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REVIEW

ADDICTION SSA

Effects of brief substance use interventions delivered in general medical settings: a systematic review and meta-analysis

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Abstract

Aims: To estimate effects of brief substance use interventions delivered in general medical settings.

Methods: A systematic review and meta-analysis of randomized trials conducted since 1990 of brief substance use interventions in patients of any age or severity level recruited in general medical settings. Primary outcomes were any measure of substance use or substance-related consequences (indexed with Hedges' g and risk ratios). Mixed-effects meta-regressions were used to estimate overall effects and predictors of effect variability. Analyses were conducted separately by brief intervention (BI) target substance: alcohol only or drugs.

Findings: A total of 116 trials (64 439 participants) were identified; 111 (62 263 participants) provided effect size data and were included in the meta-analysis. Drug-targeted BIs yielded significant small improvements in multiple drug/mixed substance use (Hedges' g ($\overline{g}$) = 0.08; 95% CI = 0.002, 0.15), but after adjusting for multiple comparisons, they did not produce significant effects on cannabis use ($\overline{g}$ = 0.06; 95% CI = 0.001, 0.12), alcohol use ($\overline{g}$ = 0.08; 95% CI = −0.0003, 0.17), or consequences ($\overline{g}$ = 0.05; 95% CI = 0.01, 0.10). Drug-targeted BIs yielded larger improvements in multiple drug/mixed substance use when delivered by a general practitioner ($\overline{g}$ = 0.19; 95% CI = 0.187, 0.193). Alcohol-targeted BIs yielded small beneficial effects on alcohol use ($\overline{g}$ = 0.12; 95% CI 0.08, 0.16), but no evidence of an effect on consequences ($\overline{g}$ = 0.05; 95% CI = −0.04, 0.13). However, alcohol-targeted BIs only had beneficial effects on alcohol use when delivered in general medical settings ($\overline{g}$ = 0.17; 95% CI = 0.10, 0.24); the findings were inconclusive for those delivered in emergency department/trauma centers ($\overline{g}$ = 0.05; 95% CI = 0.00, 0.10).

Conclusions: When delivered in general medical settings, alcohol-targeted brief interventions may produce small beneficial reductions in drinking (equivalent to a reduction in 1 drinking day per month). There is limited evidence regarding the effects of drug-targeted brief interventions on drug use.

KEYWORDS
Brief intervention, emergency department, meta-analysis, primary care, systematic review

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INTRODUCTION

Given the detrimental sequelae associated with heavy episodic drinking and other drug use [1–5], a growing body of research has evaluated preventive interventions targeting alcohol and other drug use (referred herein collectively as "substance use"; whereas "drug use" is used to refer specifically to any licit/illicit substance use other than alcohol). One approach is the brief intervention (BI), defined here as a talk or counseling intervention delivered in a circumscribed time frame that aims to promote substance-related behavior change [6]. BIs are often incorporated into a screening, brief intervention, and referral to treatment model: patients are initially screened to identify unhealthy use, with BIs then tailored to patients' substance use levels and supplemented with treatment and/or referrals to other substance-related services. By definition, BIs are short in contact time, typically lasting <1 hour [7,8]; otherwise, BIs can vary in structure, targets, clinician/interventionist, and intervention philosophy.

BIs may be well-suited for delivery in some general medical (GM) settings, where a range of non-specialized healthcare services are provided to patients of various ages with a wide array of health conditions. In these settings, clinicians have numerous opportunities to screen and discuss alcohol and other drug use with non-treatment-seeking patients, but limited time to deliver services beyond treatment of the presenting condition. Given the brevity of screening and BIs in GM settings, if effective, these interventions offer a potentially cost-efficient method for addressing unhealthy substance use, particularly among non-treatment-seeking patients [9–13]. Recent estimates suggest alcohol screening and BIs delivered in primary care may result in a cost-effectiveness ratio of €5400 per quality adjusted life year gained [14], with BIs offering similar benefits, but lower cost, than more intensive brief treatments [15]. Because BIs delivered in GM settings have the potential advantages of low cost and minimal clinician effort [16,17], an important question is whether and under what circumstances they meaningfully reduce alcohol and other drug use.

Despite extensive research on drug and alcohol BIs delivered in GM settings, findings of this research have not been summarized in a rigorous evidence synthesis that includes both alcohol- and other drug-targeted BIs and includes GM settings other than primary care settings. Further, to date, there has not been a comprehensive synthesis that focuses on variability in effects of BIs. Prior reviews indicate that alcohol BIs delivered in healthcare settings can be effective in reducing self-reported alcohol use, but effect sizes vary widely and many studies report null findings [8,18–25]. Moreover, there are fewer existing trials evaluating the efficacy of BIs targeting drugs other than alcohol [26,27]. In the absence of quantitative syntheses, prior narrative reviews have highlighted the inconsistency of BI effects on drug use [18,26,28–31], leading for calls to reconsider how unhealthy substance use is addressed in primary care settings [32].

Effects of BIs may, therefore, vary depending on whether the intervention targets alcohol or drugs, but findings may also vary depending on characteristics of the BIs, patients, clinicians, settings, and study methodology. For instance, BIs may be more effective when they feature clinician advice [33,34], or incorporate decisional balance and goal-setting exercises when targeting alcohol use among adolescents, [20] but not necessarily among adult populations [35,36]. BIs may also be more effective among younger adults, males, and Latino patients, although results have varied significantly across trials [8,20,37,38]. Prior reviews also suggest BIs may be more effective when delivered in primary care versus hospital/emergency department settings [20,39]. Finally, variation in effects—and null findings in particular—may be attributable to whether trials rigorously assessed BI efficacy or instead tested real-world clinical effectiveness [40–43], or to other aspects of trial quality [44,45].

A comprehensive and up-to-date synthesis examining whether and under what conditions BIs delivered in GM settings reduce alcohol and other drug use is needed to summarize the accumulating literature on the efficacy of BIs for reducing drug use and associated consequences.

Study objectives

This systematic review and meta-analysis sought to (i) estimate the overall efficacy of alcohol and other drug BIs in GM settings; (ii) determine whether outcome domain, study methodology (comparator type, reporting quality, and risk of bias), intervention features (target [alcohol or other drug], setting, and duration), and participant characteristics (age, gender, and race/ethnicity composition) were associated with BI efficacy; and (iii) assess study quality and publication bias in this literature.

METHODS

Protocol and registration

The protocol for this review was pre-registered in the PROSPERO registry CRD42018086832 [46] and the analysis plan was pre-registered on the Open Science Framework [47].

Eligibility criteria

Eligible studies were those using a randomized controlled trial (RCT) design to evaluate the effects of an alcohol or other drug BI delivered in a GM setting relative to a less active comparison condition (e.g. no treatment, sham, and treatment as usual). Trials had to be reported in 1990 or later and report at least one post-BI outcome of substance use or substance-related consequences. BIs must have been delivered in four or fewer sessions to participants recruited in a GM setting (defined as emergency departments, community based, university based, outpatient, inpatient, private provider, student health centers, or other GM settings such as primary care). BIs delivered in specialized clinics, substance use treatment facilities, or pharmacies were outside

the review scope. Given our focus of examining overall efficacy and variability in effects, eligible BIs were not required to implement a screening assessment before the BI (although 97% of included studies used patient samples screened as having problematic substance use; see Table 1). Eligible samples included patients of all ages and baseline severity levels.

Search strategy

We used a comprehensive search to identify trials. The following databases (hosts) were searched from 1990 through March 31, 2020: PubMed; Nursing/Academic Edition (EBSCO); ERIC, Applied Social Sciences Index and Abstracts, Dissertations and Theses Global, Social Services Abstract (ProQuest); PsycINFO (PsycNET); Cochrane Central Register of Controlled Trials; World Health Organization (WHO) International Clinical Trials Registry; and National Institutes of Health (NIH) RePORTER. See Supporting information for full PubMed search strategy. We checked the bibliographies of all identified studies, including prior reviews and meta-analyses, and conducted hand-searches of the 1990 to 2020 tables of contents in *Addiction*, *Addictive Behaviors*, *Campbell Systematic Reviews*, and *Journal of Studies on Alcohol and Drugs*.

Study selection and data extraction

Study selection and data extraction were conducted by research assistants trained and supervised by the first author. At the first stage of data collection, two reviewers independently screened titles/abstracts to eliminate clearly irrelevant studies. Any study deemed potentially relevant by at least one reviewer proceeded to the second stage, during which two reviewers independently screened the full text to make a final eligibility determination. At the third stage, two reviewers independently extracted data for all eligible trials. Any disagreements at the second and third stages of screening and coding were resolved by the first author. All data extraction followed a standardized coding protocol using the procedures defined below (see Supporting information for the coding manual).

Effect sizes

For continuous outcomes, effect sizes were represented with the small-sample corrected standardized mean difference (Hedges' *g*); with positive values indicating beneficial BI effects [48]. For binary outcomes, effects were represented with risk ratios (relative risks), coded such that values >1.0 indicated beneficial BI effects. All outlying effect sizes were double-checked for accuracy and Winsorized to less extreme values (see analysis plan in Supporting information). For the 12 trials that used cluster RCT designs, standard errors of effect sizes were adjusted to account for the design effect [49].

Study reporting quality, risk of bias, and design assessment

Our coding of study reporting quality, risk of bias, and study design is detailed in the study protocol [47]. Risk of bias assessments were collected using the Cochrane Collaboration's risk of bias tool for RCTs [50], with high, low, or unclear risk of bias in six domains. Ratings across domains were summarized in an overall risk of bias categorization, defined as: low (all domains rated low), high (any domain rated high), and unclear (any domain rated unclear and no domains rated high).

Study level moderators

We collected data on effect size moderators related to interventionist/setting, BI features, and aggregate study demographics. For interventionist/setting, we measured GM setting type (emergency department/trauma center vs other GM setting) and interventionist delivering most of the BI (general practitioner, primary care clinician, behavioral specialist, and other clinician/interventionist). For BI features, we measured delivery modality (in-person, telephone, or electronic), intervention duration (in minutes), and presence/absence of booster sessions. For aggregate study demographics, we measured age group (adolescent/young adult [up to age 25] only vs mixed ages/adult only), % female, and % white.

Statistical methods

All meta-analyses were conducted using meta-regression models with robust variance estimates to accommodate dependent effect sizes [51]. Random-effects meta-regression models were used to estimate overall mean effect sizes, and mixed-effects meta-regression models (i.e. random study level effects and fixed moderator effects) were used for all moderator analyses. Results are only presented for statistical models with adequate degrees of freedom after accounting for small sample adjustments to the robust variance estimates [52]. All analyses were conducted separately by the BI target substance: alcohol only or drugs; the drug-targeted BIs included those targeting a single drug (e.g. cannabis), multiple drugs depending on patient screening results (e.g. cannabis, cocaine), or a combination of both alcohol and other drugs (e.g. alcohol and cannabis). Analyses were also conducted separately by outcome domain (alcohol, cannabis, mixed alcohol/other drug use, and substance-related consequences). All main effects meta-analyses were conducted separately for continuous and binary outcome measures, with results adjusted for pre-test values. The Benjamini-Hochberg procedure was used to control type I error rates for all analyses within an outcome domain [53].

To maximize analytic sample sizes, all moderator meta-analyses pooled continuous and binary outcomes simultaneously by

TABLE 1 Characteristics of studies, participant samples, and interventions included in qualitative and quantitative syntheses (k = 116)

Study and design characteristics	*% (n)*[a]	*Intervention features*	*% (n)*[a]
Country/region[b]		*Setting*[b]	
Asia	4 (5)	Emergency department	41 (48)
Australia/New Zealand	8 (9)	Community	34 (39)
South Africa	4 (5)	University	22 (25)
South America	3 (3)	Outpatient	11 (13)
US/Canada	59 (68)	Inpatient	5 (6)
US Midwest	22 (15)	Private provider	9 (11)
US Northeast	43 (29)	Student health center	6 (7)
US South	10 (7)	Other	18 (21)
US West	21 (14)	*Modality*[c]	
Multiple US regions	4 (3)	In person	75 (88)
Western Europe	21 (24)	Computer/tablet/smartphone	20 (24)
Multiple	2 (2)	Telephone	5 (6)
Sample type[b]		*Booster*[c]	
Screened/elevated risk	97 (112)	Booster delivered	33 (40)
Universal/unscreened	3 (4)	No. boosters, median (range)[e]	1 (1–4)
Design[b]		Duration (minutes), M (SD)[c]	26.2 (25.7)
RCT	90 (104)	*Components*[c, f]	
Cluster RCT	10 (12)	Advice	62 (75)
Comparison group type[c]		Information booklet	59 (71)
Treatment as usual/usual care	45 (55)	Decisional balance exercise	32 (39)
General health booklet	34 (41)	Goal-setting exercise	54 (66)
Sham intervention	7 (8)	Homework activity	4 (5)
No pre-test assessment usual care	3 (4)	Personalized normative feedback	75 (89)
Other	11 (14)	Training	16 (19)
Follow-up timing (w), M (SD)[d]	34.8 (43.0)	Referrals	26 (30)
Percent attrition, M (SD)[b]		Video	4 (5)
Overall	25.0 (17.7)	Website	5 (6)
Differential	5.8 (7.0)	Other	37 (46)
Implementation monitoring[b]		Clinician/interventionist characteristics	% (*n*)
Yes	61 (71)	*Typical clinician/interventionist*[c]	
No	4 (5)	General practitioner (non-primary clinician)	10 (12)
Not reported	35 (40)	Primary care provider	19 (23)
Implementation problems[b]		Behavioral specialist	28 (34)
Yes	14 (16)	Other specialist clinician	2 (2)
Possible	18 (21)	Peer	7 (9)
Not reported	68 (79)	Graduate student/trainee	2 (2)
Intention-to-treat analysis[b]		Other interventionist	33 (41)
Yes	51 (59)		
Possible	23 (26)		
No	26 (30)		
CONSORT diagram[b]			
Yes	83 (94)		
No	17 (20)		

(Continues)

TABLE 1 (Continued)

Study and design characteristics	*% (n)*[a]	*Intervention features*	*% (n)*[a]
Overall risk of bias[b]		*Profession*[c]	
Unclear	75 (87)	Medical doctor	21 (26)
High	25 (29)	Physician's assistant	1 (1)
Participant characteristics	*M* (*SD*)[h]	Nurse	11 (14)
Average age[b]	34.1 (12.4)	Other medical specialist	2 (2)
Sample age group, % (n)[b]		Psychologist	8 (10)
Adolescent/young adult	24 (28)	Social worker	6 (8)
Mixed or adult only	76 (88)	Other behavioral health specialist	13 (16)
Percent female composition[b]	38.7 (22.7)	Other lay provider	16 (20)
Race/ethnicity composition[b]		Could not tell	23 (29)
Percent Asian	13.9 (30.9)		
Percent Black	28.9 (25.0)		
Percent Latinx	24.2 (27.2)		
Percent White	59.9 (27.6)		

k = number of studies.
[a]Percentages and counts shown unless otherwise indicated.
[b]Estimates calculated at study level.
[c]Estimates calculated at intervention or comparison group level, as appropriate.
[d]Estimates calculated at effect size level.
[e]Number (No.) of boosters calculated only among studies delivering boosters; one study (Córdoba *et al*. 1998) provided a variable number of boosters and is not included in estimates.
[f]Interventions could use multiple components; percentages reflect proportion of all intervention groups using each component.
[h]Means and standard deviations shown unless otherwise indicated. See Supporting Information Table S1 for a version of this table with descriptive details disaggregated by BI target (i.e. by trials of drug-targeted or alcohol-targeted BIs).

converting risk ratios into standardized mean differences using the Cox transformation [54]. Moderation models included a control variable indicating whether the effect size was derived from continuous/binary data. Differences between moderator subgroups were assessed for statistical significance using the coefficients from the mixed-effects meta-regression models, with results presented as predicted subgroup means from those models. Heterogeneity was assessed using τ^2, I^2, and 95% prediction intervals [55]. The prediction interval (PI) provides a useful representation of the variability in effects across settings/contexts, and provides an expected range of true effects in future similar trials [55,56]. Publication bias was assessed using contour-enhanced funnel plots and Egger regression tests [57,58]. Sensitivity analyses were conducted to assess the impact of Winsorizing effect sizes, imputation of missing cluster size and intraclass correlation values (for cluster-RCTs), and the approximated within-study effect size correlation. Mean effect estimates were not found to be sensitive to any of these modeling decisions. Trial authors were contacted to obtain any missing statistical information needed for effect size estimation. Because missing data on effect size moderators was limited and a missing at random assumption could not be reasonably justified, imputation was not used to recover missing values.

RESULTS

Study characteristics

A total of 116 trials (37 drug-targeted; 79 alcohol-targeted) with 64 439 participants met eligibility criteria and were included in the overall synthesis (Figure 1; see Supporting information for references to included trials); 111 of those 116 trials (62 263 participants; 22 966 drug-targeted; 39 297 alcohol-targeted) provided effect size data and were included in the meta-analysis. The majority (81%) of drug-targeted interventions were general substance use interventions targeting the patients' primary drug of choice, with only 19% targeting a specific drug (e.g. cannabis, prescription opioids, benzodiazepines). Most trials were conducted in the United States or Canada (59%). Nearly all (97%) trials used a screened or elevated risk sample, most (90%) used an individually randomized design, and approximately half (45%) used a treatment as usual comparison. The average age of participants was 34.1 years (SD = 12.4), and samples were composed of majority male (mean proportion female = 38.7%, SD = 22.7) and white (mean proportion = 59.9%, SD = 27.6) participants. One-quarter (25%) of trials were rated as high overall risk of bias, with 75% rated as unclear (Table 1).

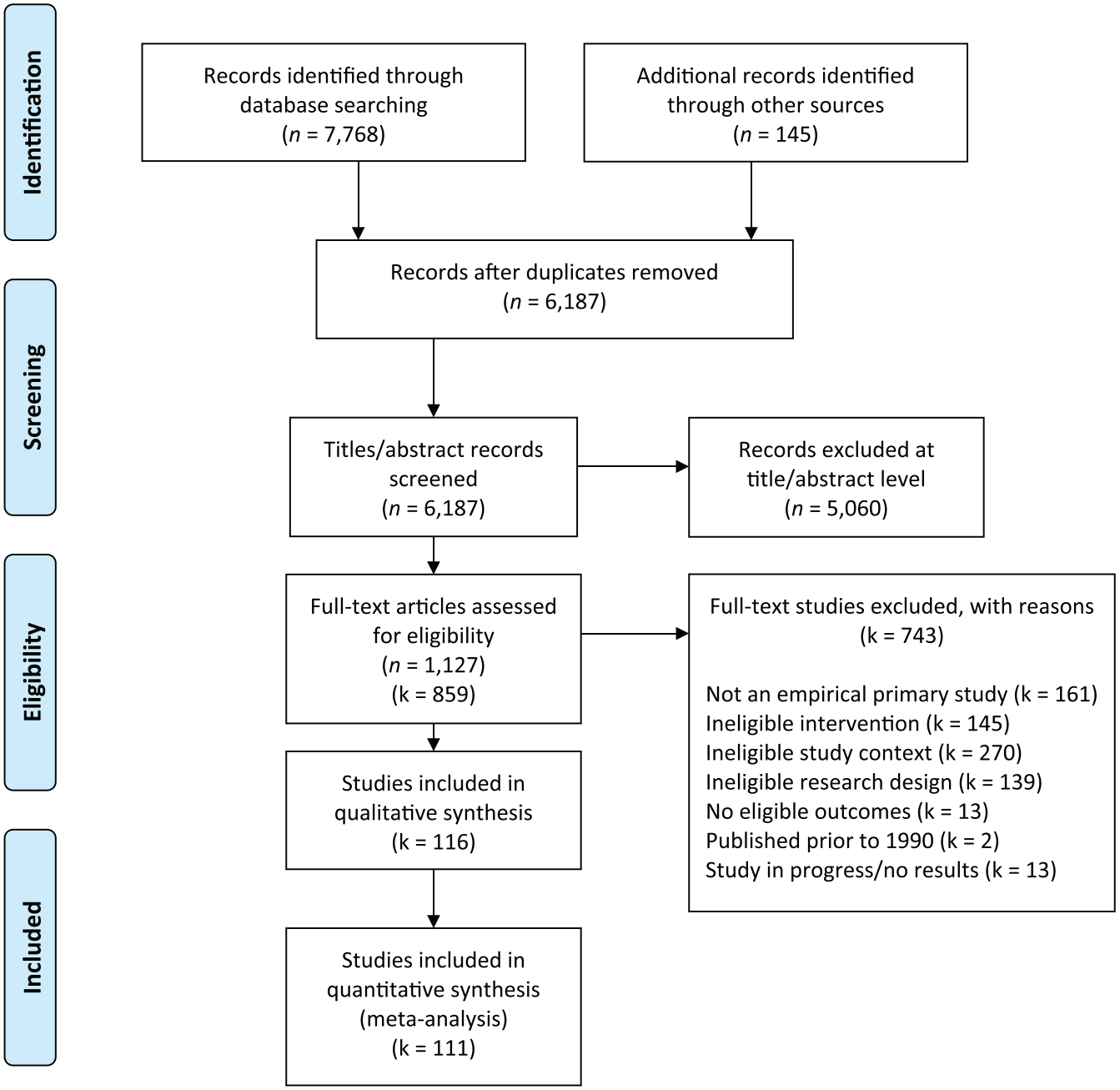

FIGURE 1 PRISMA flow diagram displaying numbers of reports and studies included in review

Forty-one percent of BIs were delivered in emergency departments, 34% in community healthcare settings, and 22% in university-based healthcare settings. Most BIs (75%) were delivered in-person, and one-third (33%) were delivered with at least one booster session. The average duration of BIs was 26 minutes (SD = 25.7); the most common intervention components reported were personalized normative feedback (75%), prescriptive advice (62%), information booklets (59%), and goal-setting exercises (54%). The BI interventionist was most commonly a behavioral specialist (28%), primary care clinician (19%), or other general practitioner other than the patient's primary care clinician (10%).

Average effects

Drug-targeted interventions

Overall, there was no evidence that BIs targeting drugs had a significantly beneficial or harmful effect on participants' cannabis use, alcohol use, or substance-related consequences after adjusting for multiple comparisons (Table 2). These meta-analyses likely had limited statistical power, however, given the small number of trials evaluating drug-targeted BIs (k = 16). The mean effect for continuously measured multiple drug/mixed substance use outcomes was

TABLE 2 Pre-test-adjusted mean effect sizes, 95% CIs, and heterogeneity statistics by brief intervention target, outcome domain, and effect size type

	Drug-targeted interventions				*Alcohol-targeted interventions*			
Outcome domain	$\overline{ES}$ *[95% CI]*	*[95% PI]*	τ^2	I^2 *(%)*	$\overline{ES}$ *[95% CI]*	τ^2 *[95% PI]*	τ^2	I^2 *(%)*
Effect size type								
Alcohol use								
SMD	0.08 [−0.0003, 0.17]$_{12,\ 71}$	[−0.09, 0.26]	0.00	27.17	**0.12 [0.08, 0.16]**$_{60,\ 396}$	[−0.12, 0.37]	0.01	51.21
RR	1.01 [0.92, 1.11]$_{8,\ 39}$	[0.93, 1.10]	0.00	0.00	**1.11 [1.04, 1.19]**$_{27,\ 105}$	[1.05, 1.19]	0.00	0.00
Cannabis use								
SMD	0.06 [0.001, 0.12]$_{13,\ 53}$	[0.004, 0.11]	0.00	0.00	—	—		—
RR	—	—		—	—	—		—
Multiple drug/mixed substance use								
SMD	**0.08 [0.002, 0.15]$_{16,\ 93}$**	[−0.10, 0.25]	0.01	27.28	—	—		—
RR	—	—		—	—	—		—
Consequences								
SMD	0.05 [0.01, 0.10]$_{12,\ 80}$	[−0.21, 0.31]	0.01	48.33	0.05 [−0.04, 0.13]$_{15,\ 64}$	[−0.10, 0.19]	0.00	18.41
RR	—	—		—	1.06 [0.94, 1.18]$_{8,\ 38}$	[0.95, 1.17]	0.00	0.00

Results in boldface are significantly different from null value (i.e. indicating no difference between intervention and comparison conditions) after Benjamini-Hochberg adjustment for multiple comparisons. $\overline{ES}$ = average effect size; CI = 95% confidence interval with robust standard errors; PI = 95% prediction interval; SMD = bias-adjusted standardized mean difference (Hedges' *g*); RR = risk ratio;
— = indicates results not available because of inadequate effect sizes and/or degrees of freedom; subscripts indicate *k* = number of studies, *n* = number of effect sizes.

statistically significant ($\overline{g}$ = 0.08, 95% CI = 0.002, 0.15; *k* = 16; *n* = 93), suggesting that on average, drug-targeted BIs yielded significant, but small reductions in participants' mixed substance use. Between-study heterogeneity was minimal (τ^2 = 0.01), although 27% of observed variability was attributable to true heterogeneity, so considerable variation in effects could be expected in similar future trials (95% PI = −0.10, 0.25).

Alcohol-targeted interventions

For alcohol-targeted BIs, syntheses were only estimable for two outcome domains: alcohol use and substance-related consequences (Table 2). Overall, alcohol-targeted BIs were associated with significant, but small reductions in alcohol use; this was consistent in the models pooling effects from continuous ($\overline{g}$ = 0.12, 95% CI = 0.08, 0.16; *k* = 60; *n* = 396) and dichotomous data (RR = 1.11, 95% CI = 1.04, 1.19; *k* = 27, *n* = 105). Between-study heterogeneity was minimal (τ^2 = 0.01; τ^2 = 0.00), but 51% of the observed variability was attributable to true heterogeneity, suggesting considerable variation in effects could be expected in similar future trials (95% PI_g = −0.12, 0.37). Finally, there was no evidence that alcohol-targeted BIs were associated with substance-related consequences, although there was a small amount of heterogeneity in these effects and results should be interpreted cautiously given the small number of contributing trials.

Moderation effects

Drug-targeted interventions

There was limited availability of effect sizes from drug-targeted BI trials across moderator levels, resulting in a small number of interpretable findings. Moreover, there was generally insufficient power to reliably assess whether drug-targeted BIs were significantly more (or less) effective in reducing alcohol use, cannabis use, or consequences outcomes across the measured moderators. Nonetheless, results from the planned moderator analyses indicated that after adjusting for multiple comparisons, drug-targeted BIs yielded larger improvements in multiple drug/mixed substance use outcomes when delivered by a general practitioner ($\overline{g}$ = 0.19, 95% CI = 0.187, 0.193) compared to other interventionists ($\overline{g}$ = 0.21, 95% CI = −0.26, 0.68, for primary care providers; $\overline{g}$ = 0.04, 95% CI = −0.34, 0.42 for behavioral specialists; $\overline{g}$ = 0.05, 95% CI = −0.88, 0.97 for peer providers; $\overline{g}$ = 0.06, 95% CI = −0.04, 0.17 for others).

Drug-targeted BI effects on multiple drug/mixed substance use outcomes were significant and positive when delivered without a booster ($\overline{g}$ = 0.12, 95% CI =0.05, 0.19) versus with a booster ($\overline{g}$ = 0.07, 95% CI = −0.08, 0.22); when no implementation problems were reported ($\overline{g}$ = 0.11, 95% CI = 0.05, 0.17) versus with possible problems ($\overline{g}$ = 0.05, 95% CI = −1.77, 1.87); and when compared to a treatment as usual condition ($\overline{g}$ = 0.15, 95% CI = 0.06, 0.23) versus other control ($\overline{g}$ = 0.08, 95% CI = −0.02, 0.18); however, none of these

TABLE 3 Moderator effects for alcohol-targeted interventions, by outcome domain

	Outcome domain	
	Alcohol use	***Consequences***
Categorical moderators		
Comparison group type		
Other types	**0.12 [0.06, 0.19]**$_{62, 501}$	0.03 [−0.13, 0.20]$_{20, 102}$
Treatment as usual	**0.10 [0.03, 0.17]**$_{62, 501}$	0.06 [0.00, 0.13]$_{20, 102}$
Implementation monitoring		
Yes	**0.10 [0.05, 0.15]**$_{62. 501}$	0.06 [−0.01, 0.13]$_{20, 102}$
Not reported	**0.14 [0.05, 0.23]**$_{62, 501}$	—
Implementation problems		
Yes	0.15 [−0.04, 0.35]$_{62, 501}$	—
Possible	0.05 [−0.02, 0.13]$_{62, 501}$	—
Not reported	**0.11 [0.06, 0.16]**$_{62, 501}$	—
Intention-to-treat analysis		
Yes	**0.10 [0.05, 0.15]**$_{61, 497}$	0.09 [0.02, 0.16]$_{20, 102}$
Possible	0.11 [−0.02, 0.24]$_{61, 497}$	—
No	**0.14 [0.03, 0.26]**$_{61, 497}$	—
CONSORT diagram reported		
Yes	**0.08 [0.04, 0.12]**$_{62, 501}$	0.03 [−0.04, 0.11]$_{20, 102}$
No	**0.24 [0.07, 0.41]**$_{62, 501}$	—
Overall risk of bias		
High	0.02 [−0.07, 0.11]$_{62, 501}$	—
Unclear	**0.14 [0.08, 0.19]**$_{62, 501}$	0.07 [0.01, 0.14]$_{20, 102}$
Setting		
Emergency department	0.05 [0.00, 0.10]$_{62, 501}$	0.00 [−0.08, 0.08]$_{20, 102}$
Other general medical setting	**0.17 [0.10, 0.24]**$_{62, 501}$	0.11 [0.02, 0.20]$_{20, 102}$
Modality		
In-person	**0.14 [0.08, 0.20]**$_{61, 497}$	—
Computer/tablet/smartphone	0.10 [0.01, 0.18]$_{61, 497}$	—
Telephone	0.01 [−0.07, 0.10]$_{61, 497}$	—
Booster delivered		
Yes	**0.16 [0.07, 0.25]**$_{62, 501}$	—
No	**0.10 [0.04, 0.15]**$_{62, 501}$	0.03 [−0.04, 0.11]$_{20, 102}$
Age group		
Adolescent/young adult	**0.11 [0.04, 0.18]**$_{62, 501}$	—
Mixed or adult only	**0.12 [0.06, 0.17]**$_{62, 501}$	0.02 [−0.06, 0.10]$_{20, 102}$
Continuous moderators		
Overall attrition	−0.28 [−0.78, 0.22]$_{58, 493}$	0.15 [−0.33, 0.64]$_{20, 102}$
Differential attrition	0.47 [−0.82, 1.77]$_{52, 371}$	0.19 [−4.60, 4.99]$_{16, 69}$
Efficacy-to-effectiveness scale score	−0.01 [−0.03, 0.01]$_{62, 501}$	−0.02 [−0.05, 0.02]$_{20, 102}$
Duration	0.00 [−0.003. 0.004]$_{54, 443}$	0.00 [−0.01, 0.003]$_{16, 90}$
Proportion female	−0.21 [−0.52, 0.09]$_{58, 487}$	0.24 [−0.05, 0.52]$_{19, 100}$
Proportion White	0.02 [−0.23, 0.28]$_{33, 280}$	—

Predicted mean effect sizes and 95% CIs presented for categorical moderators. Unstandardized coefficients and 95% CIs presented for continuous moderators. Results in boldface are significantly different from zero after Benjamini-Hochberg adjustment for multiple comparisons. *k* = number of studies; *n* = number of effect sizes; — = not estimable because of limited degrees of freedom.

group contrasts was statistically significant after adjusting for multiple comparisons. Similarly, effects were slightly larger in studies that did not use ITT analyses ($\bar{g}$ = 0.12, 95% CI = 0.08, 0.16 vs $\bar{g}$ = 0.11, 95% CI = −0.001, 0.22), but again, this group contrast was not statistically significant after adjusting for multiple comparisons.

Finally, drug-targeted BIs were associated with significantly worse (i.e. higher) levels of substance use consequences when delivered by a primary care provider ($\bar{g}$ = − 0.05, 95% CI = −0.06, −0.049) compared to other interventionists ($\bar{g}$ = − 0.15, 95% CI = −0.26, 0.68 for general practitioners; $\bar{g}$ = 0.06, 95% CI = −0.03, 0.15 for behavioral specialists; $\bar{g}$ = 0.11, 95% CI = −0.27, 0.49 for peer providers; $\bar{g}$ = 0.08, 95% CI = 0.01, 0.15 for others).

Alcohol-targeted interventions

Study reporting and design characteristics

Overall, the effects of alcohol-targeted BIs did not substantially differ across trials based on their comparison group type, attrition level, use of implementation monitoring, reporting of implementation problems, or use of an ITT analysis (Table 3). However, results indicated a substantially smaller reduction in alcohol use in trials that reported a CONSORT diagram ($\bar{g}$ = 0.08, 95% CI = 0.04, 0.12) versus those that did not ($\bar{g}$ = 0.24, 95% CI = 0.07, 0.41), and in studies with a high overall risk of bias ($\bar{g}$ = 0.02, 95% CI = −0.07, 0.11) compared to those with unclear overall risk ($\bar{g}$ = 0.14, 95% CI = 0.08, 0.19).

Intervention features

Alcohol-targeted BIs yielded no evidence of a significant effect on alcohol use outcomes when delivered in emergency departments/trauma centers ($\bar{g}$ = 0.05, 95% CI = −0.00, 0.10) compared to other GM settings ($\bar{g}$ = 0.17, 95% CI = 0.10, 0.24). This pattern also emerged for substance use consequences. In person delivery of alcohol-targeted BIs appeared to be associated with a larger reduction in alcohol use ($\bar{g}$ = 0.14, 95% CI = 0.08, 0.20) compared to delivery using a computer, tablet, or smartphone ($\bar{g}$ = 0.10, 95% CI = 0.01, 0.18), although this difference was not statistically significant (P = 0.38). Use of an intervention booster was associated with a larger reduction in alcohol use ($\bar{g}$ = 0.16, 95% CI = 0.07, 0.25) compared to BIs without a booster ($\bar{g}$ = 0.10, 95% CI = 0.04, 0.15). There was no evidence that duration of the BI significantly moderated efficacy on alcohol use or consequences.

Participant characteristics

A similar reduction in alcohol use was observed in studies that tested alcohol-targeted BIs in adolescent/young adult samples (all participants ≤30; $\bar{g}$ = 0.11, 95% CI = 0.04, 0.18) and in adult or mixed-age sample ($\bar{g}$ = 0.12, 95% CI = 0.06, 0.17). Alcohol-targeted BI effects on alcohol use did not significantly vary by aggregate proportion of female or white participants.

Publication bias

Contour-enhanced funnel plots and regression tests for funnel plot asymmetry suggested potential publication bias (also known as small study bias) for alcohol and cannabis use outcomes, but not for alcohol and other drug use and consequences outcomes (see Tanner-Smith *et al*. [47]). Meaningful interpretation of funnel plots was not possible, however, given limited variability in sample sizes across trials, large sample sizes in most trials, and observed heterogeneity in effects [59].

Discussion

This review synthesized findings from 116 trials and 64 439 total participants to estimate variability in the efficacy of alcohol/other drug focused BIs delivered in GM settings. We found few trials evaluating the efficacy of drug-targeted BIs; synthesizing evidence from 16 studies, we found no evidence that BIs targeting drug use significantly improved or worsened patients' use or substance-related consequences. These null effects were generally consistent across the settings, participants, and study design characteristics assessed, but results should be interpreted cautiously given the smaller body of literature on drug-targeted BIs (vs alcohol-targeted BIs). Our results suggested potential small beneficial effects when drug-targeted BIs were delivered by a general practitioner. For alcohol-targeted BIs, after synthesizing evidence from 60 studies, results were consistent with prior literature indicating small beneficial reductions in self-reported alcohol use, roughly equivalent to a reduction from 11.6 to 10.7 drinking days per month. Effects were larger for alcohol BIs delivered in-person or in a general medical setting (vs emergency department/trauma center settings), but were also larger in trials with higher risk of bias. These small effects of alcohol BIs may not be clinically meaningful at the individual level given that similar future trials are expected to yield effects no larger than 0.25 SD reductions for alcohol use; however, these small effects may still be clinically meaningful at the population level. Future research should consider the population effects of BIs, distinct from individual effects, where small mean changes over large numbers of people could potentially reduce population level harms. Further, effects of this magnitude could be clinically meaningful for certain population subgroups, such as adolescents and young adults, if a one-day reduction in drinking could interrupt a trajectory from experimentation to an alcohol use disorder.

Consistent with prior work, our results provide limited evidence that screening and BIs for drug use are efficacious for reducing drug use [27–29,60] despite consistent evidence of small beneficial effects for alcohol BIs [8,18,20]. Although identification and management of drug use may be reasonable to consider in clinical practice (for diagnosis/management of other health conditions, creating opportunities for future conversations, and inviting care-seeking), given the lack of

evidence regarding the efficacy of drug BIs, new strategies and approaches should also be explored for addressing patients' drug use. And although our finding that drug BIs may have small beneficial effects when delivered without booster sessions could be spurious, it does accord with prior literature suggesting that adding boosters may not improve the efficacy of BIs [61–64].

Our results also suggested alcohol BIs may have the smallest effects when delivered in emergency departments or trauma centers, versus other GM settings. This is likely because of differences in expectations/relationships between clinicians and patients in other GM settings that include primary care settings (e.g. patients may have longer duration and more trusting relationships with primary care providers than with emergency care providers), as well as differences across settings in patient baseline substance use severity, physical and mental health, and socioeconomic status [65]. Finally, our results indicated that any beneficial effects of alcohol BIs may be upwardly biased in trials with poorer reporting quality, so practitioners and policymakers should exercise caution when considering the magnitude of alcohol BI effects without first evaluating trial reporting quality.

The findings from this meta-analysis should be interpreted in light of several limitations. First, given the small number of trials examining drug-targeted BIs ($k = 16$), we did not have adequate power to assess heterogeneity in effects for several of the moderators of interest. Moreover, as telehealth models have become increasingly prevalent because of the COVID-19 pandemic, future research may need to examine variability in BI effects delivered via telehealth. Second, because patient characteristic moderators were collected at the study level (e.g. proportion female), we were unable to assess whether BIs were more or less effective for certain types of patients (e.g. by demographics or level of substance use severity) given the risk of ecological fallacy when using aggregate level data to make inferences about individuals. Future syntheses using individual participant data meta-analysis approaches will be better suited for examining variability in BI effects across individual patient characteristics such as age, race, ethnicity, comorbidities, and baseline substance use [66]. Third, given inconsistent reporting in individual trials, it was not possible to estimate subgroup effects for specific types of GM settings (e.g. primary care vs general hospital) or patient age groups (e.g. adolescents only). Finally, this synthesis was limited to evidence on the efficacy of BIs delivered in GM settings and did not examine efficacy in other settings (e.g. alcohol or drug treatment centers, reproductive clinics).

CONCLUSION

Unhealthy alcohol and other drug use continues to be a widespread public health concern, necessitating the identification of effective preventive approaches for decreasing risk (for which there is modest evidence in the existing literature) and for interrupting trajectories toward clinical substance use disorders (for which there is no evidence in the literature). Given their brevity, low cost, and minimal clinician effort, BIs have emerged as a promising approach for addressing substance use. When delivered in GM settings, alcohol-targeted BIs are likely to produce small reductions in drinking, but the literature does not include enough trials of drug-targeted BIs to ascertain whether they consistently reduce drug use or associated consequences. Clinical research should continue testing alcohol and drug BIs, as well as developing other novel approaches for addressing alcohol and drug use in healthcare settings, particularly those using telehealth models that maximize patient reach when in-person intervention is not possible [67]. Research on telehealth approaches could also determine whether providing ongoing support, referrals, and other resources available by telehealth after a BI is delivered leads to increased intervention efficacy.

PROTOCOL REGISTRATION DETAILS

The protocol for this review was pre-registered in PROSPERO (CRD42018086832) and the analysis plan was pre-registered in OSF (osf.io/m48g6).

ETHICAL APPROVAL

The University of Oregon Institutional Review Board (IRB) reviewed the protocol for this review and determined that the study activities did not meet the definition of research with human subjects according to Title 45 CFR 46.102 (d-f) and therefore, did not require IRB approval.

DECLARATIONS OF INTEREST

E.E.T.-S., N.J.P., and M.S.C. have no conflicts of interest to declare. R.S. reports personal fees from University of Oregon to support this work. R.S. also reports non-financial support from Alkermes, personal fees from American Society of Addiction Medicine, American Medical Association, National Council on Behavioral Healthcare, Kaiser Permanente, UpToDate/Wolters Kluwer, Yale University, National Committee on Quality Assurance, Oregon Health Sciences University, RAND Corporation, Leed Management Consulting/Harvard Medical School, Partners, Beth Israel/Deaconess Hospital, American Academy of Addiction Psychiatry, Group Health Cooperative, Checkup and Choices, International Network on Brief Interventions for Alcohol and Other Drugs (INEBRIA) supported via funds from Systembolaget, Smart Recovery, Karolinska Institute, Institute for Research and Training in the Addictions, Medical Malpractice Expert Witness, Charles University, Brandeis University, and Massachusetts Medical Society outside the submitted work; he also reports research consulting to ABT Corporation (not remunerated). R.S. is an author of primary studies included in this review, but was not involved in the data extraction or data analysis of those studies for this review.

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AUTHOR CONTRIBUTIONS

Emily Tanner-Smith: Conceptualization; funding acquisition; investigation; methodology; project administration; supervision. **Nicholas Parr:** Formal analysis; investigation; methodology; visualization. **Maria Schweer-Collins:** Investigation; methodology. **Richard Saitz:** Conceptualization; funding acquisition; supervision.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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