Brief Behavioral Interventions for Substance Use in Adolescents: A Meta-analysis

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abstract

CONTEXT: Adolescents with problematic substance use (SU) are at risk for far-reaching adverse outcomes.

OBJECTIVE: Synthesize the evidence regarding the effects of brief behavioral interventions for adolescents (12–20 years) with problematic SU.

DATA SOURCES: We conducted literature searches in Medline, the Cochrane Central Register of Controlled Trials, Embase, Cumulative Index to Nursing and Allied Health Literature, and PsyCInfo through October 31, 2019.

STUDY SELECTION: We screened 33 272 records and citations for interventions in adolescents with at least problematic SU, retrieved 1831 articles, and selected 22 randomized controlled trials of brief interventions meeting eligibility criteria for meta-analysis.

DATA EXTRACTION: We followed Agency for Healthcare Research and Quality guidelines. We categorized brief interventions into components, including motivational interviewing (MI), psychoeducation, and treatment as usual. Outcomes included SU (abstinence, days used per month) for alcohol and cannabis, and substance-related problem scales. Strength of evidence (SoE) was assessed.

RESULTS: Both pairwise and network meta-analyses were conducted by using random effects models. Compared to treatment as usual, the use of MI reduces heavy alcohol use days by 0.7 days per month (95% credible interval [CrI]: −1.6 to 0.02; low SoE), alcohol use days by 1.1 days per month (95% CrI −2.2 to −0.3; moderate SoE), and overall substance-related problems by a standardized net mean difference of 0.5 (95% CrI −1.0 to 0; low SoE). The use of MI did not reduce cannabis use days, with a net mean difference of −0.05 days per month (95% CrI: −0.26 to 0.14; moderate SoE).

LIMITATIONS: There was lack of consistently reported outcomes and limited available comparisons.

CONCLUSIONS: The use of MI reduces heavy alcohol use, alcohol use days, and SU-related problems in adolescents but does not reduce cannabis use days.

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Rates of alcohol and cannabis use remain perniciously high among adolescents. According to 2019 US national data, 24% of eighth-graders reported lifetime alcohol use and 14% reported cannabis use. Among 12th-graders, rates were more than twice as high, 59% for alcohol use and 44% for cannabis. Adolescents who engage in alcohol and cannabis use are at increased risk of negative health outcomes, including sexually transmitted infections, unintended pregnancies, school dropout, and premature separation from their guardians. Moreover, untreated adolescent drinking and cannabis use often persist into adulthood, increasing the risk of adult substance use disorders (SUDs) and cooccurring problems. With these far-reaching negative consequences, we underscore the importance of identifying effective early interventions for adolescent alcohol and cannabis use that can be easily used in primary care settings.

Brief interventions (BIs), consisting of 1 or 2 behavioral therapy sessions, are conceptually well suited to use by primary care physicians and staff to address adolescent alcohol and cannabis use. BIs are highly scalable and can be delivered across multiple settings serving adolescents, such as primary health care clinics, emergency departments, schools, and outpatient behavioral health centers. BIs are also compatible with a public health approach that promotes early substance use (SU) detection and intervention across the risk continuum, as opposed to a disease-oriented approach focused only on adolescents meeting full SUD diagnostic criteria. Furthermore, BIs are aligned with a harm-reduction approach, whereby adolescents are not asked to commit to abstinence but rather are encouraged to set personalized goals to reduce their risk. The conceptual fit of BIs within the remit of primary care has been recognized by the American Academy of Pediatrics and other leading national organizations. Pairing BIs with universal screening in primary care settings has been touted as a practical, integrated approach for achieving population-level reductions in adolescent alcohol and cannabis use.

In previous qualitative systematic reviews, researchers have deemed BIs that use a motivation-building approach, broadly defined as motivational interviewing (MI), as probably efficacious but not meeting the threshold for identification as well-established interventions. This is consistent with the US Preventive Services Task Force determination that there is insufficient evidence to recommend screening and BIs for adolescents in primary care.

Previous meta-analyses are used to support the use of BIs (particularly MI) in adolescents with risky drinking, albeit with variable effect estimates across outcome measures. Evidence supporting BIs in cannabis users is mixed. Confidence in these conclusions from previous meta-analyses is hindered, however, by several limitations: (1) failure to assess overall strength of evidence (SoE) informed by formal assessments of the risk of bias (RoB) in individual trials; (2) reliance on standardized effect size estimates; (3) pairwise comparisons pooling multiple types of BI; and (4) grouping outcomes for multiple “illicit substances” in the analysis (eg, assuming that change in cannabis days is equivalent to change in cocaine days).

This work was conducted as part of an extensive, peer-reviewed systematic review (SR) of interventions for SU in adolescents. The full comparative effectiveness review and review protocol are available at https://doi.org/10.23970/AHRQEPCCER225 (PROSPERO identifier CRD42018115388). We present our systematic review with network meta-analyses, summarizing the effects of BIs in adolescents, 12 to 20 years of age, with problematic alcohol and/or cannabis use.

**METHODS**

We used established methodologies as outlined in the Agency for Healthcare Research and Quality (AHRQ) *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*. The key questions and protocol were discussed in depth with a panel of key informants and technical experts.

**Search Strategy and Study Selection**

A medical librarian with expertise in designing searches for systematic reviews conducted literature searches in Medline, the Cochrane Central Register of Controlled Trials, Embase, and Cumulative Index to Nursing and Allied Health Literature from inception to October 31, 2019. The overall search was designed to cover the full range of key questions in the full report and is broader than the scope of interventions and outcomes addressed here. In the searches, we included terms for substances (including a list of known substances) crossed with terms for disorders and also terms for treatments (including a list of known treatments). The search was further crossed with terms for the adolescent age group and terms for primary studies and systematic reviews. All searches were designed to be maximally sensitive. Full search strategies can be found in the online supplement. We further searched ClinicalTrials.gov and the US Food and Drug Administration websites for unpublished and ongoing studies. Reference lists of available clinical practice guidelines and existing systematic reviews were scanned for eligible studies. The results of all studies were deduplicated and screened by 2
reviewers using the online program abstrackr (http://abstrackr.cebm.brown.edu/). Accepted citations were retrieved and reviewed in full text.

For the research question addressed here, studies had to be randomized controlled trials (RCTs) in which researchers compared ≥2 interventions with at least 10 participants per arm. RCTs had to have been focused on adolescents, aged 12 to 20 years inclusive (ie, ≥80% of the population had to be within this age range), who met criteria for at least 1 SUD or for problematic SU (excluding tobacco). Problematic use was operationally defined as meeting at least 1 of the following criteria: (1) referral for treatment by self, parent, school, other professional, or the justice system; (2) screened by using a validated tool, with a BI given to those who met prespecified criteria indicating elevated risk; (3) reported SU at least once per month; or (4) identified after a substance-related consequence, such as an alcohol-related emergency department visit. Although in the full systematic review, a range of interventions was evaluated, to be eligible for the current analysis at least 1 of the evaluated interventions had to be designated as brief, defined as 1 or 2 sessions. We excluded interventions focused on drinking in the college setting because (1) this population is developmentally distinct from adolescents with problematic SU and (2) and such studies have been the focus of multiple previous systematic reviews.23–25

**Intervention Coding**

Two members of the team with expertise in psychology and complex interventions created a categorization schema to capture the salient aspects of the behavioral interventions and independently assigned ≥1 intervention code(s) for each arm in each study. Disagreements were resolved by consensus.

An intervention was coded as MI if at least 1 session was focused on building the adolescent’s motivation to reduce SU and/or attain abstinence. Motivation enhancement therapy, a more structured and specific approach to building the adolescent’s motivation, was also categorized as MI. Interventions that referenced a general goal to build the adolescent’s motivation to change were not coded as containing MI unless there was a stand-alone, manual-guided MI component.

Interventions were categorized as psychoeducation if they explicitly aimed to reduce the adolescent’s SU through provision of education about substance-related harms. Because most SU interventions involve some degree of education, we coded an intervention as psychoeducation only if there was explicit reference to a stand-alone psychoeducation module.

Interventions designed to be comparators to active interventions that were not directed at treating SU were categorized as treatment as usual (TAU). Examples included wait lists or pamphlets regarding issues other than SU.

In 3-arm studies comprising 2 treatment arms that were not distinguishable by using our taxonomy (eg, computer-delivered MI versus therapist-delivered MI versus TAU), we pooled the nondistinguishable arms and included the pooled arm in meta-analyses.

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**FIGURE 1**

Literature flow diagram. Transition-aged youth were 21 to 25 years of age. CINAHL, Cumulative Index to Nursing and Allied Health Literature; NRCS, nonrandomized comparative study.
Outcome Extraction

SU Frequency Scales

We examined outcomes related to frequency of use of specific substances (eg, alcohol, cannabis), whether reported as continuous measures reflecting frequency of use or as categorical measures of abstinence. For alcohol, we considered both frequency of heavy alcohol use (eg, mean days of heavy alcohol use per 30 days) and frequency of any use (eg, percent days of alcohol use per 30 days). For cannabis, we considered only frequency of any use.

Aggregate outcomes that combined multiple substances were classified into 1 of 3 mutually exclusive categories: (1) alcohol and other drugs, (2) illicit drug use (excluding alcohol but including cannabis and other drugs, regardless of local laws), and (3) other drugs (excluding alcohol and cannabis).

SU-Related Problem Scales

We also examined scales that measured problems related to SU. We extracted the mean value of the various scales reflecting substance-related problems. When a study reported several scales, each associated with a specific substance (ie, alcohol or cannabis), we chose the scale with the highest mean severity.

Assessment of Study RoB

Two senior investigators assessed the RoB (methodologic quality) of each study on the basis of predefined criteria, using the Cochrane RoB tool for RCTs.26

Meta-analyses and SoE Assessments

We conducted pairwise meta-analyses, using both frequentist and Bayesian frameworks, and network meta-analyses, using the Bayesian framework. Analyses were done by using R27 with the metafor28 and gemtc packages.29 Network meta-analysis is an extension of pairwise meta-analysis that allows simultaneous comparison of multiple interventions by combining direct evidence (when interventions are compared head-to-head) and indirect evidence (when interventions are compared through other reference interventions across studies). In Bayesian analyses, we used empirical previous distributions for the between-study heterogeneity variance.30–32

Outcomes related to frequency of SU were converted to a common metric of mean number of use days per 30 days. We analyzed outcomes evaluated ~3 months after baseline assessment. Effects were estimated for net mean differences (NMDs), that is, the between-arm differences in the within-arm changes from baseline (difference-in-differences). Standardized net mean differences (SNMDs) were calculated for SU-related problem scales. Abstinence outcomes were compared to odds ratios (ORs). As a sensitivity analysis, we included all available substance-specific outcomes (ie, use days, scales, and nonlinear transformations of use days) and calculated a summary SNMD effect. Statistical heterogeneity was explored qualitatively. The a priori subgroup analyses of interest (male versus female, racial and ethnic minorities, socioeconomic status, and family characteristics) were too sparse for meaningful meta-regression or subgroup analysis.

RESULTS

In our search for the full AHRQ systematic review, 33 732 citations were returned. Of 1831 abstracts accepted in initial screening and retrieved for full-text review, 988 that were focused on older adults were excluded (Fig 1). An additional 626 articles were rejected for reasons provided in Figure 1. In the full systematic review, 118 studies were included, and the review was also comprised of studies of nonbrief behavioral interventions and pharmacologic interventions. Here, we report on the results most relevant for primary care practitioners, the 22 studies that were used to evaluate BIs for adolescents with problematic alcohol or cannabis use.34–55 The baseline and intervention details of these 22 studies are summarized in

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>NMD (95% CI/CrI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arnaud et al., 2017</td>
<td>−0.6 (−1.2 to −0.1)</td>
</tr>
<tr>
<td>Bernstein et al., 2010</td>
<td>−1.0 (−1.9 to −0.1)</td>
</tr>
<tr>
<td>Colby et al., 2018</td>
<td>−2.0 (−3.4 to −0.5)</td>
</tr>
<tr>
<td>D’Amico et al., 2018</td>
<td>−0.1 (−0.4 to 0.3)</td>
</tr>
<tr>
<td>Winters et al., 2007</td>
<td>−0.7 (−1.3 to −0.2)</td>
</tr>
<tr>
<td>REML RE (direct)</td>
<td>−0.7 (−1.1 to −0.2)</td>
</tr>
<tr>
<td>Bayes RE (direct)</td>
<td>−0.7 (−1.6 to 0.0)</td>
</tr>
</tbody>
</table>

FIGURE 2

Heavy alcohol use: forest plot depicting individual study effects with summary estimates of the relative effect of MI versus TAU. An NMD <1 favors MI. “Direct” is used to indicate direct (pairwise) comparisons. CI, confidence interval; RE, random effect; REML, restricted maximum likelihood.
Supplemental Table 1. Despite superficial heterogeneity of study inclusion criteria with respect to the targeted substance(s), in most studies, researchers enrolled adolescents using some combination of alcohol and cannabis, with a minority using other drugs.

Interventions were coded as MI, psychoeducation, or TAU. Although included in the network meta-analysis, there was insufficient evidence to evaluate effects of either psychoeducation versus TAU or MI versus psychoeducation. The outcomes reported by each study are detailed in Supplemental Table 2. Aggregate outcomes (ie, alcohol and other drug use, illicit drug and other drug use) were rarely reported, precluding meta-analysis.

**RoB and SoE**

RoB summaries are presented graphically (Supplemental Fig 7) for the 22 included studies. The most common methodologic concerns involved lack of blinding of participants (all RCTs had a high RoB), personnel (21 had a high RoB), and outcome assessors (12 had a high RoB). The evidence profile used to define overall SoE by outcome is provided in Supplemental Table 3.

**Alcohol Outcomes: Heavy Alcohol Use**

In 7 studies with 2821 participants, researchers reported a measure of heavy alcohol use. In all 7 studies, researchers directly compared MI with TAU (Supplemental Fig 8). Across the 5 studies that reported days of heavy alcohol use (1248 participants), the NMD was −0.7 (95% credible interval [CrI] −1.6 to 0.0) days per month of heavy alcohol use, favoring MI (Fig 2). This corresponds to a Bayesian posterior probability of 97.3% that MI is superior to TAU. Results were similar in a sensitivity analysis that included 2 additional studies (N = 1573) that reported a scale reflecting heavy alcohol use. Because of moderate RoB and imprecision, we deemed there to be low SoE supporting this conclusion.

**Alcohol Outcomes: Alcohol Use Days**

In 10 studies (N = 2153 participants), a measure of the frequency of alcohol use was reported. As shown in the evidence network (Supplemental Fig 9), in 9 studies, researchers directly compared MI to TAU, and, in 1 study, researchers evaluated MI versus psychoeducation. In 7 of the 9 studies in which researchers directly compared MI to TAU, days of alcohol use was reported. The summary estimate from the Bayesian network meta-analysis for the NMD used to compare MI to TAU was −1.1 (95% CrI −2.2 to −0.3) alcohol use days per month (Fig 3), favoring MI. Conclusions were unchanged in a sensitivity analysis in which the 2 studies that reported a scale were included. Because of moderate RoB but adequate precision, we deemed there to be moderate SoE supporting this conclusion.

**Alcohol Outcomes: Alcohol Abstinence**

Abstinence from alcohol use was reported in 7 studies (N = 2482 participants). As shown in the evidence network (Supplemental Fig 10), in 5 studies, researchers compared MI to TAU, and 2 studies were used to evaluate MI versus psychoeducation. The summary OR comparing MI to TAU was 1.9 (95% CrI 0.9 to 6.0), favoring MI (Supplemental Fig 11). The CrI for this effect is wide and compatible with no effect. Because of moderate RoB and imprecision that included a null effect, we rated the SoE as insufficient.

**Cannabis Outcomes: Cannabis Use Days**

In 13 studies, the effect of BI on cannabis use days was analyzed (N = 2386). In all studies in the network, the number of cannabis use days was reported. The summary estimate from the Bayesian network meta-analysis for the NMD used to compare MI to TAU was −1.1 (95% CrI −2.2 to −0.3) alcohol use days per month (Fig 3), favoring MI. Conclusions were unchanged in a sensitivity analysis in which the 2 studies that reported a scale were included. Because of moderate RoB but adequate precision, we deemed there to be moderate SoE supporting this conclusion.
from the Bayesian network meta-analysis for the effect of MI versus TAU was \(-0.05\) (95% CrI \([-0.26\) to 0.14]) days per month (Fig 4). This result is used to support the conclusion that MI is not more effective than TAU in reducing cannabis use days. Because of moderate RoB, we rated the SoE as moderate.

**Cannabis Outcomes: Cannabis Abstinence**

In 6 studies, cannabis abstinence outcomes were reported (\(N = 1119\)).\(^{36,39,45,46,50,55}\) Of these, MI was compared to TAU in 4 studies and MI versus psychoeducation was evaluated in 2 studies (Supplemental Fig 13). The summary OR for MI versus TAU was 1.5 (95% CrI: 0.7 to 3.4) (Supplemental Figs 13 and 14). Because of moderate RoB and imprecision compatible with a null effect, we rated the SoE as insufficient.

**SU Problem Scales**

In 9 studies, 1 of 8 SU problem scales (\(N = 1854\)) was reported.\(^{35,40-43,46,53-55}\) Of these, psychoeducation was compared to MI in 3 studies and MI versus TAU was evaluated in 6 studies (Supplemental Fig 15). After standardizing the scales, the pooled estimate from the network meta-analysis was \(-0.5\) (95% CrI: -1.0 to 0) SNMD units, ie, MI is more effective than TAU to reduce SU-related problems (Fig 5). Because of moderate RoB and imprecision, we rated the SoE as low.

**DISCUSSION**

We found that the use of MI reduces heavy alcohol use (low SoE) and overall alcohol use (moderate SoE) compared to TAU in adolescents with problematic alcohol use. By contrast, we found that the use of MI does not reduce days of cannabis use compared to TAU (moderate SoE). One interpretation of these findings is that adolescent cannabis use is more resistant to change than adolescent drinking. We also found evidence that MI may reduce overall substance-related problems relative to TAU (low SoE).

Our findings for alcohol use outcomes are generally consistent with those of previous systematic reviews and meta-analyses that have been focused on adolescent drinking. In a systematic review of experimental and quasi-experimental studies, Tanner-Smith and Lipsey\(^{17}\) pooled data across multiple outcomes and interventions using standardized effect size metrics. They concluded that adolescents aged 11 to 18 years who received BIs for alcohol use had lower levels of self-reported alcohol consumption and alcohol-related problems than those who received TAU and that MI strategies were the most effective BIs for adolescent drinking.\(^{17}\) We use our replication of these findings using network meta-analysis, “natural units” of days of use, and rigorous SoE assessments to speak to the robustness of the results.

Comparison of our findings for cannabis use with previous meta-analyses is complicated by the fact that cannabis use has often been conflated with “illicit drug use.” For example, Tanner-Smith et al\(^{19}\) concluded that MI explicitly targeting alcohol use in adolescents and young adults did not reduce concurrent use of “other illicit drugs,” whereas MI explicitly targeting both alcohol and illicit drug use was more effective than TAU in reducing “use of both substances.” In a systematic review, Li et al\(^{20}\) similarly examined the effects of brief MI on “illicit drug use” among adolescents. In this review, the researchers included 10 included
RCTs whose participants predominately reported cannabis use (80%) but also reported using multiple illicit substances, including cocaine (30%), amphetamines, and 3,4-methylenedioxymethamphetamine (20%). Li et al.\textsuperscript{20} aggregated “extent of drug use outcomes” (drug use frequency, abstinence, problems related to drug use, etc) and found no evidence for an effect of MI compared to TAU (standardized effect size of 0.05 [95% confidence interval: $-0.06$ to $0.17$]). In a recent meta-analysis, Halladay et al.\textsuperscript{21} focused specifically on the effectiveness of BIs on cannabis use outcomes in adolescents and emerging adults. They reported no significant difference in frequency of cannabis use at 1 to 3 months postintervention between BI and passive control, with a standardized mean difference of $-0.05$ (95% confidence interval: $-0.14$ to $0.03$).

Our findings, specific to cannabis use in the adolescent age group, are consistent with the Halladay et al.\textsuperscript{21} meta-analysis, and, with them, we suggest that using MI is no more effective than using TAU to reduce days of cannabis use. Given the apparent heterogeneity of treatment effects for alcohol and cannabis, it may be problematic to interpret intervention effects when the substance targeted is unclear, particularly when outcomes pertain to multiple substances (eg, “alcohol and other drugs” or “illicit drugs”), as has been done in previous systematic reviews.\textsuperscript{17,20,56} If treatment effects vary by substance, estimates of effect on such composite outcomes will be determined by the relative proportion of alcohol, cannabis, and other drug use in individual studies. Because many researchers enroll adolescents with mixed use of alcohol, cannabis, and (less commonly) other drugs, we recommend that, in future systematic reviews, researchers should report substance-specific effects.\textsuperscript{57}

### Limitations

The results of our systematic review must be considered in the context of several design decisions. First, we aggregated BIs from studies across settings, which may have masked meaningful contextual factors that can modify treatment effectiveness. Second, although some consider any SU in adolescents to be problematic,\textsuperscript{10} others argue that some experimentation with alcohol and cannabis is normative in adolescence.\textsuperscript{58} Our goal was to estimate treatment effects in participants with use that has been variously described as “risky,” “unhealthy,” “hazardous,” or “harmful”\textsuperscript{16} but not yet meeting criteria for diagnosis of a SUD. Therefore, in consultation with our subject matter experts and a panel of experts in the field, we developed pragmatic inclusion criteria for problematic SU, when evaluating individual studies.

The included studies varied with regards to the primary substance of use, with researchers generally including users of alcohol, cannabis, combinations of specific drugs (eg, alcohol and cannabis), and/or unspecified substances in their studies. Some researchers reported outcomes for multiple substances but rarely explicitly identified when the intervention was targeted to a specific substance.

Finally, in the absence of information about the comparison interventions, we chose to categorize them as TAU. Consequently, the TAU category comprised a heterogeneous collection of often poorly described interventions that could be efficacious. This conservative approach may result in underestimates of treatment effects. No classification schema can be used to perfectly capture the complexity of possible interventions or be fully robust to the variable reporting in published reports. To support evidence synthesis, future researchers are encouraged to more clearly describe intervention components received by study participants, including those assigned to TAU. For example, rather than simply stating that an intervention was designed to “build motivation” or “build skills,” investigators should...
clearly explicate the underlying theoretical orientation and components of the intervention, to allow inferences as to whether the intervention was delivered with consistency and quality.

Because of the lack of consistently reported outcomes across studies, the number of available comparisons was substantially reduced. The available evidence was consequently too sparse to allow a meaningful examination of factors that modify treatment effect, such as identification of key ingredients of successful interventions or examination of how intervention effects differ across demographic groups and participant factors, such as SU severity, substance of primary use, and cooccurring diagnoses. In future RCTs, researchers are encouraged to both use a consistent set of outcome measures and specify and evaluate putative mediators and moderators of treatment effect.

Contributions of the Current Review

In the current review, we address the limitations of previous systematic reviews in several ways. We examine the specific effects of BIs on alcohol and cannabis outcomes, rather than reporting aggregate effects reflecting use of multiple substances (eg, illicit drug use). When possible, we report intervention effects in “natural units” (eg, days of use) instead of standardized mean differences to facilitate direct interpretation.60 Furthermore, we employ network meta-analysis, which allows comparisons of >2 interventions (ie, MI, psychoeducation, and TAU) in a single, coherent analysis using both direct and indirect evidence.61 Finally, the, in current analysis, we include a rigorous SoE assessment of the body of evidence that is based on RoB and other ratings.

CONCLUSIONS

Compared to TAU, MI for adolescents with problematic SU is used to reduce both heavy alcohol use and overall days of alcohol use. We use these findings to lend further support to calls for wider implementation10 of MI for adolescents with problematic alcohol use in primary care settings.

Unfortunately, we found no evidence that decreased cannabis use results from brief MI. Given the ubiquity of cannabis use in adolescents, there is a vital need for additional research to identify effective interventions targeting problematic cannabis use by adolescents in primary, urgent, and emergency care settings. We use our finding (albeit with low SoE) that MI may decrease problems related to the use of alcohol and/or cannabis, such as missed school or work, to support further investigation of interventions focused on harm reduction in adolescent substance users.

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ABBREVIATIONS

AHRQ: Agency for Healthcare Research and Quality
BI: brief intervention
Crl: credible interval
MI: motivational interviewing
NMD: net mean difference
OR: odds ratio
RCT: randomized controlled trial
RoB: risk of bias
SNMD: standardized net mean difference
SoE: strength of evidence
SU: substance use
SUD: substance use disorder
TAU: treatment as usual

Dr Steele conceptualized and designed the review, designed data collection instruments and supervised data collection, performed data analysis and interpretation of data, and drafted and revised the manuscript; Dr Becker assisted in conceptualization and design, categorized intervention components, reviewed data collection, and critically reviewed the manuscript; Dr Danko assisted in conceptualization and design, categorized intervention components, and critically reviewed the manuscript; Dr Balk assisted in conceptualization and design, reviewed data collection, collected data including risk of bias assessments, and critically reviewed the manuscript; Ms Adam performed the literature search, participated in data collection and interpretation of data, and critically reviewed the manuscript; Dr Saldanha participated in data collection, risk of bias assessments, and interpretation of data and reviewed and revised the manuscript; Dr Trikalinos oversaw protocol conception and design, performed primary meta-analyses, supplemental analysis, and interpretation of data, and critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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