95% CI range, 0.77 to 0.98), respectively (6 studies, n = 5735).

Harms of Screening

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

No eligible studies were identified.

Benefits of Interventions

Key Question 4. Do interventions to reduce drug use reduce drug use or improve other risky behaviors? Do interventions to reduce drug use reduce morbidity or mortality or improve other health, social, or legal outcomes?

Psychosocial Interventions

Fifty-two trials (reported in 65 publications) evaluated a psychosocial intervention for unhealthy drug use or drug use disorders (n = 15 659) (eTable 8 in the Supplement).[54-118] Twenty-seven trials

enrolled patients identified through screening and 25 trials enrolled patients seeking substance use treatment or with known substance use ("treatment-seeking"). The severity of baseline substance use varied considerably, with only 5 trials (all among treatment-seeking persons)[55,69-72] requiring patients to meet *DSM* criteria for drug use disorder.

The primary substance used was cannabis in 29 trials, stimulants in 6 trials, opioids in 2 trials, and mixed or multiple drugs in 15 trials. Among the trials reporting mixed or multiple drug use, the proportion of patients reporting opioid use ranged from 5% to 26%. Five trials evaluated interventions in adolescents, 8 in young adults (18-25 years), and 7 trials in mixed populations of adolescents or young adults. Thirty-two trials evaluated adults or mixed populations of adults and adolescents, including 3 trials of postpartum adults and 2 trials of pregnant adults.

Thirty-seven trials evaluated a brief psychosocial intervention and 19 trials evaluated more intensive interventions (number of sessions ranged from 2 to 14, except 1 trial with 57 sessions); some of these trials were multigroup (eTable 9 in the Supplement). The most commonly used techniques in the psychosocial intervention trials were motivational interventions and CBT. The mode of delivery was in-person in 37 trials; by computer, internet, or telephone in 12 trials; and by multiple modes of delivery in 3 trials. The control intervention consisted of a minimal intervention in 30 trials, waitlist in 11 trials, and usual care in 11 trials. Minimal intervention controls typically consisted of brief education.

Eight trials were rated good quality and the remainder were rated fair quality. Methodological limitations in the fair-quality trials included high attrition, failure to blind or unclear blinding of outcome assessors, and unclear randomization methods. In these trials, blinding of patients and clinicians was not feasible, given the nature of the interventions. Attrition at 3 to 4 months ranged from 2% to 67% and at 6 to 12 months from 2% to 46%.

Results of the psychosocial trials are presented in **Table 2** and in eTable 10 in the Supplement. Psychosocial interventions were associated with increased likelihood of abstinence from drug use vs control conditions at 3 to 4 months (15 trials, n = 3636; risk ratio [RR], 1.60 [95% CI, 1.24 to 2.13]; I^2 = 61%; absolute risk difference [ARD], 9% [95% CI, 5% to 15%]) (eFigure 1 in the Supplement) and at 6 to 12 months (14 trials, n = 4031; RR, 1.25 [95% CI, 1.11 to 1.52]; I^2 = 38%; ARD, 6% [95% CI, 2% to 10%]) (Table 2; eFigure 2 and eTable 10 in the Supplement). At 3 to 4 months, psychosocial interventions were also associated with decreased number of days of drug use during the last 7 days vs controls (19 trials, n = 5085; mean difference [MD], −0.49 day [95% CI, −0.85 to −0.13]; I^2 = 89%) (eFigure 3 in the Supplement) and drug use severity (17 trials, n = 4437; standardized MD, −0.18 [95% CI −0.32 to −0.05]; I^2 = 73%) (eFigure 5 in the Supplement), but these associations were smaller and not statistically significant at 6 to 12 months for drug use days (15 trials, n = 5095; MD, −0.08 [95% CI, −0.30 to 0.11]; I^2 = 45%) (eFigure 4 in the Supplement) or severity (13 trials, n = 3798; standardized MD, −0.10 [95% CI, −0.24 to 0.02]; I^2 = 65%) (eFigure 6 in the Supplement).

At 3 to 4 months, the associations with drug use days were statistically significantly greater among trials of treatment-seeking vs screen-detected populations (10 trials, n = 1664; MD, −0.91 [95% CI, −1.52 to −0.31] vs 9 trials, n = 3421; MD, −0.10 [95% CI, −0.31 to 0.12]; P = .02) and for intensive vs brief interventions (10 trials, n = 2364; MD, −0.88 [95% CI, −1.50 to −0.28] vs 9 trials, n = 2721; MD, −0.13 [95% CI, −0.36 to 0.12]; P = .03) (Table 2). Otherwise, statistically significant differences were not present in stratified analyses, although effects were generally stronger across outcomes in trials of treatment-seeking vs screen-detected populations, cannabis use vs other types of drug use, intensive vs brief interventions, and (for abstinence) in-person vs other modes of delivery.

Data on effects of psychosocial interventions on other health, social, and legal outcomes were limited. These data, however, generally showed no differences between psychosocial interventions vs control conditions in the likelihood of injection drug use or sexual risk behaviors[56-59,98,102,105,119]; the risk of emergency department visits or hospital admissions[107,119]; measures related to mental health, quality of life, or function[55,56,58,80,81,84,89,107,119]; the likelihood of driving after cannabis use[66,67,85]; and risk of incarceration or involvement in criminal activity.[56-58,88,102]

Pharmacological Therapies

Opioid Agonist Therapy (Methadone and Buprenorphine) | Seven trials (reported in 9 publications) (n = 1109) reported effects of opioid agonist therapy (buprenorphine or methadone) vs placebo or no medication (waitlist or usual care) for opioid use disorder (eTable 11 in the Supplement).[120-128] Two trials evaluated oral methadone, with dosing of up to 90 mg/d in one trial and averaging 78 mg/d in the other trial (eTable 12 in the Supplement). The other 5 trials evaluated buprenorphine: sublingual administration in 3 trials (dose, 8-24 mg/d), implant in 1 trial (4 implants, with a total dose of 320 mg), and both sublingual and implant in 2 separate groups in the remaining trial.[124] The duration of treatment ranged from 3 to 12 months (6 months in 4 trials and 3, 4, or 12 months in 1 trial each). Oral methadone and sublingual buprenorphine were administered daily under direct observation, although some trials allowed take-home doses for weekends and holidays. In 5 of the 7 trials, all patients received some drug use counseling (individual, group, or both). The intensity of counseling ranged from "minimal" (not described) to "standard" counseling for 45 to 60 minutes on a weekly or twice-weekly basis. Two trials of bridging therapy with methadone or buprenorphine did not include a counseling intervention.

In all 7 trials of opioid agonist therapy, the main type of opioid used was heroin; 2 trials reported prescription opioids as the main opioid used by about one-third of patients. Four trials were conducted in the US, 2 trials in Europe, and 1 trial in Malaysia. In all trials, patients were treatment-seeking. Patients were enrolled from inpatient settings in 1 trial, from the community in 1 trial, and from outpatient addiction treatment settings in 5 trials. In all but 1 trial, treatment was administered in outpatient addiction treatment settings.

Study participants were predominantly men (proportion of women ranged from 25%-43%), and mean age ranged from 29 to 43 years. No study was conducted in adolescents, and no trial stratified outcomes by patient sex. In studies that reported the duration of drug use, the mean ranged from 5 to 20 years. Three studies reported the mean number of days of heroin use during the last 30 days, ranging from 19 to 30 days.

Two studies were rated good quality and the remainder were rated fair quality. Methodological shortcomings in the fair-quality trials included unclear randomization or allocation concealment methods and unclear or high attrition. Both methadone trials used

Table 3. Summary of Pooled Findings: Pharmacological Interventions (Key Question 4)

Outcome, Timing	Study characteristics	Group analyzed	No. of trials	Effect size, RR (95% CI)	I^2, %	*P* value
Opioid agonists						
Relapse						
All time points	All trials	All participants	4	0.75 (0.59 to 0.82)	75	
	Drug	Buprenorphine	3	0.59 (0.21 to 1.31)	84	.78
		Methadone	1	0.71 (0.61 to 0.84)		
	Type of counseling	Standard counseling	3	0.59 (0.21 to 1.31)	84	.78
		No counseling	1	0.71 (0.61 to 0.84)		
	Study quality	Good	2	0.75 (0.65 to 0.85)	0	.54
		Fair	2	0.46 (0.08 to 2.19)	93	
	Buprenorphine administration route	Sublingual	2	0.46 (0.08 to 2.19)	93	.70
		Implant	1	0.77 (0.68 to 0.88)		
Retention in treatment						
All time points	All trials	All participants	7	2.58 (1.78 to 4.59)	71	
	Drug	Buprenorphine	5	2.52 (1.89 to 4.74)	51	.54
		Methadone	2	2.22 (0.63 to 7.56)	92	
	Type of counseling	Standard counseling	5	2.09 (1.54 to 3.33)	56	.79
		Minimal or no counseling	3	2.78 (0.93 to 13.74)	86	
	Study quality	Good quality	2	3.15 (1.90 to 4.81)	42	.72
		Fair quality	5	2.34 (1.41 to 9.20)	73	
	Buprenorphine administration route	Sublingual	4	2.95 (1.97 to 12.06)	57	.46
		Implant	2	2.27 (1.58 to 3.31)	0	
Naltrexone						
Relapse						
All time points	All trials	All participants	12	0.72 (0.62 to 0.85)	78	
	Route of administration	Oral	11	0.76 (0.65 to 0.88)	70	.13
		Injection or implant	2	0.41 (0.06 to 2.40)	98	
	Timing of outcome assessment	Receiving treatment	10	0.71 (0.59 to 0.84)	82	.36
		After intervention	2	0.93 (0.54 to 1.50)	0	
	Study quality	Good quality	3	0.67 (0.48 to 0.94)	84	.52
		Fair quality	9	0.76 (0.61 to 0.91)	78	
	Naltrexone dose (oral administration)	≤50 mg/d	7	0.69 (0.58 to 0.81)	47	.70
		>50 mg/d	4	0.97 (0.81 to 1.11)	0	
Retention in treatment						
All time points	All trials	All participants	9	1.71 (1.13 to 2.49)	67	
	Route of administration	Oral	8	1.59 (1.00 to 2.38)	61	.37
		Injection or implant	2	2.48 (0.58 to 11.75)	94	
	Timing of outcome assessment	Receiving treatment	8	1.89 (1.36 to 2.65)	59	.05
		After intervention	1	0.39 (0.14 to 1.14)		
	Study quality	Good	3	2.10 (1.21 to 4.13)	78	.33
		Fair	6	1.43 (0.78 to 2.47)	67	
	Naltrexone dose (oral administration)	≤50 mg/d	6	1.84 (1.22 to 2.71)	49	.18
		>50 mg/d	2	0.82 (0.14 to 4.48)	73	

Abbreviation: RR, risk ratio.

an unblinded design—one trial compared methadone vs usual care and the other trial compared methadone vs wait-list control.

Results of trials of methadone and buprenorphine are summarized in **Table 3** and eTable 13 in the Supplement. After 4 to 12 months of treatment, opioid agonist therapy was associated with decreased risk of relapse vs controls (4 trials, n = 567; RR, 0.75 [95% CI, 0.59 to 0.82]; I^2 = 75%; ARD, −35% [95% CI, −67% to −13%]) (eFigure 7 in the Supplement) and an increased likelihood of treatment retention (7 trials, n = 1099; RR, 2.58 [95% CI, 1.78 to 4.59]; I^2 = 71%; ARD, 39% [95% CI, 23% to 54%]) (eFigure 8 in the Supplement). There was no significant difference between type of drug (methadone or buprenorphine), buprenorphine administration method (sublingual or by implant), counseling intensity, or trial quality and effects on relapse or retention.

Evidence on health outcomes associated with opioid agonist therapy vs placebo or no opioid agonist was very limited. Only 3 trials reported on a measure of global function or well-being with no clear effect. Mortality was reported in 2 trials of buprenorphine with a total of 4 deaths, all in patients randomized to placebo. No trial reported on the social or legal outcomes of opioid agonist therapy.

Naltrexone | Thirteen trials (in 14 publications) (n = 1718) evaluated naltrexone vs placebo or no naltrexone for opioid use disorder (generally based on meeting *DSM-II-R*, *DSM-III*, or *DSM-IV* criteria) (eTable 14 in the Supplement).[125,129-141] All patients in the trials received drug use counseling, usually described as individual or group counseling ranging from 3 times per week to biweekly. Details on counseling methods, however, were limited. Eleven trials assessed oral naltrexone, 1 trial injectable naltrexone (300 mg every 4 weeks), and 1 trial had 2 active groups of a naltrexone implant (1000 mg twice a month) and oral naltrexone (eTable 15 in the Supplement). The oral naltrexone dose was 50 mg daily in 7 trials, up to 150 mg daily in 2 trials, and 100 or 150 mg 2 or 3 times weekly in 3 trials. Treatment duration was 6 months in 10 trials and 2, 3, or 9 months in the other 3 trials. Outcomes were assessed at the end of treatment in all trials except for 2 trials that evaluated outcomes 6 or 10 months after treatment completion. Five trials were conducted in Russia, 2 in Israel, 2 in the US, 2 in Europe, 1 in Malaysia, and 1 in China. Patients were recruited from inpatient settings, drug treatment settings, or from the criminal justice system (eg, parolees). No study recruited patients from primary care settings. In all cases, naltrexone treatment was administered in outpatient settings.

Where reported, heroin was the primary opioid of use in all or most patients in naltrexone treatment trials. Studies enrolled predominantly men (proportion of women ranged from 0% to 31%), and no trial reported outcomes stratified by patient sex. The mean age ranged from 21 to 29 years, with no trials of adolescents. All trials required patients to be withdrawn from opioids prior to initiation of naltrexone. Four trials described inpatient or residential withdrawal from opioids; details were otherwise not well reported.

Three studies were rated good quality and the remainder were rated fair quality. Methodological shortcomings in the fair-quality trials included unclear randomization or allocation concealment methods and unclear or high attrition. All trials were blinded.

Results of the naltrexone trials are presented in Table 3 and in eTable 16 in the Supplement. In pooled analyses, naltrexone was associated with decreased risk of relapse vs placebo or no naltrexone (12 trials, n = 1599; RR, 0.73 [95% CI, 0.62 to 0.85]; ARD, -18% [95% CI, -26% to -10%]) (eFigure 9 in the Supplement), as well as an increased likelihood of treatment retention (9 trials, n = 1404; RR, 1.71 [95% CI, 1.13 to 2.49]; I^2 = 67%; ARD, 15% [95% CI, 5% to 22%]) (eFigure 10 in the Supplement). There was no significant difference in the likelihood of relapse or treatment retention based on route of naloxone administration. Results were similar when analyses were restricted to trials of oral naltrexone at a dose of 50 mg/d and to good-quality trials.

Evidence on the effects of naltrexone vs placebo or no naltrexone on health outcomes (eg, global function, quality of life, depression, and anxiety) was limited, with no consistent evidence of a benefit of naltrexone compared with placebo or no naltrexone. Mortality was rare, with a total of 3 deaths (2 in naltrexone groups and 1 in placebo groups) in 5 trials.

Harms of Interventions

Key Question 5. What are the harms of interventions to reduce drug use (including illicit drug use and nonmedical pharmaceutical drug use)?

Psychosocial Interventions

Four trials of psychosocial interventions (n = 1196) reported no adverse events in either intervention or control groups (eTable 10 in the Supplement).[94,98,99,142] Harms were otherwise not reported, with no serious adverse events noted.

Pharmacological Therapies

Opioid Agonist Therapy (Buprenorphine or Methadone) | Four trials of buprenorphine vs placebo reported harms[122-125]; no trials of methadone reported harms (eTable 13 in the Supplement). There was no significant difference between buprenorphine vs placebo in risk of serious adverse events, which were uncommon (2 trials, n = 450; RR, 0.32 [95% CI, 0.09 to 1.12]; I^2 = 0%)[123,124]; 1 trial reported no hospitalizations due to serious medication-related adverse events.[125] One trial (n = 83) found no significant difference between buprenorphine vs placebo in risk of withdrawal due to adverse events (RR, 0.89 [95% CI, 0.06 to 13.7]),[125] and 1 trial (n = 287) found no difference in risk of any adverse event (RR, 1.14 [95% CI, 0.90 to 1.43]).[124] Buprenorphine was also not associated with increased risk of diaphoresis (3 trials, n = 476; RR, 1.15 [95% CI, 0.55 to 2.73]; I^2 = 44%)[122,124,125] or nausea (3 trials, n = 393; RR, 1.13 [95% CI, 0.41 to 6.07]; I^2 = 30%).[122,124] Buprenorphine was associated with increased risk of constipation vs placebo, based on 2 trials (n = 246; RR, 2.36 [95% CI, 1.16 to 4.92]; I^2 = 0%; ARD, 12% [95% CI, -5% to 41%]).[123,125]

Naltrexone | Eleven trials of naltrexone vs placebo or no medication reported harms (n = 1645) (eTable 16 in the Supplement).[125,129-136,139,140] For withdrawal from study due to adverse events, 3 trials found no difference between naltrexone vs placebo or no medication, but the estimate was imprecise (n = 836; RR, 1.54 [95% CI, 0.35 to 8.31]; I^2 = 0%).[133-135] Three other trials (n = 181) reported no study withdrawals due to adverse events.[125,130,139] Three studies (n = 638) found no differences in serious adverse events, but the estimate was imprecise (RR, 1.24 [95% CI, 0.11 to 10.21]; I^2 = 59%).[125,134,135] Three trials (n = 163) found no differences between naltrexone and control groups in risk of gastrointestinal adverse events (constipation, diarrhea, and nausea or vomiting).[125,130,140]

Benefits of Naloxone Preemptive Prescribing

Key Question 6. Does naloxone reduce morbidity or mortality, or improve other health outcomes, in persons with opioid use disorder or misuse?

No eligible studies were identified.

Harms of Naloxone Preemptive Prescribing

Key Question 7. What are the harms of naloxone in persons with opioid use disorder or misuse?

No eligible studies were identified.

Table 4. Summary of Evidence

Intervention	Study design	Summary of findings[a]	Consistency and precision	Other limitations	Strength of evidence	Applicability
KQ1: Benefits of screening						
NA	No studies	NA	NA	NA	Insufficient	NA
KQ2: Screening accuracy						
NA (test accuracy only)	28 Observational studies (n = 65 720)[b]	Thirty different screening tools evaluated, including brief frequency-based tools, risk assessment tools, and indirect screeners Among adolescents, sensitivity of frequency-based and risk assessment tools for detecting any cannabis use or unhealthy cannabis use ranged from 0.68 to 0.98 (95% CI, 0.64 to 0.99) and specificity ranged from 0.82 to 1.00 (95% CI, 0.80 to 1.00) Among adults, sensitivity of frequency-based and risk assessment tools for detecting unhealthy use of "any drug" ranged from 0.71 to 0.94 (95% CI, 0.62 to 0.97) and specificity ranged from 0.87 to 0.97 (95% CI, 0.83 to 0.98) Instruments were less accurate in detecting unhealthy use of prescription opioids or sedatives then other specific drugs, especially cannabis; sensitivity and specificity of frequency-based and risk assessment tools for detecting any prenatal drug use (not including alcohol) was lower than the estimates found for nonpregnant adults and ranged from 0.37 to 0.76 (95% CI, 0.24 to 0.86) and from 0.68 to 0.83 (95% CI, 0.55 to 0.91)	Reasonably consistent and imprecise	Each instrument was not evaluated in more than 1 or 2 studies No studies restricted inclusion to young adults specifically (the age group with the highest prevalence of use) Low prevalence of some drugs makes it difficult to determine if the screening tools are accurate for those substance Few studies included biologic confirmation of drug use Few studies among pregnant persons using brief screeners	Low	Most studies conducted in US-based primary care population, although included studies represented samples with generally higher prevalence of drug use and drug use disorders than US national estimates Higher representation of nonwhite and low SES participants
KQ3: Harms of screening						
NA	No studies	NA	NA	Insufficient	NA	NA
KQ4a and KQ4b: Efficacy of interventions						
Psychosocial interventions	52 trials (n = 15 659) Screen-detected populations: 27 trials (n = 10 227) Treatment-seeking populations: 25 trials (n = 5432)	Drug use abstinence: 3 to 4 mo: 15 trials; RR, 1.60 (95% CI, 1.24 to 2.13); I^2 = 61%; ARD, 9% (95% CI, 5% to 15%) 6 to 12 mo: 14 trials; RR, 1.25 (95% CI, 1.11 to 1.52); I^2 = 38%; ARD, 10% (95% CI, 3% to 16%) Drug use days (in last 7 d): 3 to 4 mo: 19 trials; MD, −0.49 d (95% CI, −0.85 to −0.13); I^2 = 89% 6 to 12 mo: 15 trials; MD, −0.08 d (95% CI, −0.30 to 0.11); I^2 = 45% Drug use severity: 3 to 4 mo: 17 trials; SMD, −0.18 (95% CI, −0.32 to −0.05); I^2 = 73% 6 to 12 mo: 13 trials; SMD, −0.10 (95% CI, −0.24 to 0.02); I^2 = 65% Mortality: reported in 4 trials with few events Other health, social, and legal outcomes: few trials, with inconsistent effects	Substantial clinical heterogeneity and inconsistency Effects present in trials of treatment-seeking but not screen-detected populations Effects also generally stronger in trials that evaluated cannabis use than other type of drug use, trial of adult than trial of adolescents or young adults, and trial of more intensive than brief interventions No stratified analysis explained inconsistency	Overall risk of bias moderate; attrition was high Trials of psychosocial interventions could not be effectively blinded Methods for measuring drug use outcomes varied Reporting bias not detected	Moderate	Studies varied in terms of whether patients were screen-detected or treatment-seeking, recruitment setting, and severity and type of drug use Most trials evaluated psychosocial interventions that used cognitive behavioral therapy or motivational interventions, but treatment intensity varied Brief interventions are usually designed to be feasible for delivery in primary care settings

(continued)

Table 4. Summary of Evidence (continued)

Intervention	Study design	Summary of findings[a]	Consistency and precision	Other limitations	Strength of evidence	Applicability
Naltrexone for opioid use disorder	13 trials (n = 1718)	Drug use relapse: 11 trials; RR, 0.73 (95% CI, 0.62 to 0.85); I^2 = 78%; ARD, −18% (95% CI, −26% to −10%) Retention in treatment: 9 trials; RR, 1.71 (95% CI, 1.13 to 2.49); I^2 = 67%; ARD, 15% (95% CI, 5% to 22%) Mortality: Reported in 5 trials, with very few events Other health, legal, and social outcomes: few trials, with inconsistent effects	For drug use relapse and retention in treatment, inconsistency in magnitude but not direction of effect Estimates reasonably precise Results consistent in stratified and sensitivity analyses	Overall risk of bias moderate; attrition was high Methods for defining drug use relapse and retention in treatment varied Reporting bias not detected	Moderate	All trials enrolled treatment-seeking persons with opioid use disorder due to heroin use Naltrexone administered in conjunction with drug use counseling Most trials evaluated oral naltrexone, some trials recruited patients from the criminal justice system, and around one-half of naltrexone trials were conducted in countries in which opioid agonist therapy is not available
Opioid agonist therapy (buprenorphine or methadone) for opioid use disorder	7 trials (n = 1109) Buprenorphine: 5 trials (n = 679) Methadone: 2 trials (n = 430) All trials conducted in treatment-seeking individuals	Drug use relapse: 4 trials; RR, 0.75 (95% CI, 0.59 to 0.82); I^2 = 75%; ARD, −35% (95% CI, −67% to −3%) Retention in treatment: 7 trials; RR, 2.58 (95% CI, 1.78 to 4.59); I^2 = 71%; ARD, 39% (95% CI, 23% to 54%) Results very similar when stratified by buprenorphine or methadone Mortality: reported in 2 trials, with very few events Other health, legal, and social outcomes: few trials, with inconsistent effects	For drug use relapse and retention in treatment, inconsistency in magnitude but not direction of effect Estimates reasonably precise Results consistent in stratified and sensitivity analyses	Overall risk of bias moderate; attrition was high Two trials used an open-label design Methods for defining drug use relapse used urine drug test findings Reporting bias not detected	Moderate	All trials enrolled treatment-seeking persons with opioid use disorder, primarily due to heroin use Opioid agonist therapy usually administered in conjunction with drug use counseling Opioid agonist therapy usually administered in addiction treatment setting No trial evaluated newly FDA--approved, injectable buprenorphine
KQ5: Harms of interventions						
Psychosocial interventions	4 trials (n = 1198)	No harms reported in either intervention of control groups No serious adverse events noted	Findings consistent but imprecise	Overall risk of bias moderate Harms only reported in a few trials; however, serious harms not expected with this type of intervention	Low-moderate	See entry for efficacy of psychosocial interventions
Naltrexone for opioid use disorder	11 trials (n = 1645)	Withdrawal due to adverse events: 3 trials; RR, 1.54 (95% CI, 0.35 to 8.31); I^2 = 0% Serious adverse events: 3 trials; RR, 1.24 (95% CI, 0.11 to 10.21); I^2 = 59% Constipation: 2 trials; RR, 0.97 (95% CI, 0.37 to 2.39); I^2 = 0% Diarrhea: 2 trials; RR, 1.94 (95% CI, 0.70 to 6.53); I^2 = 0%	Findings consistent but imprecise	Overall risk of bias moderate Harms reporting was inconsistent, and harms not reported by all trials	Low-moderate	See entry for efficacy of naltrexone
Opioid agonist therapy (buprenorphine or methadone) for opioid use disorder	4 trials (n = 639) on buprenorphine; no studies on methadone	Serious adverse events: 2 trials; RR, 0.33 (95% CI, 0.09 to 1.12); I^2 = 0% Withdrawal due to adverse events: 1 trial; RR, 0.89 (95% CI, 0.06 to 13.7) No hospitalizations due to serious medication-related adverse events: 1 trial Constipation: 2 trials; RR, 2.36 (95% CI, 1.17 to 4.92); I^2 = 0%; ARD, 12% (95% CI, −5% to 41%) Diaphoresis: 3 trials; RR, 1.15 (95% CI, 0.55 to 2.73); I^2 = 44% Nausea: 2 trials; RR, 1.13 (95% CI, 0.41 to 6.07); I^2 = 30%	Some inconsistency and imprecision	Overall risk of bias moderate Harms reporting was inconsistent, and harms not reported by all trials	Low-moderate	See entry for efficacy of opioid agonist therapy

(continued)

Table 4. Summary of Evidence (continued)

Intervention	Study design	Summary of findings[a]	Consistency and precision	Other limitations	Strength of evidence	Applicability
KQ6: Efficacy of naloxone preemptive prescribing						
NA	No studies	NA	NA	NA	Insufficient	NA
KQ7: Harms of naloxone preemptive prescribing						
NA	No studies	NA	NA	NA	Insufficient	NA

Abbreviations: ARD, absolute risk difference; FDA, US Food and Drug Administration; MD, mean difference; NA, not applicable; RR, risk ratio; SES, socioeconomic status; SMD, standardized mean difference.

[a] Comparisons are against placebo or no medication for pharmacological interventions and against waitlist, a minimal intervention, or usual care for psychosocial interventions.

[b] N includes 1 US-based community sample (n = 42 923) that only evaluated a single-item alcohol question for predicting problematic drug use. Without this study, total n = 22 797.

Discussion

This review updates the 2008 USPSTF review on screening for drug use in adolescents and adults.[5] A summary of findings, including an assessment of the strength of evidence for each KQ, is presented in **Table 4**. Consistent with the 2008 review, no studies were identified on the benefits and harms of screening (vs no screening) for drug use in primary care. However, evidence indicates that several screening instruments, including single-item drug frequency questions[18,20,45,48]; the Substance Use Brief Screen[18]; the Tobacco, Alcohol, Prescription Medication, and Other Substance Use tool[25,49]; and the Drug Abuse Screening Test (10 items),[20] can detect unhealthy drug use with reasonable accuracy. Both frequency-based and risk assessment screening instruments generally have sensitivity greater than or equal to 0.80 and specificity greater than or equal to 0.85 for identifying unhealthy drug use and drug use disorders among adults when validated against a structured diagnostic interview. Based on the range in test accuracy estimates and a prevalence of drug use among adults of 11%,[3] the positive predictive value of screening instruments is approximately 40%. In patients who screen positive, further assessment to define patients' risk level may help determine the appropriateness for treatment, such as the procedure recommended by the National Institute on Drug Abuse.[143]

Compared with the 2008 review, substantially more evidence is available to support the effectiveness of psychosocial interventions and FDA-approved medications to improve drug use outcomes among persons with unhealthy drug use or a diagnosed drug use disorder. When trials in screen-detected and treatment-seeking populations were combined in the meta-analyses, psychosocial interventions were associated with an increased likelihood of drug use abstinence, decreased number of drug use days, and decreased drug use severity at 3 to 4 months. Beneficial effects at 6 to 12 months were only observed for drug use abstinence. Most trials of psychosocial interventions recruited patients with cannabis use or mixed drug use and used CBT or motivational interventions ranging in intensity from 1 or 2 sessions to ongoing treatment for months. Based on overall pooled estimates, psychosocial interventions were associated with a number needed to treat of 17 for 1 additional case of drug use abstinence at 6 to 12 months. Effects were generally greater in treatment-seeking populations than in screen-detected populations, stronger for cannabis use than other drug use outcomes, stronger for shorter-term (3- to 4-month) than longer-term (6- to 12-month) outcomes, and stronger for more intensive interventions vs brief interventions. Few trials evaluated psychosocial interventions among adolescents or pregnant persons.

Both opioid agonist therapy (methadone and buprenorphine) and naltrexone were associated with a decreased risk of relapse and increased likelihood of treatment retention among individuals with an opioid use disorder after 4 to 12 months of treatment, compared with no treatment. Trials of pharmacologic treatment were primarily conducted in persons using heroin, and medications were typically administered in conjunction with drug use counseling, in accordance with recommended practice.[14,144] Based on pooled estimates, the number needed to treat to avoid 1 additional case of relapse was 3 for opioid agonists and 6 for naltrexone. There was no evidence that the effectiveness of pharmacologic treatment varied

according to type of medication, administration method, intensity of co-occurring counseling, or trial quality.

Evidence on the effects of psychosocial and medications for opioid use disorder on health outcomes (eg, such as global function, quality of life, depression, and anxiety) was very limited and showed no consistent evidence of a benefit of treatment compared with no treatment. While assessment and reporting of harms in trials of pharmacotherapies was suboptimal, it indicated no increase in risk of serious adverse events or study withdrawal due to adverse events vs placebo or pharmacotherapy. Trials of psychosocial interventions generally did not report harms, although serious harms are not anticipated with this type of intervention.

As described in the full report,[8] evidence on the benefits and harms of preemptive prescribing of naloxone in primary care settings for reducing overdose risk in persons with opioid use disorder or misuse is not available. To date, the effectiveness of naloxone has mainly been demonstrated in the context of evaluations of community opioid overdose prevention and naloxone distribution programs.[145,146]

Limitations

This study had several limitations. First, for screening accuracy, despite inclusion criteria designed to result in the selection of studies highly applicable to US primary care, many screening studies were conducted in populations with high prevalence of drug use or high numbers of known drug users, and some of the larger studies were conducted among non–clinic-based samples. As such, the instrument accuracy reported in the included studies may not reflect the accuracy for all US primary care settings.

Second, trials of psychosocial interventions were characterized by marked variability in patient populations, interventions, outcomes, recruitment and treatment settings, and other factors, likely contributing to the substantial statistical heterogeneity observed in pooled analyses. Furthermore, evidence was lacking on the effectiveness of psychosocial treatments among adolescents and pregnant people as well as for treatment of stimulant use. Most trials of medication therapy were among adults with opioid use disorder due to heroin use and not prescription opioid misuse.

Third, trials primarily focused on intermediate outcomes, such as drug use or retention in treatment, and there was little direct evidence on the effects of interventions on mortality or other clinical, social, and legal outcomes.

Conclusions

Several screening instruments with acceptable sensitivity and specificity are available to screen for drug use, although there is no evidence on the benefits or harms of screening. Pharmacotherapy and psychosocial interventions are effective at improving drug use outcomes, but evidence of effectiveness remains primarily derived from trials conducted in treatment-seeking populations.

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Concept and design: Patnode, Perdue, Rushkin, O'Connor, Chou.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Patnode, Rushkin, Dana, Blazina, Bougatsos, Grusing, Fu, Chou.
Critical revision of the manuscript for important intellectual content: Patnode, Perdue, Blazina, O'Connor, Chou.
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