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e-Interventions for Alcohol Misuse

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PREFACE

Quality Enhancement Research Initiative's (QUERI) Evidence-based Synthesis Program (ESP) was established to provide timely and accurate syntheses of targeted healthcare topics of particular importance to Veterans Affairs (VA) clinicians, managers and policymakers as they work to improve the health and healthcare of Veterans. The ESP disseminates these reports throughout the VA, and some evidence syntheses inform the clinical guidelines of large professional organizations.

QUERI provides funding for four ESP Centers and each Center has an active university affiliation. The ESP Centers generate evidence syntheses on important clinical practice topics, and these reports help:

- develop clinical policies informed by evidence;
- guide the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- set the direction for future research to address gaps in clinical knowledge.

In, 2009, the ESP Coordinating Center was created to expand the capacity of HSR&D Central Office and the four ESP sites by developing and maintaining program processes. In addition, the Center established a Steering Committee comprised of QUERI field-based investigators, VA Patient Care Services, Office of Quality and Performance, and Veterans Integrated Service Networks (VISN) Clinical Management Officers. The Steering Committee provides program oversight, guides strategic planning, coordinates dissemination activities, and develops collaborations with VA leadership to identify new ESP topics of importance to Veterans and the VA healthcare system.

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EXECUTIVE SUMMARY

INTRODUCTION

Alcohol misuse is the third leading cause of preventable death in the United States and the third leading cause of morbidity and mortality worldwide. The associated costs amount to more than 1% of the gross national product in high- and middle-income countries. Substance use disorders, including alcohol use disorder (AUD), are among the most common and most costly conditions in Veterans presenting for treatment in the Veterans Health Administration (VHA) system.

Traditional treatment for AUD—intensive, but time-limited initial interventions, then less intensive follow-up care—can be prohibitive because of barriers such as sufficient funding, time, and adequately trained personnel. Even screening and brief interventions for less severe alcohol misuse, which have been recommended by the U.S. Preventive Services Task Force (USPSTF), require financial and clinical resource investments that can be problematic. Thus, electronic interventions (e-interventions) may prove a useful way to extend the reach of traditional interventions for alcohol misuse or AUD.

Eighty-seven percent of the U.S. population uses the Internet. Thus, e-interventions have the potential to reach those individuals with drinking problems who wish to remain anonymous; those who live at great distance from, cannot afford, or have little time for traditional therapy; and shift workers who need treatment to be available during non-standard business hours. Given that Veterans can encounter most, if not all, of these barriers to accessing care for alcohol misuse, e-interventions may prove a promising new avenue, especially for the younger, more Internet-savvy Veterans returning from Iraq and Afghanistan.

Definitions

Alcohol misuse: Excess daily consumption (>4 drinks/day in men, >3 drinks/day in women and men over age 65) or excess total consumption (>14 drinks/week in men, >7 drinks/week in women and men over age 65)

Alcohol use disorder (AUD): A disease characterized by the harmful consequences of repeated alcohol use (*eg*, social or physical problems), a pattern of compulsive use (*eg*, use in situations in which it is physically hazardous), and sometimes, physiological dependence on alcohol (tolerance or symptoms of withdrawal)

Standard drink: In the United States, a standard drink contains 14 grams alcohol, equivalent to:

- 12 ounces of beer (5% alcohol by volume)
- 5 ounces of wine (12% alcohol by volume)
- 1.5 fluid ounces of 80-proof spirits

Although prior reviews have evaluated computer-based interventions for alcohol misuse, our study includes a broader array of e-interventions, evaluates effects separately for student and non-student populations, and focuses on studies that report longer term, clinically important outcomes. In order to inform policy on alcohol misuse for VHA, we offer a systematic review of the randomized controlled trials (RCTs) assessing CD-ROM-based, web-based, interactive voice response (IVR), or mobile applications of e-interventions for alcohol misuse. We assess for changes in alcohol consumption, effects on medical health, and social or legal consequences of alcohol misuse.

METHODS

We conducted a primary review of the literature by systematically searching, reviewing, and analyzing the scientific evidence as it pertains to the following key questions (KQs):

- KQ 1: For e-interventions targeting adults who misuse alcohol or who have a diagnosis of AUD, what level, type, and modality of user support is provided, by whom, and in what clinical context?
- KQ 2: For adults who misuse alcohol but do not meet diagnostic criteria for AUD, what are the effects of e-interventions compared with inactive controls?
- KQ 3: For adults at high risk of AUD (*eg*, AUDIT-C ≥8), or who have a diagnosis of AUD, what are the effects of e-interventions compared with inactive controls?
- KQ 4: For adults who misuse alcohol, are at high risk of AUD, or have a diagnosis of AUD, what are the effects of e-interventions alone or used in combination with face-to-face therapy compared with face-to-face therapy alone?

Data Sources and Searches

In consultation with an expert librarian, we searched MEDLINE (via PubMed), The Cochrane Library, Embase, and PsycINFO from January 1, 2000, to August 18, 2014, for peer-reviewed, English-language RCTs. We used Medical Subject Heading (MeSH) terms and selected free-text terms for the conditions and therapy types of interest as well as the electronic delivery mode. We further reviewed the bibliographies of exemplar trials and systematic reviews. As a check for publication bias, we searched ClinicalTrials.gov to identify completed but unpublished trials.

Study Selection

Using prespecified inclusion and exclusion criteria, 2 trained investigators assessed titles and abstracts for relevance to the KQs. Full-text articles identified as potentially relevant were further examined by 2 investigators; disagreements were resolved through consensus. We included RCTs conducted in adults with alcohol misuse or AUD that compared an e-intervention to an inactive or active control and reported relevant outcomes at ≥6 months.

Data Abstraction and Quality Assessment

Data from included articles were abstracted into the final form by a trained investigator and confirmed by a second investigator. Data elements abstracted included patient descriptors, setting, features and dose of the e-intervention, characteristics of the comparator, and outcomes. When data were incomplete or missing, we contacted authors to request the data.

We assessed the quality (risk of bias) of each study using criteria specific for RCTs and summarized the overall risk of bias as low, moderate, or high. In addition to rating the quality of individual studies, we evaluated the overall strength of evidence (SOE) for selected outcomes as high, moderate, low, or insufficient using the domains: directness, risk of bias, consistency of treatment effects, precision of treatment effects, and risk of publication bias.

Data Synthesis and Analysis

While synthesizing abstracted data, we classified the e-interventions according to the level of supplementary human support provided, as follows:

- Level 1: No support; e-intervention only
- Level 2: Some support; e-intervention supplemented by non-counseling meetings with study staff
- Level 3: Therapeutic support; e-intervention supplemented by counseling with trained staff

We grouped studies into those that enrolled participants with alcohol misuse and those that enrolled participants at high risk of or with AUD. Because of important differences in the study samples and intervention designs, we planned a priori to analyze studies conducted in college student samples separately from studies conducted in other adult samples.

When meta-analysis was feasible—for alcohol consumption, meeting recommended alcohol consumption limits, binge drinking (students only), and social problems from drinking (students only)—we computed summary estimates of effect, stratified by condition for 6 and 12 months. The primary outcome—alcohol consumption—was measured using different units across trials. Therefore, we converted to a common unit (grams [g]/week) and combined using mean differences (MDs). Since studies used different outcome measures for social problems from drinking, we used the standardized mean difference (SMD) to summarize treatment effects. Dichotomous outcomes were analyzed using summary risk ratios (RRs). We evaluated for statistical heterogeneity in treatment effects using Cochran's Q and I^2 statistics. We planned subgroup analyses to explore potential sources of heterogeneity, specifying a priori: follow-up rates, treatment dose, and the level of support given with the intervention. However, planned subgroup analyses could not be performed because subgroups did not meet the prespecified minimum of 4 studies per subgroup. When there were at least 3 studies at low or moderate risk of bias, we performed sensitivity analyses to compute summary estimates after excluding studies at high risk of bias.

Where quantitative synthesis was not feasible, we analyzed the data qualitatively. We gave more weight to the evidence from higher quality studies. We focused on identifying patterns in the efficacy and safety of the interventions and finding potential reasons for inconsistency in treatment effects. When evaluating the overall SOE, we considered a difference of 3 standard U.S. drinks/week or an SMD $\geq$0.4 as clinically significant and defined precise effects as those with 95% confidence intervals (CIs) that excluded smaller effects.

RESULTS

Results of Literature Search

From 722 citations screened, we reviewed 84 full-text articles and identified 26 trials that met eligibility criteria. The populations were divided between college students (n=12) and other groups of adults (n=14). Men and women were both well-represented, and in the adult studies, the majority of participants had some college education. One study was conducted in a VA sample. Only 3 trials specifically recruited subjects who were at high risk of or had been

diagnosed with AUD. The other 23 trials recruited subjects who misused alcohol. Three trials examined IVR, and the other 23 compared an e-intervention with an inactive control. IVR is slightly different from what is generally thought of when the term "e-intervention" is used in that IVR is a technology that allows a computer to interact with humans through the use of voice and signaling over analog telephone lines. Six trials involved face-to-face therapy. A single trial used a mobile device as the delivery platform. The most commonly reported outcomes were effects on alcohol consumption, reductions in consumption to meet drinking limits, binge drinking, and the social and legal consequences of drinking.

Summary of Results for Key Questions (KQs)

KQ 1: Characteristics of and User Support for E-Interventions

Of 26 studies, only 12 relied on any type of supplementary human support, and only 4 of these included support of a therapeutic nature. Most of the studies examined a one-time intervention, delivered online or at a desktop computer, that compared an individual's alcohol consumption to their peer group norm. Generally, interventions designed for college students were less complex, having fewer and shorter sessions, and using a more limited number of strategies. Studies in other groups of adults were more intense, including studies that used therapeutic support ranging from 1.5 to 5 hours and that targeted subjects with more severe drinking problems. Other key findings are summarized below:

- Most interventions were a single session, designed to moderate alcohol consumption in individuals who screened positive on an alcohol questionnaire (*eg*, AUDIT or AUDIT-C).
- The most common components of the e-interventions were personalized normative feedback (PNF), information comparing an individual's alcohol consumption patterns to the normative behavior of a reference group, and psycho- or alcohol-specific education including the negative consequences of drinking.
- When supplementary human support was utilized (n=12), it was limited, consisting only of technical support from a research assistant in half the cases. In other cases, it was often given in combination with IVR or other telephonic or face-to-face treatment in subjects at high risk of or with AUD.
- Although many e-interventions for alcohol misuse have been studied, few have been evaluated in more than a single study meeting criteria for this review.

KQ 2: Effects of E-Interventions Compared with Inactive Controls in Adults who Misuse Alcohol

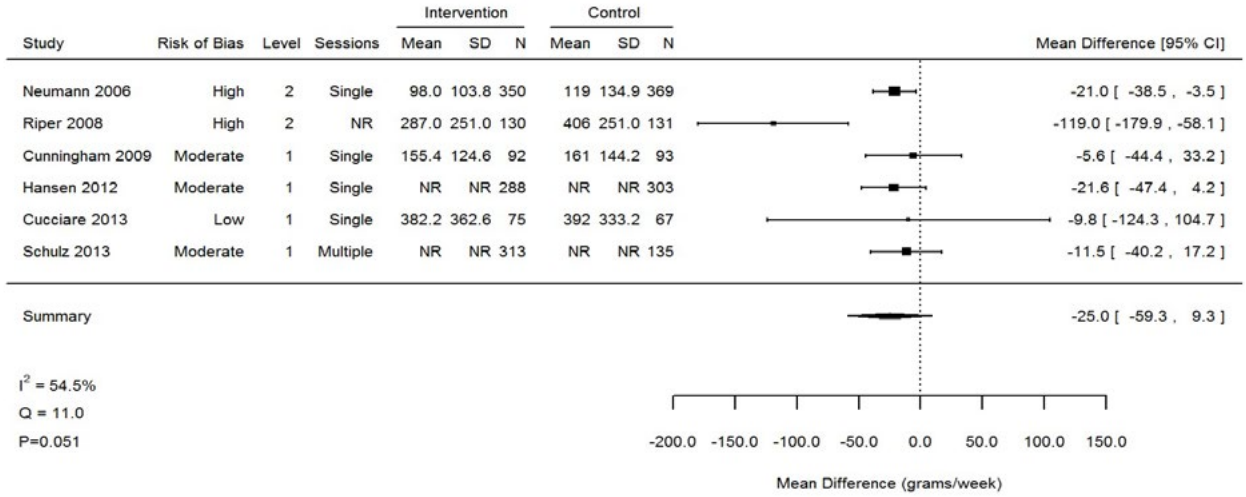
Twenty-two studies (13,929 participants) evaluated the effects of e-interventions versus inactive controls in participants with alcohol misuse. Most studies were judged to be at low (n=7) or moderate (n=12) risk of bias. Overall, the available data suggest that long-term effects of e-interventions on alcohol outcomes are modest or absent. Other key findings are summarized below:

- The most commonly reported outcome was weekly alcohol consumption, but treatment effects were relatively small and varied significantly across studies.

  - In 6 adult studies at 6-month follow-up, e-interventions were associated with a small, statistically insignificant reduction in alcohol consumption (MD -25.0 g/ week; 95% CI, -59.3 to 9.3; Figure ES-1). A sensitivity analysis limited to studies at low or moderate risk of bias found a small, statistically significant reduction in alcohol consumption (MD -14.7 g/week; 95% CI, -26.4 to -3.0).
  - In 8 student studies at 6-month follow-up, e-interventions were associated with a modest, statistically insignificant reduction in alcohol consumption (MD -12.4 g/ week; 95% CI, -26.6 to 1.9; Figure ES-2).

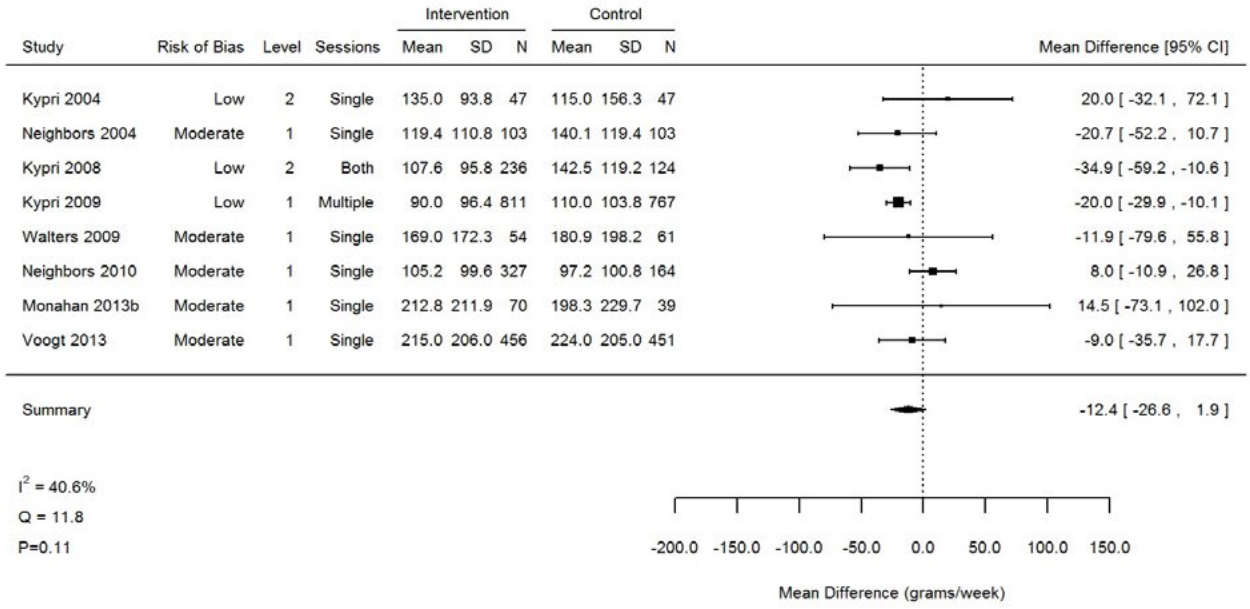
- Few studies in adults reported effects on meeting drinking limit guidelines (n=5), reducing binge-drinking episodes (n=2), or decreasing alcohol-related social problems (n=1).
- In 4 student studies, e-interventions did not result in a significant reduction in binge drinking (MD -0.1; 95% CI, -1.0 to 0.9) at 6 month follow-up.
- In 7 student studies, e-interventions showed no effect on the negative social consequences of alcohol (MD -0.04; 95% CI, -0.22 to 0.13) at 6-month follow-up.
- Longer term effects (≥6 months) of e-interventions on alcohol consumption and its associated effects on health and well-being were modest or absent in the data currently available.

Figure ES-1. Alcohol Consumption at 6 Months in Studies of Adults*



*Hansen 2012 and Schulz 2013: Means and SDs were not available, as only mean difference and CI were given.
Abbreviations: CI=confidence interval; N=number of participants; NR=not reported; SD=standard deviation

Figure ES-2. Alcohol Consumption at 6 Months in Studies of College Students



Abbreviations: CI=confidence interval; N=number of participants; SD=standard deviation

KQ 3: Effects of E-Interventions Compared with Inactive Controls in Adults at High Risk of AUD (eg, AUDIT-C ≥8) or with a Diagnosis of AUD

Only 3 studies (2 moderate, 1 high risk of bias) compared e-interventions with inactive controls in 533 patients with a diagnosis of AUD. Neither computerized feedback plus telephone counseling nor an IVR system decreased alcohol consumption or risk of relapse. A multi-component smartphone program used to support recovery following residential treatment increased abstinence (odds ratio [OR] 1.94; 95% CI, 1.14 to 3.31) and decreased risky drinking days at 12-month follow-up.

KQ 4: Effects of E-Interventions Alone or Used in Combination with Face-to-Face Therapy Compared with Face-to-Face Therapy Alone in Adults who Misuse Alcohol

Six trials (1090 participants) compared e-interventions alone or in combination with face-to-face brief motivational interviewing (BMI) with BMI alone. All studies enrolled individuals with alcohol misuse. They varied markedly with regard to setting, subject, and intervention characteristics. Studies were judged to be at low (n=2) or moderate risk of bias (n= 4). Overall, this diverse group of studies did not find a benefit of e-interventions alone or as an adjunct to face-to-face BMI compared with face-to-face BMI alone for college students or midlife primary care patients who misuse alcohol.

The effects of e-interventions alone (n=3) or in combination with BMI (n=3) versus BMI alone are summarized below:

- Combination of e-intervention plus BMI versus BMI alone in adults: IVR plus BMI was the only e-intervention compared with face-to-face treatment in non-collegiate populations. Two studies found no improvement in primary drinking outcomes with the addition of IVR.

- Combination of e-intervention plus BMI versus BMI alone in students: One study found no improvement in 12-month outcomes when computerized PNF was added to BMI.
- E-intervention versus BMI: All 3 head-to-head comparisons were conducted in college students. BMI was generally more effective. Both heavier alcohol consumption (50 g to 81 g more per week) and increased binge drinking frequency (2 to 2.5 more episodes per month) were associated with the e-intervention.

DISCUSSION

Key Findings and Strength of Evidence

We identified 26 RCTs involving over 14,000 participants with alcohol misuse, at risk of AUD, or with AUD. Participants were selected for these trials based on one or more alcohol consumption criteria, but only 3 studies based inclusion on an assessment of AUD. Studies were divided roughly equally between college students and other groups of adults. Adult participants were typically midlife (median age=41.4 years), and the majority had at least some college education, with baseline alcohol consumption in excess of 14 drinks per week. Most trials compared e-interventions with inactive controls. E-interventions were typically accessed online, consisted of one session lasting 30 minutes or less, and were completed without supplementary human support; PNF was the predominant strategy. A single trial used a mobile device as the delivery platform.

We summarize the SOE for selected outcomes in Table ES-1. Overall, there was low SOE that e-interventions compared to inactive controls did not decrease alcohol consumption outcomes in participants with alcohol misuse. In patients with AUD, a multicomponent smartphone application decreased the risk of relapse after residential treatment (SOE=low). Treatment effects varied across studies, and we were unable to explain the heterogeneity. Sensitivity analyses restricted to studies at low or moderate risk of bias were generally consistent with the primary analyses.

Consistent with previous literature, qualitative examination suggested that more intensive treatments were associated with larger decreases in alcohol consumption. Compared with face-to-face treatment, e-interventions alone or in combination with face-to-face treatment were not associated with decreased alcohol use. IVR e-interventions may be less effective than face-to-face treatment. Other outcomes were reported infrequently (*eg*, social or legal consequences of alcohol use, health-related quality of life) or not at all (*eg*, alcohol-related medical problems).

Table ES-1. Summary SOE Ratings

Outcome	Number of Studies (Participants)	Study Design/ Risk of Bias	Effect Estimate	SOE
KQ 2: E-intervention vs control in alcohol misuse				
Alcohol consumption (weekly)	17 (10,122)	RCT/Moderate	Statistically insignificant reduction of 2 U.S. standard drinks per week	Low
Met alcohol consumption limits	6 (4932)	RCT/Low	Statistically insignificant increase in adults: RR 1.22 (95% CI, 0.79 to 1.89)	Low
Alcohol consumption (binge drinking)	8 (5043)	RCT/Low	Small, statistically insignificant difference	Moderate
Alcohol-related social problems	8 (5765)	RCT/Low	No difference	Low (adults) Moderate (students)
KQ 3: E-intervention vs control in AUD				
Alcohol consumption (maintain abstinence)	3 (533)	RCT/Moderate	Increase in abstinence for adults with smartphone e-intervention: OR 1.94 (95% CI, 1.14 to 3.31) No difference with IVR or e-intervention feedback	Low Insufficient
Alcohol-related social problems	2 (409)	RCT/Moderate	No difference	Low
KQ 4:E-intervention vs face-to-face counseling				
Alcohol consumption (weekly)	3 (438)	RCT/Moderate	About 3.5 to 6 U.S. standard drinks/week higher with e-intervention in students	Low
Alcohol-related social problems	1 (210)	RCT/Moderate	Small, statistically insignificant difference in students	Insufficient
KQ 4: E-intervention + face-to-face counseling vs face-to-face counseling alone				
Alcohol consumption (weekly)	3 (668)	RCT/Moderate	No consistent difference	Low
Alcohol-related social problems	0	NA	No studies	Insufficient

Abbreviations: AUD=alcohol use disorder; CI=confidence interval; e-intervention=electronic intervention; IVR=interactive voice response; KQ=key question; NA=not applicable; OR=odds ratio; RCT=randomized controlled trial; RR=risk ratio; SOE=strength of evidence

Clinical and Policy Implications

We found a relatively small number of trials reporting longer term effects of e-interventions to address alcohol misuse. Based on the available literature, we generally found low strength of evidence of a small effect of e-interventions on longer term (≥6 months) alcohol misuse outcomes. Although prior research has found positive effects of e-interventions on alcohol consumption over the short term, those effects were also generally not maintained at longer term

follow-up. We also found limited evidence that e-interventions are not as effective as face-to-face treatment. Exploratory qualitative analyses suggest that more intensive interventions, with higher level supplementary human support (*eg*, phone counseling), could improve engagement and effectiveness. Our findings contrast with a review conducted for the USPSTF, which found that behavioral counseling decreased alcohol consumption by 3 to 4 drinks per week at long-term (≥12 months) follow-up. Most trials in the USPSTF review used multi-contact, in-person interventions, in contrast to the single-session, computer-delivered interventions in the present review. The USPSTF recommended that "health care providers should screen adults aged 18 years or older for alcohol misuse and provide brief behavioral counseling to reduce alcohol misuse for patients with risky or harmful drinking." Based on our review, e-interventions cannot currently be recommended as a substitute for in-person, multi-contact counseling.

If better e-interventions can be developed, they have the potential to overcome many barriers to conventional alcohol treatment felt by both patients (*eg*, distance, time, stigma) and professionals (*eg*, training, resources). Since annual screening with the AUDIT-C is already implemented in VA primary care clinics, effective e-interventions could meet a need for Veterans who decline traditional therapy.

Further research using other platforms and expanding the strategies employed are needed. VHA has introduced some smartphone applications (*eg*, assessment, referral), and e-interventions could be adapted to this medium, including cognitive-behavioral coping strategies and exercises tailored to the individual who would then be able to carry them with them and practice throughout the day. This is potentially very cost-effective both in terms of human resources and infrastructure expenditures. However, privacy and information security issues must be adequately addressed before initiation.

Strengths and Limitations

Our systematic review extends prior reviews by following a protocol-driven, transparent process, engaging stakeholders and policy makers, including the most recently published RCTs, and taking an inclusive approach to the definition of e-interventions. Nevertheless, there are important limitations.

Data could be biased because it was collected via self-report. It has been found that assessment itself is associated with decreased alcohol consumption similar to the placebo effect. There was relatively low intensity in most of the interventions, as well as low variability in the types of support offered in the interventions. These limitations constrained our evaluation of factors contributing to variable treatment effects and limit the reliability of the conclusions to be drawn about e-interventions as a general approach.

Applicability

The VHA screens Veterans annually for alcohol misuse with the AUDIT-C. Among those who screen positive, 80% have alcohol misuse, while 20% exceed the threshold for probable AUD. The majority of trials in this review used similar methods to enroll participants, and exclusion criteria were relatively few. Other reasons these results may have limited applicability to the VHA are that only one study was conducted in a VA sample and over one-half of the studies were conducted outside of the United States. In addition, the VA population tends to be older, less educated, and have more comorbidities than the participants in the included studies.

Research Gaps/Future Research

The finding that very low intensity e-interventions may yield small decreases in alcohol use supports further research to investigate whether higher intensity interventions would have longer term effects; whether e-interventions would be effective in patients who are older, have less education, or more comorbidities; whether more portable platforms such as iPods and smartphones would improve compliance; and whether e-interventions could be efficacious in patients with more severe problems with alcohol (*ie*, AUD). All of these questions could be answered by properly designed RCTs. There is also some question about the validity of self-reported outcomes. This could be addressed by studies that use bioverification measures or mobile monitoring.

Conclusions

We found limited evidence for small or no effects of e-interventions compared with controls on long-term (≥6 months) alcohol outcomes in participants who screened positive for alcohol misuse. Findings were even more limited for participants with AUD or comparisons of e-interventions to face-to-face treatment. Further research is needed to determine with higher confidence whether e-interventions can produce long-term benefits for alcohol-related outcomes. In particular, given the limited number and duration of intervention episodes in the studies reviewed, it is possible that these e-interventions were not designed to be robust enough to produce significant, enduring effects on alcohol misuse. As reported in previous reviews, brief in-person interventions produce sustained reductions in alcohol consumption in participants with alcohol misuse. Current evidence does not support substitution of e-interventions for brief, in-person treatment. Future research on e-interventions should include evaluations of more intensive or longer duration e-interventions for alcohol misuse.

ABBREVIATIONS TABLE

AUD	Alcohol use disorder
AUDIT	Alcohol Use Disorders Identification Test
AUDIT-C	Alcohol Use Disorders Identification Test for Clinicians
BMI	Brief motivational interviewing
CD-ROM	Compact disc read-only memory
CI	Confidence interval
e-intervention	Electronic intervention
g	Gram(s)
IVR	Interactive voice response
KQ	Key question
MD	Mean difference
MeSH	Medical Subject Heading
OR	Odds ratio
PNF	Personalized normative feedback
RCT	Randomized controlled trial
RR	Risk ratio
SMD	Standardized mean difference
SOE	Strength of evidence
USPSTF	U.S. Preventive Services Task Force
VA	Veterans Affairs
VHA	Veterans Health Administration

EVIDENCE REPORT: E-INTERVENTIONS FOR ALCOHOL MISUSE

INTRODUCTION

The economic, social, and health burden of alcohol misuse is widely recognized,[1] as is the need for effective interventions to reduce this burden.[2,3] Alcohol misuse constitutes the third leading cause of morbidity and mortality worldwide[4-6] and is the third leading cause of preventable death in the United States, after tobacco use and obesity.[7,8] Alcohol misuse contributes to a multitude of medical and psychiatric illnesses and presents across all medical specialties. The associated costs amount to more than 1% of the gross national product in high- and middle-income countries.[6,9] Veterans, who account for approximately 21.8 million people in the United States,[10] are among those significantly affected by addiction.[11] Substance use disorders, including alcohol use disorder (AUD), are among the most common and costly conditions among Veterans presenting for treatment in the Veterans Health Administration (VHA) system.[12,13] Among Veterans with at least one primary care visit in VHA within the past year, 589,094 (14.5%) screened positive for alcohol misuse, and 396,374 had a diagnosis of AUD with or without another substance use disorder (Daniel Kivlahan, PhD, e-mail communication, July 2014).

Studies on alcohol misuse conceptualize the target problem differently, and the recently introduced *Diagnostic and Statistical Manual of Mental Disorders,* 5th edition (DSM-5),[14] criteria include important revisions to the nosology. The key change for DSM-5 was to integrate "alcohol abuse" and "alcohol dependence" diagnoses into a single disorder, "alcohol use disorder" (AUD), with mild, moderate, and severe subclassifications. To provide clarity on the use of terminology for alcohol consumption patterns and related problems, Table 1 provides operational definitions for the terms used in this report.

Table 1. Definitions of the Spectrum of Alcohol Misuse*

Term	Definition (Reference Time Period: 1 Year)
Risky Use or Hazardous Use	Excess daily consumption (>4 drinks/day in men, >3 drinks/day in women and men over age 65) or excess total consumption (>14 drinks/week in men, >7 drinks/week in women and men over age 65) associated with increased risk of health problems.
Harmful use	A pattern of drinking that is already causing damage to health. The damage may be either physical *(eg,* liver damage) or mental *(eg,* depressive episodes).
Alcohol abuse (DSM-IV criteria)†	A maladaptive pattern of alcohol use leading to clinically significant impairment or distress *(eg,* failure to fulfill major obligations). Continued use despite persistent or recurrent social or interpersonal problems caused or exacerbated by alcohol.

Term	Definition (Reference Time Period: 1 Year)
Alcohol dependence (DSM-IV criteria)†	A maladaptive pattern of alcohol use leading to clinically significant impairment or distress, which may include symptoms associated with alcoholism or addiction: tolerance, withdrawal, excessive amounts consumed or time spent drinking, unsuccessful attempts to decrease use, pattern continues despite persistent problems caused by or associated with alcohol.
Alcohol use disorder (AUD) (DSM-5 criteria)†	This new category integrates the 2 DSM-IV disorders "alcohol abuse" and "alcohol dependence" into a single disorder for DSM-5: An individual continues pattern of alcohol use despite significant substance-related problems in one or more of the following areas: impaired control over use *(eg,* inability to decrease consumption), social impairment *(eg,* failing an obligation or foregoing a favorite activity), health consequences (physical or mental), and physiological dependence *(eg,* cravings). The disorder is classified as mild, moderate, or severe depending on number of symptoms.

*The term "alcohol misuse" (sometimes termed "unhealthy alcohol use") is an umbrella term for a spectrum of potentially problematic patterns of alcohol use. This table is adapted with permission from Table 1 in Jonas et al, 2012,8 and uses terminology from the DSM-IV[15] for alcohol abuse and alcohol dependence, and from the DSM-5[14] for AUD. The source table was abbreviated and updated to reflect the DSM-5 terminology for this report in collaboration with Dr. Jonas.
†Not all exact criteria are listed.

Abbreviations: AUD=alcohol use disorder; DSM-5=Diagnostic and Statistical Manual of Mental Disorders, 5th edition; DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, 4th edition

Traditional treatment approaches for AUD, which usually consist of initial intensive and time-limited interventions followed by less intensive follow-up care,[12] can be prohibitive for individuals seeking treatment for a variety of reasons. Even the use of screening and brief interventions for less severe alcohol misuse, which have been shown to be effective, are constrained by barriers such as adequate funding, time, and adequately trained personnel.[16-18] Thus, electronic interventions (e-interventions) may prove to be a useful way to extend the reach of interventions for alcohol misuse. With 87% of the U.S. population using the Internet,[19] e-interventions have the potential to reach individuals with drinking problems who wish to remain anonymous, have little time for traditional therapy, need therapy to be available during non-standard business hours due to shift work, live at great distance from traditional therapy, or cannot afford such therapy.[20,21] Given that Veterans can encounter most, if not all, of the barriers to accessing care for alcohol misuse, e-interventions may prove a promising avenue, especially for the younger, more Internet-savvy Veterans returning from recent deployments in places such as Iraq and Afghanistan.

Prior reviews focus on student or young adult populations,[22-24] do not include the most recent trials,[21,25,26] include studies with only short-term outcomes[27] or studies restricted to web-based interventions,[22,25] or combine alcohol and other substance use in the same analyses.[28] To inform

policy for VHA, we focused on studies that reported longer term, clinically important outcomes and evaluated effects separately for student and non-student populations. We offer a systematic review of randomized controlled trials (RCTs) assessing CD-ROM-based, web-based, interactive voice response (IVR), or mobile applications of e-interventions for alcohol misuse in order to assess for changes in alcohol consumption, alcohol-related health problems, alcohol-related social or legal problems, health-related quality of life (HRQOL), functional status, medical utilization, and adverse effects. We intend the evidence synthesis to be used to inform the decision whether to disseminate e-interventions for alcohol misuse in VHA, and how best to implement programs.

METHODS

TOPIC DEVELOPMENT

We followed a standard protocol for this review. The topic was nominated after a process that included a preliminary review of published peer-reviewed literature and consultation with investigators, Veterans Affairs (VA) and non-VA experts, and key stakeholders (Mental Health Web Services, Mental Health Services, and Mental Health Quality Enhancement Research Initiative [QUERI]).

The key questions (KQs) are:

- KQ 1: For e-interventions targeting adults who misuse alcohol or who have a diagnosis of AUD, what level, type, and modality of user support is provided (*eg*, daily telephone calls, weekly email correspondence), by whom (*eg*, professional counselor, technical support staff), and in what clinical context (adjunct to therapy or primary intervention)?
- KQ 2: For adults who misuse alcohol but do not meet diagnostic criteria for AUD, what are the effects of e-interventions compared with inactive controls?
- KQ 3: For adults at high risk of AUD (*eg*, AUDIT-C ≥8), or who have a diagnosis of AUD, what are the effects of e-interventions compared with inactive controls?
- KQ 4: For adults who misuse alcohol, are at high risk of AUD, or have a diagnosis of AUD, what are the effects of e-interventions alone or used in combination with face-to-face therapy compared with face-to-face therapy alone?

SEARCH STRATEGY

We conducted a primary review of the literature by systematically searching, reviewing, and analyzing the scientific evidence as it pertains to the KQs. To identify relevant articles, in consultation with an expert librarian, we searched MEDLINE (via PubMed), The Cochrane Library, Embase, and PsycINFO from January 1, 2000 to August 18, 2014, for peer-reviewed publications of trials that compared e-interventions with a waitlist control, usual care, or face-to-face therapy in adults who misuse alcohol or who have a diagnosis of AUD.

We used Medical Subject Heading (MeSH) terms and selected free-text terms for the conditions of interest; cognitive-behavioral therapy and closely related therapies, including brief counseling and health education; and the electronic delivery mode, including computer-assisted, Internet, and terms for mobile devices. We added validated search terms for RCTs.[29] We limited the search to RCTs published in English. The exact search strategies used are provided in Appendix A. We further searched the bibliographies of exemplar trials and systematic reviews for missed publications.[23-28,30,31]

To assess for possible publication bias, we searched ClinicalTrials.gov (www.clinicaltrials.gov) to identify completed but unpublished studies meeting our eligibility criteria.

All citations were imported into 2 electronic databases (for referencing, EndNote® Version X5, Thomson Reuters, Philadelphia, PA; for data abstraction, DistillerSR; Evidence Partners Inc., Manotick, ON, Canada).

STUDY SELECTION

Using prespecified inclusion and exclusion criteria, 2 investigators assessed titles and abstracts for relevance to the KQs. Full-text articles identified by either investigator as potentially relevant were retrieved for further review and examined by 2 investigators against the eligibility criteria. Disagreements on inclusion, exclusion, or the major reason for exclusion were resolved by discussion or by a third investigator. The criteria to screen articles for inclusion or exclusion at both the title-and-abstract and full-text screening stages are detailed in Table 2. In addition, trials with 3 or more arms were examined for appropriateness of all arms for inclusion. For example, any active arm that did not include an e-intervention or evidence-based face-to-face treatment was not abstracted for inclusion in the analysis.

Table 2. Inclusion and Exclusion Criteria

Study Characteristic	Inclusion Criteria	Exclusion Criteria
Population	Adults 18 years or older with alcohol misuse (*eg*, positive alcohol screen; KQ 2), at high risk of AUD, or with diagnosis of AUD (KQ 3)	Pregnant women
Intervention	Intervention must be a computer-based therapy adhering to evidence-based treatment principles and providing individually delivered treatment for alcohol misuse delivered by CD-ROM, web-based, IVR, mobile phones, or in-home electronic devices (*eg*, Health Buddy™) and may be combined with various levels of supplementary human support.	Interventions targeted at dyads (*eg*, couple) or primary prevention Computerized screening only
Comparator	The comparator for KQ 2 and KQ 3 was usual care not involving psychotherapy; waitlist; or information or attention control. For KQ 4, the comparator was face-to-face treatment.	Any comparator where the effect of the electronic aspect of the intervention could not be isolated
Outcome	Studies must report effects on at least one of the following relevant outcomes: alcohol consumption, alcohol-related health problems, alcohol-related legal or social problems, HRQOL, functional status measures, medical utilization, or adverse effects from treatment.	–
Timing	Outcomes reported at ≥6 months from randomization and initiation of intervention	Outcomes reported at <6 months
Setting	Outpatients in any setting (general medical, emergency room, and community) or participants not engaged in clinical care who are enrolled through self-assessments. We included studies where enrollment was inpatient but the majority of the intervention was delivered outpatient.	Inpatient settings for intervention delivery
Study design	RCTs with n ≥50. The sample size requirement is designed to exclude small pilot studies that typically are underpowered and have more methodological problems than larger trials. Studies with small samples and no treatment effect are also less likely to be published, increasing the risk of publication bias.	RCTs with n <50

Study Characteristic	Inclusion Criteria	Exclusion Criteria
Publications	English-language publication Published from 2000 to present* Peer-reviewed, full publication Study conducted in North America, the European Union, or Australia/New Zealand†	Non-English language Published before 2000 Abstract only

*Rationale is that the Internet was developed in the 1990s and not used routinely for interventions until 2000. Based on our assessment of studies included in existing systematic reviews, the earliest relevant publication was in 2004.
†Rationale is to include economically developed countries with sufficient similarities in healthcare system and culture to be applicable to U.S. medical care.

Abbreviations: AUD=alcohol use disorder; CD-ROM=compact disc read-only memory; HRQOL=health-related quality of life; IVR=interactive voice response; KQ=key question; n=number of participants; RCTs=randomized controlled trials

DATA ABSTRACTION

Before general use, the abstraction form templates, designed specifically for this report, were piloted on a sample of included articles and revised to ensure that all relevant data elements were captured and that there was consistency and reproducibility between abstractors. Data elements included descriptors to assess applicability, quality elements, intervention/exposure details, and outcomes. Key data elements abstracted included patient descriptors (including age, education, baseline alcohol use); setting, features and dose of the e-intervention, characteristics of the comparator, and outcomes as described in Table 2. Key features relevant to applicability included the match between the sample and target populations (*eg*, age, education level) and the training and experience of the clinician. Data from published reports were then abstracted into the final abstraction form by a trained investigator. All data abstractions were confirmed by a second investigator. Disagreements were resolved by consensus or by obtaining a third investigator's opinion. When data from published reports were missing or incomplete, we contacted study authors to request the data.

We abstracted the following key information for each included study:

- Study characteristics and design
  - Study identifiers—Author last name, year published, ID number
  - Study design—RCT, patient level or group level
  - Location (country) and recruitment setting (clinic, *etc*) of study
  - Number of study arms; types of comparison groups
  - Inclusion and exclusion criteria (identified by screen only or diagnostic criteria, *etc*)
  - Recruitment (*eg*, internet, advertisement); source (*eg*, campus, clinic)
  - Number of participants eligible for, randomized, enrolled in, and completing study
  - Analysis method for alcohol consumption: analysis of covariance (ANCOVA), mixed model, other
  - Did analysis account for missing data? (*ie*, mixed models or multiple imputation)
- Population characteristics
  - Sex, race, and age of sample

  - Inclusion of active duty or Veteran participants
  - Alcohol consumption at baseline (*eg*, drinks/week)
  - Are there important differences in alcohol diagnosis or severity (amount of consumption)?

- Description of the intervention and comparator
  - Comparator used (*eg*, waitlist, treatment as usual, informational or attention control, face-to-face treatment)
  - Comparator delivery, if applicable
  - Overall e-intervention classification (degree of support provided)
  - Type, delivery mode, and location of computer platform
  - "Brand" name of intervention
  - Theoretical basis of intervention (cognitive-behavioral therapy, motivational interviewing, *etc*)
  - Components of intervention
    - Group or individual
    - Number of sessions and minutes per session
    - Types of interactivity (*eg*, email, text messaging, telephone, peer component)
    - Techniques used (*eg*, personalized normative feedback [PNF], psychoeducation, negative consequences, tailored materials, *etc*)
  - Therapist credentials, level of therapist support (feedback, email, phone, *etc*)
  - Technical support, if offered

- Outcomes
  - Time points measured (number of follow-up assessments)
  - Study duration (longest follow-up, in weeks)
  - Treatment adherence: mean sessions completed or proportion completing all sessions
  - Patient satisfaction
  - Alcohol consumption (measured at time points closest to 6 and 12 months)
    - Standard drinks per week (and number of grams of alcohol per drink, if given)
    - Heavy drinking episodes (and definition of qualifying episode)
    - Achieved recommended drinking limits
  - Health outcomes
    - HRQOL
    - Alcohol-related accidents
    - Alcohol-related medical problems
    - Mortality
  - Utilization outcomes
    - Hospitalizations
    - Emergency department visits
  - Social or legal problems

QUALITY ASSESSMENT

We abstracted data necessary to assess the quality (risk of bias) of included trials. Across all included trials, quality criteria were applied for each RCT by 2 independent investigators. Disagreements were resolved between the 2 investigators or, when needed, by arbitration from a third investigator. We used the key risk of bias criteria described in the Agency for Healthcare Research and Quality's (AHRQ's) *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*,[32] adapted to this specific topic and customized to RCTs (Appendix B). These criteria are: adequacy of randomization and allocation concealment; comparability of groups at baseline; blinding; completeness of follow-up and differential loss to follow-up; whether incomplete data were addressed appropriately; validity of outcome measures; and conflict of interest. We assigned a summary risk of bias score (low, moderate, or high) to individual studies. Detailed quality ratings for each included study are provided in Appendix C.

DATA SYNTHESIS

While synthesizing relevant abstracted data, we developed a summary table describing the key outcomes used to test e-interventions in included RCTs. As part of this process, we classified the e-interventions according to the level of supplementary human support provided as follows:

- Level 1 (minimal): No support; e-intervention only
- Level 2 (low): Some support; e-intervention supplemented by non-counseling meetings with study staff
- Level 3 (moderate to high): Therapeutic support; e-intervention supplemented by counseling with trained staff

We grouped studies into those with eligibility criteria designed to enroll participants with alcohol misuse and those designed to enroll participants at high risk of or with AUD (*ie*, DSM-5 criteria or high threshold on screening test). Controls were grouped into inactive (waitlist, attention/information, and treatment as usual) and face-to-face active controls.

We then determined the feasibility of completing a quantitative synthesis (meta-analysis) to estimate summary effects. Feasibility depends on the volume of relevant literature, conceptual homogeneity of the trials, and completeness of results reporting. Because of important differences in the study samples and intervention designs, we planned a priori to analyze studies conducted in college samples separately from studies conducted in other adult samples.

When meta-analysis was feasible, we computed summary estimates of effect, stratified by condition (alcohol misuse versus at risk of AUD or with AUD), for both end-of-treatment and longest follow-up point ≥6 months. When trials evaluated more than one e-intervention, we averaged the effect across e-interventions.[33-36] Meta-analyses were feasible only for the e-interventions compared with inactive controls. Because the primary outcome—alcohol consumption—was measured across the trials using different units, the measurements were converted to a common unit (grams/week) and were combined using mean differences (MDs).[37,38] If means and standard deviations (SDs) were not reported, we used other statistics (*eg*, median, F values) to calculate effect sizes. Because of the relatively small number of studies, we used

a random-effects model with the Knapp and Hartung method to adjust the standard errors of the estimated coefficients.[39,40] The dichotomous outcome "met drinking limits" was analyzed using summary risk ratios (RRs). For outcomes that used different measures to evaluate the construct (*eg*, social or legal problems from alcohol misuse), we computed summary estimates using standardized mean differences (SMDs). At each time point, the SMD was calculated by subtracting the average intake of the intervention group from the average intake of the control group and dividing the result by the pooled standard deviations of the 2 groups. SMDs of 0.2 can be considered small treatment effects; 0.5, moderate effects; and ≥0.8, large effects.[41] We evaluated for statistical heterogeneity in treatment effects using Cochran's Q and I^2 statistics. An I^2 of 0% indicates no observed heterogeneity, and larger values suggest increasing heterogeneity: 25% is interpreted as low, 50% as moderate, and ≥75% as high heterogeneity.[42]

We planned subgroup analyses to explore potential sources of heterogeneity, specifying a priori: follow-up rates, treatment dose, and the level of support given with the intervention. Consistent with AHRQ's *Methods Guide*, we specified a minimum of 4 studies per subgroup to conduct the planned analyses.[43] However, because of the relatively small number of studies and lack of variability in moderator variables, subgroup analyses were not performed. When there were at least 3 studies at low or moderate risk of bias, we performed sensitivity analyses to compute summary estimates after excluding studies at high risk of bias.

We used R (R Foundation for Statistical Computing, Vienna, Austria) with the metafor package[44] to calculate the summary estimates of treatment effect. Publication bias was assessed using findings from a search of ClinicalTrials.gov. Funnel plots were not used because analyses did not meet the minimum threshold of at least 10 studies for meaningful analysis.[32]

Where quantitative synthesis was not feasible, we analyzed the data qualitatively. We gave more weight to the evidence from higher quality studies with more precise estimates of effect. A precise estimate of effect was defined as one that excluded a difference of ≤3 standard drinks per week or a SMD of ≤0.4. The qualitative syntheses focused on documenting and identifying patterns in efficacy and safety of the interventions across conditions and outcome categories. We also analyzed potential reasons for inconsistency in treatment effects across studies by evaluating differences in the study population, intervention, comparator, and outcome definitions.

RATING THE BODY OF EVIDENCE

In addition to rating the quality of individual studies, we evaluated the overall strength of evidence (SOE) for each KQ as described in AHRQ's *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.[32] In brief, this approach requires assessment of 4 domains: risk of bias, consistency, directness, and precision. These domains, along with evidence for publication bias, were considered qualitatively, and a summary rating of high, moderate, low, or insufficient SOE was assigned after discussion by 2 investigators. The 4-level rating scale consists of the following definitions:

- **High**—We are very confident that the true effect lies close to the estimate of the effect.
- **Moderate**—We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

- **Low**—Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
- **Insufficient**—Evidence on an outcome is absent or too weak, sparse, or inconsistent to estimate an effect.

When a rating of high, moderate, or low was not possible or was imprudent to make, a rating of insufficient was assigned.

PEER REVIEW

A draft of this report was reviewed by technical experts and clinical leadership. A transcript of their comments and our responses is provided in Appendix D.

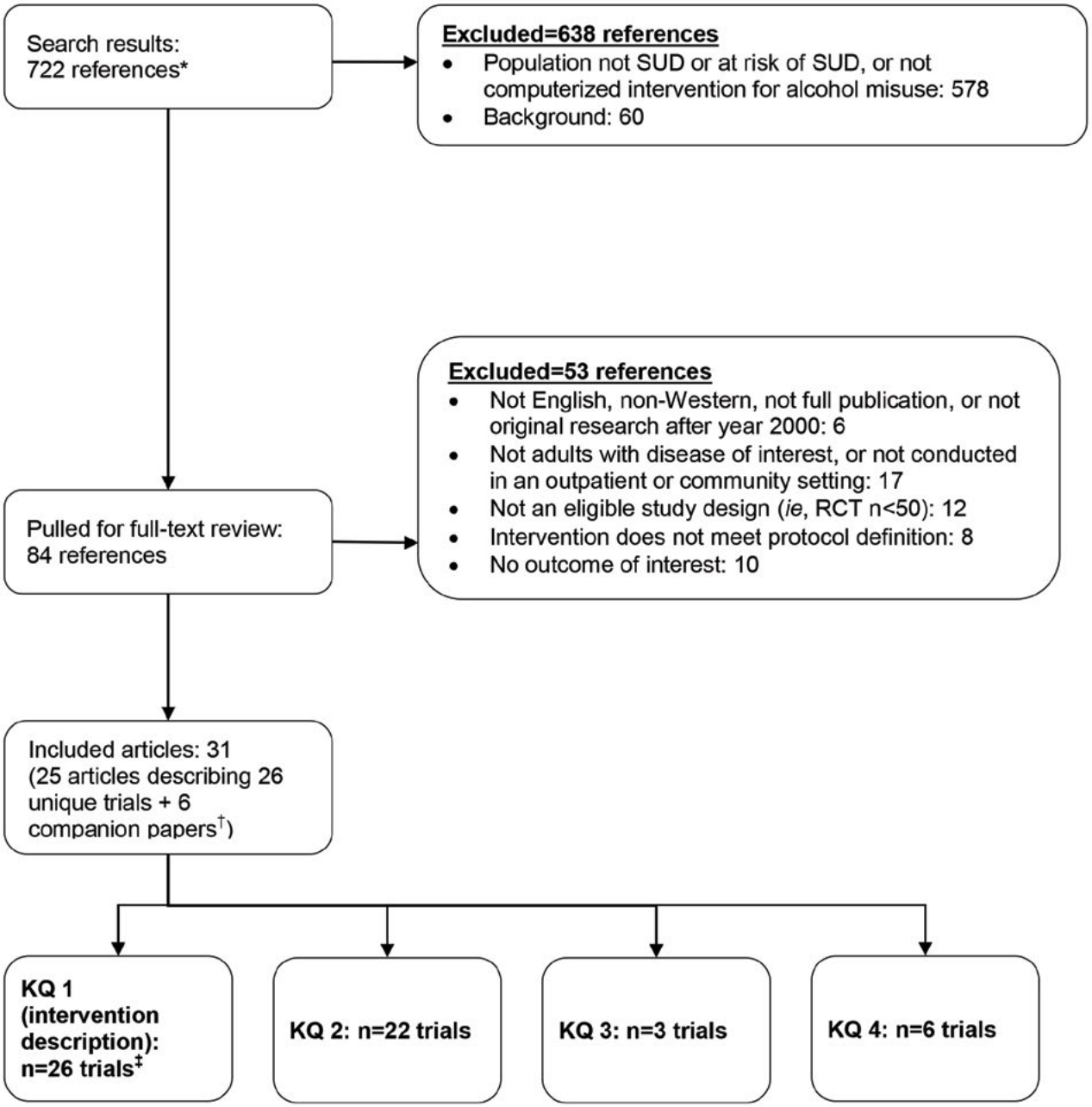
RESULTS

LITERATURE FLOW

The flow of articles through the literature search and screening process is illustrated in Figure 1. We identified 704 unique citations from a combined search of PubMed (n=319), Embase (n=154), PsycINFO (n=14), and The Cochrane Library (n=19) and a separate search for IVR studies (n=198) conducted from January 1, 2000, through August 18, 2014. We also searched the bibliographies of seminal, exemplar studies for articles not retrieved by our search (n=18), for a total of 722 citations. After applying inclusion and exclusion criteria at the title-and-abstract level, 84 full-text articles were retrieved and screened. Of these, 53 were excluded at the full-text screening stage, leaving 31 articles (representing 26 unique trials reported in 25 articles and 6 companion papers) for data abstraction. Monahan et al[45] described 2 different trials in the same publication. It was necessary to contact 12 authors for clarification of abstracted elements during the course of the data abstraction process. Eleven authors responded with the requested information.

We searched ClinicalTrials.gov (www.clinicaltrials.gov) to identify completed but unpublished studies that might meet our eligibility criteria. We found little evidence of publication bias: there were only 2 completed studies for which we could not identify a publication (NCT000658398[46] and NCT01923246[47]).

Figure 1. Literature Flow Chart



*Search results from PubMed (319), Embase (154), PsycINFO (14), and The Cochrane Library (19), IVR search (198) and manually identified studies (18)
†Manuscript reference list includes additional references cited for background and methods.
‡One article reported data from 2 trials that we analyzed separately.

DESCRIPTION OF INCLUDED STUDIES

We identified 26 trials that met eligibility criteria. Eleven trials were conducted in the United States (one in a VA sample); 15 were conducted in the European Union, Australia, or Canada. The populations were divided between college students (n=12) and other groups of adults (n=14). Adult studies enrolled midlife adults, the majority of whom had some college education (median 52%, range 8% to 83%). Across all studies, men and women were well-represented. Twenty-three trials recruited subjects who misused alcohol but did not meet criteria for AUD. Only 3 trials specifically recruited subjects who were at high risk of or had been diagnosed with AUD, but in many of the adult studies the mean weekly alcohol consumption exceeded 14 U.S. standard drinks per week. Study exclusion criteria were limited: 4 trials specifically excluded those in alcohol treatment, 3 excluded those with psychosis, and 2 excluded those with severe or terminal medical illness. Most trials were judged to be at moderate risk of bias (n=14); 5 were at low risk, and 7 were assessed as being at high risk of bias. Twenty-three trials compared an e-intervention with an inactive control, while 3 trials compared IVR (e-intervention via telephone lines) with inactive or active controls. Six studies compared e-interventions or IVR to a face-to-face control condition. A single trial used a mobile device as the delivery platform; none used the Health Buddy™ appliance. The most commonly reported outcomes were the characteristics of the interventions and their effects on alcohol consumption, reductions in consumption to meet drinking limits, binge drinking, and the social and legal consequences of drinking.

KEY QUESTION 1: For e-interventions targeting adults who misuse alcohol or who have a diagnosis of AUD, what level, type, and modality of user support is provided (*eg*, daily telephone calls, weekly email correspondence), by whom (*eg*, professional counselor, technical support staff), and in what clinical context (adjunct to therapy or primary intervention)?

Key Points

- The majority of interventions (n=14) did not utilize supplementary human support and were delivered online or at a desktop computer. A single study utilized a mobile device.
- Most interventions were a single session, designed to moderate alcohol consumption in individuals who screened positive on an alcohol questionnaire (*eg*, Alcohol Use Disorders Identification Test [AUDIT] or AUDIT for Clinicians [AUDIT-C]).
- The main components of the e-interventions were personalized normative feedback (PNF) and psychoeducation or alcohol-specific education including the negative consequences of drinking.
- When supplementary human support was utilized (n=12), it was limited, consisting only of technical support from a research assistant in half the cases. In other cases, it was often given in combination with IVR or combined with telephone or face-to-face treatment in subjects at high risk of or with AUD.

General Description

We included 26 RCTs, described in 25 publications;[33-36,45,48-67] the paper by Monahan and colleagues[45] reported results from 2 separate trials. All 26 trials were conducted in adults 18 years of age or older, but 46% were conducted specifically in college students. The included RCTs evaluated 21 unique e-interventions—IVR (3 trials) or computer-based programs (23 trials). A single trial used a mobile device as the delivery platform;[52] none used the Health Buddy™ appliance. Seventeen of the interventions used commercially available programs; however, 11 of these were each evaluated in a single study. Three programs were evaluated in 2 studies each—Electronic Check-Up to Go (e-CHUG), Alcohol 101, and Brief Alcohol Screening and Intervention for College Students (BASICS)—and these were all used in student studies. Study characteristics are described in greater details in Appendix E. Detailed descriptions of the e-interventions evaluated are provided in Appendix F. A summary of the adult versus student studies is given in Table 3.

In terms of the level of supplementary human support provided, we classified the e-interventions evaluated in the included studies as follows:

- Level 1 (minimal, n=14): No support; e-intervention only
- Level 2 (low, n=8): Some support; e-intervention supplemented by non-counseling meetings with study staff
- Level 3 (moderate or high, n=4): Therapeutic support; e-intervention supplemented by counseling from trained staff

Table 3. Characteristics of E-Interventions (KQ 1)

Characteristic	Adult Studies (n=14)	Student Studies (n=12)
Level of support:		
1 (minimal)	6	8
2 (low)	4	4
3 (moderate or high)	4	0
Number of sessions:		
1	6	8
>1	5 (3=daily IVR)	4 (2–5 sessions)
NR	3	0
Session duration:		
Median (range)	10 (10-90) minutes	30 (5-50) minutes
NR	7	0
NA (IVR)	3	0
Intervention name:		
IVR	3	0
Not named	3	3
Alcohol 101	0	2
e-CHUG	0	2
BASICS	0	2
Program used only once*	8	3

Characteristic	Adult Studies (n=14)	Student Studies (n=12)
Delivery mode:		
Accessed via the Web	8	8
Software on laptop or desktop	1	4
Mobile device	1	0
IVR	3	0
NR	1	0
Delivery location:		
Off-site (home, IVR, *etc*)	5	2
On-site (clinic, classroom, *etc*)	3	5
NR	6	5
Content of e-intervention:		
Brief intervention	10	8
PNF†	GS: 6; non-GS: 1; NR: 1	GS: 7; non-GS: 2
Psychoeducation	8	8
Alcohol-specific	3 of 8	4 of 8
Goal-setting	7	1
Negative consequences	5	4
Skills training	2	1
Self-monitoring	4	0
Tailored feedback	2	1
Relapse prevention	2	0
Other techniques (used once)‡	9	3

*Programs used only once: in adult trials: FRAMES, eScreen.se, www.drinktest.nl, Down Your Drink, Check your Drinking, minderdrinken.nl; in student trials: THRIVE, What do You Drink, College Drinkers Check-up

†For adults, the comparison group was usually a national population (n=3) or age-matched adults (n=3); for students, the comparison group was usually student peers (n=7).

‡Other treatment techniques used: for adults: CBT, computer monitoring, email, GPS, taking responsibility, text messaging, values clarification; for students: homework, decisional balance exercise,

Abbreviations: BASICS=Brief Alcohol Screening and Intervention for College Students; CBT=cognitive-behavioral therapy; e-CHUG=Electronic Check-Up to Go; E-Interventions=electronic interventions; FRAMES=feedback, responsibility, advice, menu of options, empathy, self-efficacy; GPS=global positioning system; GS=gender-specific; IVR=interactive voice response; KQ=key question; NA=not applicable; NR=not reported; PNF=personalized normative feedback; THRIVE=Tertiary Health Research Intervention Via Email

Level of Support

Over half of the e-interventions (n=14) were classified as level 1 support, which did not provide any supplementary human support, technical or therapeutic.[35,36,45,50,51,53,57,59,61,64-66,68] Eight of these were collegiate studies, and the remainder (n=6) were conducted in other adult groups. All of these studies used computerized PNF as the major component of the intervention.

Four adult[49,52,62,63] and 4 student[34,48,56,58] studies were classified as level 2 support. This usually consisted of technical support from a research assistant, so that human contact was made, but no therapy was given. Among the adult studies, Riper et al[63] used a weekly, moderated peer-support group, and Gustafson et al[52] used both a peer "bulletin board" and email contact with a therapist over the smartphone application. In the other 2 trials,[49,62] interaction with study staff was limited to screening questions and technical aid with the computer program. Among the student studies, one[48] had an in-person assessment in both the active and control conditions in addition to technical help from the staff in the e-intervention arm. In the other 3 level 2 student studies,

the only supplementary human support was technical aid from the research assistant about navigating the program.

All level 3 support studies (n=4) were conducted in non-collegiate adults.[33,54,55,60] Three of these 4 studies[54,55,60] were IVR trials. IVR is a technology that allows a computer to interact with humans through the use of voice and signaling over analog telephone lines. All of the IVR studies were 3-arm studies with one control arm and 2 active arms. In the first,[55] the intervention started with a brief intervention with the participant's primary care provider. Afterwards, participants were randomized to control, IVR, or IVR plus PNF. Participants in IVR groups were instructed to phone in to an interactive program on a daily basis and report their alcohol consumption over the previous 24 hours. Those in the PNF group received monthly PNF from their primary care provider about their consumption in the mail. The second IVR study[54] started with a motivational interview with a counselor who had either a BA or MA in psychology, supervised by a PhD in psychology, which was followed by IVR in one of the active arms. Both active arms received 2 brief (15-minute) follow-up sessions. The third IVR study[60] randomized subjects to IVR only or IVR plus follow-up phone calls with the study coordinator, whose credentials were not specified, for help or guidance in relation to the intervention. The one non-IVR level 3 study[33] also included 3 arms and provided a computerized "expert system intervention" (about which very little information was given) to both active arms, then randomized subjects either to counseling sessions via phone with "trained psychologists" at all follow-up assessment points (full care intervention) or only if needed (stepped care intervention). Whether the extra sessions were needed was determined by the answers to the follow-up questionnaires.

Intervention Intensity: Number of Planned Sessions and Mean Duration of Planned Sessions

Most e-interventions (n=14) consisted of one planned session with the computer program[33,36,45,49-51,53,56,58,59,61,62,66] and offered no further support beyond technical aid. In 5 of these 14 studies, the session lasted 10-20 minutes.[49-51,58,66] Four studies[36,45,56] had slightly more intensive e-interventions that required 30-40 minutes to complete. One study's initial session took 90 minutes to complete.[62] Four studies[33,53,59,61] did not report the length of the e-intervention, but one of these[33] was a level 3 support study in which, although there was an initial computer session, the bulk of the treatment focused on tailored, therapeutic feedback over the phone in up to 4 scheduled phone calls that lasted 30-40 minutes each.

Five studies offered 2 to 5 sessions with the e-intervention;[34,35,48,57,64]; 3 studies[52,65,67] offered subjects unlimited access to the program; one was delivered via a mobile phone application.[52] Sinadinovic et al[65] reported in response to a query that the average number of sessions was 2.66 (4.31) in the 69.3% of intervention participants who accessed the site at all. Of studies with multiple, but limited numbers of sessions, Kypri et al offered 2 short, 5- to 10- minute sessions—the initial motivational interview and a short "booster session" 1 month later—in one study[57] and repeated the 10 minute e-intervention at the 1- and 6-month follow-up in another study.[34] Schulz et al[64] provided 3 sessions (length not reported) with the computer program at 3-month intervals. Neighbors et al[35] supplied 2 to 5 computer sessions of 50 minutes each, the number and timing of which was dependent on previous adherence. Barnett et al[48] required a 45-minute session with a 25-minute "booster" session 1 month later to mimic the in-person therapy control.

The other 4 eligible studies included more supplementary human support. Riper and colleagues[63] used a weekly moderated peer support group accessed via the web for 6 weeks after the initial computerized assessment. The length of the group sessions was not reported. The remaining 3 studies were the IVR studies[54,55,60] that included a daily brief check-in call to the program for 2, 3, or 6 months. These check-in calls, averaging 3 to 5 minutes each over 60 to 180 days, totaled 3 to 9 hours of support time. In addition to the IVR time, the IVR studies had either brief initial sessions (<15 minutes) and/or follow-up sessions (40 to 120 minutes).

One study[63] did not report the number or duration of sessions, and the author did not respond to a query for this information.

Delivery Mode and Delivery Location: Online, Desktop, IVR, and On- or Off-Site

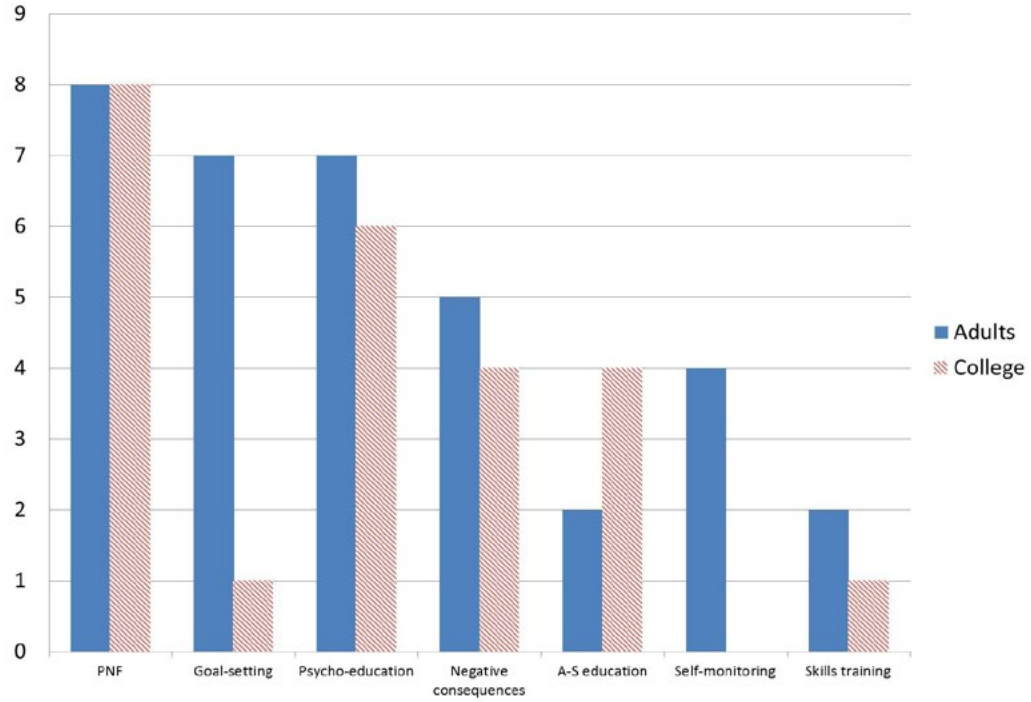
Most programs were commercially available (n=17) and accessed online (n=16). The other delivery modes were desktop- or CD-ROM-based programs (n=5), mobile phone application (n=1), or IVR (n=3). Web-delivered interventions were sometimes accessed from dedicated computers in healthcare[49] or research settings, but more often the location was not specified. Desktop-delivered interventions were typically located in a healthcare setting[50,56,62] or research lab.[45] Security features for the programs were not often reported (n=18). In the 3 IVR studies,[54,55,60] the device was linked to the participant's home phone.

E-Intervention Content: Theoretical Basis and Most Common Features

A conceptual framework for the program was reported for 16 of the e-interventions. In most cases (n=13), the e-intervention drew upon principles from motivational interviewing. Cognitive-behavioral therapy (n=4) or the Transtheoretical Model of Behavior Change (n=2) were occasionally used alone or with motivational interviewing.

The most commonly employed strategies used in the e-interventions are summarized by adult and college samples in Figure 2. Overall, PNF was the most common intervention strategy (n=16). PNF consists of a summary of the individual's alcohol intake compared to intake among the subject's peer group. The comparison group was usually gender-specific. In adult studies, they were often age-matched (n=4) or described as local or national population samples (n=3). In student studies, they were described as "student peers." After PNF, the treatment techniques used most often were goal-setting, psychoeducation or alcohol-specific education, and information about the negative consequences of alcohol misuse. Other strategies that were used infrequently included: 1) assessment of attitudes, self-efficacy, and motivation to change; 2) potential strategies to implement change such as decisional balance exercises; 3) relapse prevention strategies; and 4) links to other sources of information. The one mobile application study[52] used techniques specific to this platform— global positioning system (GPS) and texting.

Figure 2. Strategies Used in E-Interventions



Abbreviations: A-S=alcohol specific; E-Interventions=electronic interventions; PNF=personalized normative feedback

As described previously, level 1 e-interventions typically consisted of a single session that delivered PNF via computerized feedback or printout. To further illustrate level 2 and 3 interventions, we describe studies in general terms in Table 4.

Table 4. Examples of Level 2 and Level 3 Interventions (KQ 1)

Level 2: These 8 studies utilized multiple strategies beyond PNF such as the negative consequences and risks associated with alcohol intake, goal-setting, decision-making (including a decisional balance exercise in one case), measurement of motivation to change, correcting misperceptions, and skills training. In 3 cases, subjects completed an assessment that took 30 to 90 minutes.[48,56,62] Five utilized an in-person appointment with a research assistant to conduct parts of the baseline assessment, which is a larger investment on both the part of the subject and the research team.[34,49,56,58,62] Another example of a level 2 intervention used a web-moderated peer group that promoted self-monitoring, skills training, and goal-setting.[63] Finally, a level 2 intervention delivered via mobile phone offered email correspondence with a therapist, an e-bulletin board for posting messages with peers, text-messaging, and a GPS.[52]
Level 3: One study[33] used a computer psychoeducation program coupled with a brief intervention delivered by a trained psychologist, followed by 30- to 40-minute phone sessions with the psychologist at 1-, 3-, and 6-month follow-ups. Other level 3 studies[54,55,60] consisted of 1 to 4 face-to-face (n=2) or telephone-delivered (n=1) therapy sessions lasting <30 minutes, combined with daily IVR for 2, 3, or 6 months. In the IVR interventions, therapy was delivered by personnel from various disciplines (study coordinator; MD; BA- or MA-level trainee supervised by a PhD-level psychologist).[54,55,60]

Abbreviations: GPS=global positioning system; KQ=key question; IVR=interactive voice response; PNF=personalized normative feedback

Summary of Findings

Of 26 studies relevant to KQ 1, only 12 relied on any type of supplementary human support, and only 4 of these included support of a therapeutic nature. This could reflect the fact much of the research to date seems to examine whether a one-time intervention providing data generated from a computer program that compares an individual's alcohol consumption to the peer group norm (PNF) could moderate alcohol consumption in individuals with alcohol misuse. In addition to PNF, goal-setting and psychoeducation/alcohol-specific education including the negative effects and consequences of drinking were the most commonly reported strategies. Although many e-interventions for alcohol misuse are available, few have been evaluated in more than a single study. Most are accessible on the web, but whether or not a user name and password is required is usually not reported. The content of these computer programs varies widely, from one 10-minute session to an unlimited number of sessions that may take up to 45 minutes each to complete. Generally, interventions designed for college students were much less complex, having fewer, shorter sessions and using a more limited number of strategies. Studies in other groups of adults were more intense, containing the studies that used therapeutic support ranging from 1.5 to 5 hours and the studies that targeted subjects with more severe drinking problems.

KEY QUESTION 2: For adults who misuse alcohol but do not meet diagnostic criteria for AUD, what are the effects of e-interventions compared with inactive controls?

Key Points

- E-interventions identified were not intensive, typically providing one brief intervention. Existing e-interventions might not have been designed to be robust enough to produce long-term effects (≥6 months).
- Included studies generally provided data on alcohol consumption outcomes, but there were limited data on functional outcomes and quality of life.
- The available data suggest that long-term effects of e-interventions on alcohol outcomes are modest or absent.

We identified 22 studies involving 13,929 participants that met eligibility criteria for KQ 2.[33-36,45,49-51,53-59,61-67] Study characteristics are summarized in Table 5; detailed study characteristics are presented in Appendix E. Because one of the studies had 2 e-interventions and one inactive control, allowing 2 comparisons in the same study,[54] there were a total of 23 comparisons between e-interventions and inactive controls. Twelve studies were conducted in adult samples.[33,49-51,53-55,62-65,67] Of these, 4 were judged to be at low risk of bias, 6 moderate risk, and 2 high risk. Another 10 studies were conducted in student samples.[34-36,45,56-59,61,66] Of these, 3 were assessed as being at low risk of bias, 6 moderate risk, and one high risk. Across all studies, there were no differences in baseline alcohol consumption between intervention and control arms (MD 0.32 g/week; 95% confidence interval [CI], -2.87 to 3.50). In this literature, the most common study limitations increasing risk of bias were lack of participant blinding to study condition (demand characteristics) and incomplete or perceived potential for selective reporting of outcome data.

Table 5. Characteristics of E-Interventions (KQ 2)

Characteristic	Adult Studies (n=12; 7141 Participants)	Student Studies (n=10; 6788 Participants)
Delivery location/setting:		
Clinic/emergency room:	2	0
College health services	0	2
College classroom	0	1
Research lab	0	1
Home	0	2
NR	10	4
Intervention name:		
escreen	1	0
Drinktest	1	0
Down Your Drink	1	0
Check Your Drinking	1	0
Minderdrinken	1	0
Alcohol-Everything within limits	1	1
Alcohol 101	0	1
e-CHUG	0	2
BASICS	0	2
THRIVE	0	1
What Do You Drink	0	1
College Drinker's	0	1
Not named	6	3
Delivery mode:		
IVR	2	0
Accessed online	8	8
Accessed on desktop computer	1	2
NR	1	0
Number of sessions:		
1	6	8
>1	1	2
NR	2	0
IVR	2	0
Unlimited/unstructured	1	0
Comparator:		
Waitlist	4	5
Attention/information control	6	3
Treatment as usual	2	1
Face-to-face	0	1
Outcomes:		
Alcohol consumption	8	8
HRQOL	2	0
Social/legal effects	1	8
Risk of bias:		
Low	4	3
Moderate	6	6
High	2	1

Abbreviations: BASICS=Brief Alcohol Screening and Intervention for College Students; e-CHUG=Electronic Check-Up to Go; HRQOL=health-related quality of life; IVR=interactive voice response; KQ=key question; NR=not reported; THRIVE=Tertiary Health Research Intervention Via Email

Results from Studies of Adults

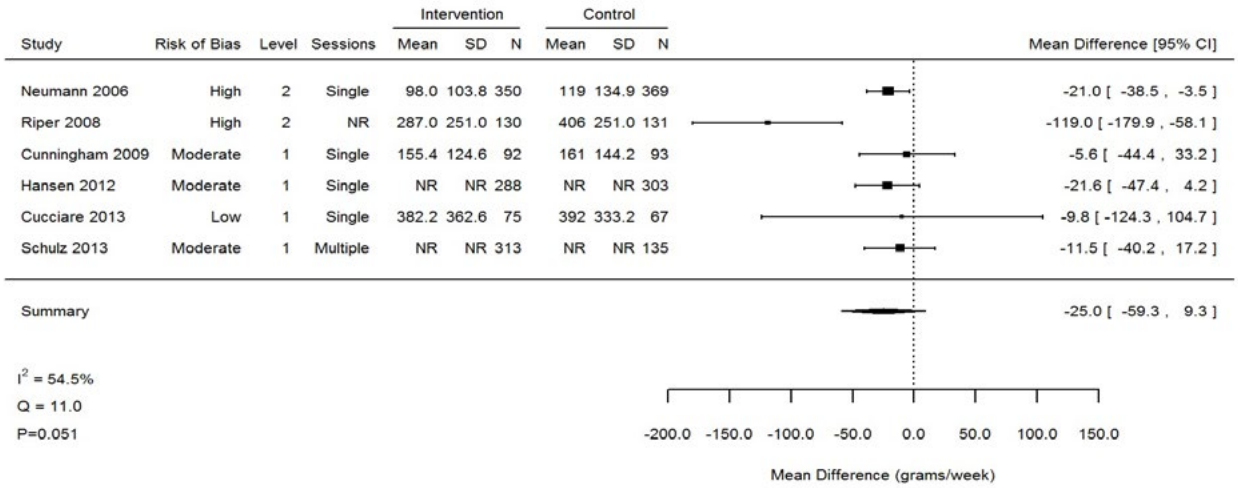
Of the 12 studies conducted in adult samples, 10 provided mean age (range 32.5 to 59.3 years, median 41.1 years). The proportion of females ranged from 0 to 57%, with a median of 41%. Race or ethnicity was reported in only 2 studies. Few data were available on education, though the 7 studies reporting enough data to determine whether participants attended college had a range of 34% to 82% of participants who had attended at least some college. Data on the location of the e-interventions were lacking. Similarly, many studies did not report the name of the e-intervention programs. Of the programs reported in studies reviewed, no specific program was used by more than one study. Most e-interventions were one-session treatments that were accessed online. Half of the studies (n=6) utilized comparison conditions that provided some information or attention as a control, while the other half used waitlist or treatment as usual as comparisons. While 8 studies reported some type of alcohol consumption outcome (grams/week, binge drinking episodes, or meeting alcohol limit guidelines), only 2 studies reported HRQOL, and only one study reported on the social/legal consequences of drinking. We categorized the level of supplementary human support provided as follows: 6 studies had level 1 (minimal) support, 3 studies had level 2 (low) support, and 3 studies had level 3 (moderate or high) support.

To aggregate alcohol consumption across studies, we converted all outcomes to grams (g) of alcohol consumed per week. This generally involved converting standard drinks (U.S., European Union, or Australia) to g/drink, multiplying times the standard drinks/unit time, and then adjusting for unit of time if not given as 1 week. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) defines a U.S. standard drink as a drink that contains 14 g of alcohol, which is often the amount found in a 12-ounce beer, 8 to 9 ounces of malt liquor, 5 ounces of table wine, or 1.5 ounces of hard liquor. The mean baseline alcohol consumption in studies enrolling adult samples ranged from 129 to 436 g/week (median=292 g/wk).

Alcohol Consumption

Figure 3 shows a forest plot of mean differences (MDs) for the 6 studies conducted with adults that had sufficient data at 6-month follow-up assessment to analyze alcohol consumption.[50,51,53,62-64] In these studies, e-interventions were associated with a small, statistically insignificant reduction in alcohol consumption (MD -25.0 g/week; 95% CI, -59.3 to 9.3). Treatment effects varied moderately (Q=11.0; p=0.051; I^2=55%). Qualitative analyses suggested that studies using more intensive treatment were associated with greater reductions in alcohol consumption. For example, the trial by Riper and colleagues[63] offered access to a moderated peer-to-peer forum, and participants received the recommendation to remain engaged with the e-intervention for 6 weeks. Reductions in alcohol consumption were large. Similarly, Bischof and colleagues[33] observed decreased alcohol consumption in adults at 12-month follow-up in a relatively intensive e-intervention that was combined with 4 phone counseling sessions. A sensitivity analysis that removed the 2 studies at high risk of bias found a small, statistically significant reduction in alcohol consumption (MD -14.7 g/week; 95% CI, -26.4 to -3.0), with little variability across studies (I^2=0.0%).

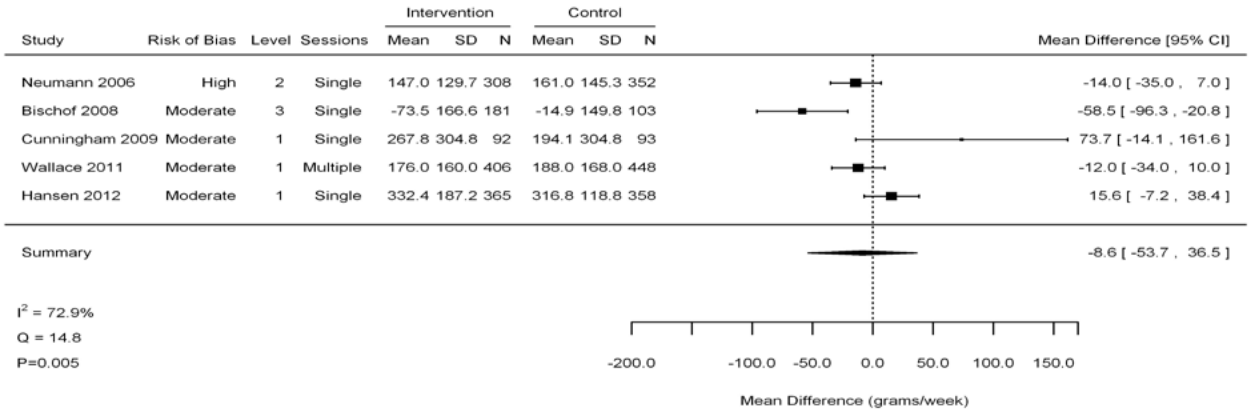
Figure 3. Alcohol Consumption at 6 Months in Studies of Adults*



*Hansen 2012 and Schulz 2013: Means and SDs were not available, as only mean difference and CI were given.
Abbreviations: CI=confidence interval; N=number of participants; NR=not reported; SD=standard deviation

Five studies reported sufficient data to analyze 12-month follow-up assessments of alcohol consumption;[33,51,53,62,67] 3 of the studies were also analyzed at the 6-month time point.[51,53,62] Figure 4 shows a forest plot for these studies. E-interventions were associated with a very small, statistically insignificant reduction in alcohol consumption at 12 months (MD -8.6 g/week; 95% CI, -53.7 to 36.5), with high heterogeneity in treatment effects (Q=14.8; p=0.005; I^2=73%). A sensitivity analysis that removed the one study at high risk of bias was consistent with the primary analysis (MD -5.5 g/week; 95% CI, -79.0 to 68.1; I^2=79.1%).

Figure 4. Alcohol Consumption at 12 Months in Studies of Adults



Abbreviations: CI=confidence interval; N=number of participants; SD=standard deviation

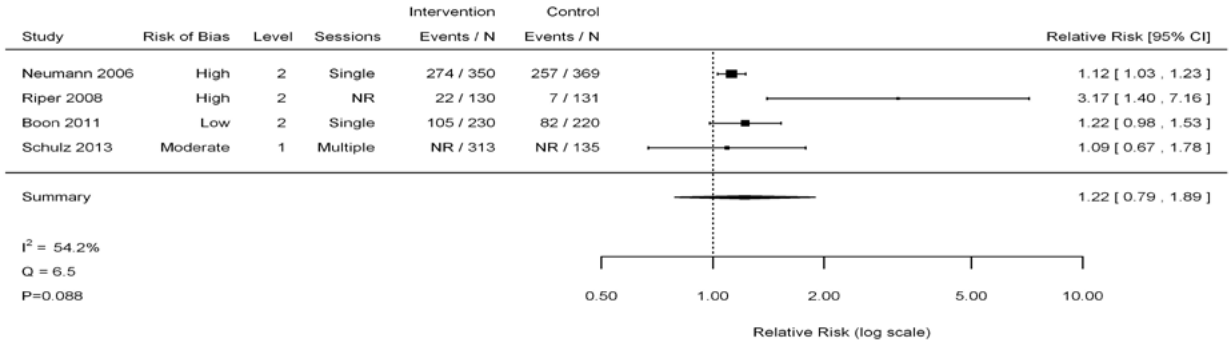
An additional study with relevance to this question was not included in meta-analyses due to the unique characteristics of its intervention and study sample, namely, face-to-face motivational interviewing plus IVR in individuals with HIV.[54] In this study, a brief motivational interviewing (BMI) intervention was paired with a daily IVR system for tracking drinking behavior. Another arm of the study employed BMI only and is described under KQ 4. Relative to inactive control, the BMI plus IVR arm resulted in similar amounts of alcohol consumption at 6- and 12-month follow-up assessments.

Alcohol Reduction to Meet Drinking Limit Guidelines

The operational definition of drinking limit guidelines varied across studies. Studies typically defined limits by a weekly total of standard drinks (*eg*, <20).[49,63] However, one study[62] combined the weekly limit with a daily limit (≤5 drinks for men, ≤3 for women), whereby exceeding either the weekly or the daily limit would count as not meeting the guideline. The studies varied considerably in the proportion of participants meeting drinking limit guidelines at the 6-month follow-up. The 4 studies with data on this outcome reported 17%, 23%, 46%, and 78% meeting drinking limit guidelines in the e-treatment groups at 6 months.

Figure 5 shows a forest plot of risk ratios (RRs) for the 4 studies conducted in adults that had sufficient data at 6-month follow-up assessment to analyze the proportion of participants meeting drinking limit guidelines.[49,62-64] In these studies, e-interventions were associated with a small, statistically insignificant increase in the risk of meeting guidelines (RR 1.22; 95% CI, 0.79 to 1.89). There was low to moderate heterogeneity in effect sizes (Q=6.5; p=0.088; I^2=54%).

Figure 5. Alcohol Reduction to Meet Drinking Limit Guidelines at 6 Months in Studies of Adults*



*Schulz 2013 did not report event rates. Intervention effects are based on adjusted estimates reported from a logistic regression model.

Abbreviations: CI=confidence interval; N=number of participants; NR=not reported; SD=standard deviation

There were no studies with sufficient data to analyze 12-month follow-up assessments of meeting drinking limit guidelines.

An additional study targeted alcohol misuse with comorbid illicit drug use.[65] This study enrolled participants online and provided a brief online intervention where participants could monitor drinking and get PNF with motivational interviewing-based recommendations. This was compared to an assessment-only condition. Drinking limits in this study were defined as AUDIT <8. At 6-month follow-up, the 2 groups had similar proportions of participants with AUDIT <8.

Binge Drinking

Two studies in adults reported the effects of e-treatment on binge drinking.[50,53] Both trials reported 6-month data, but no 12-month data. Due to the limited number of trials, we did not conduct meta-analysis. One study enrolled military Veterans with alcohol misuse and compared treatment as usual in a primary care setting to treatment as usual plus a brief online alcohol intervention.[50] Binge drinking was defined as ≥5 drinks on one occasion for men, and ≥4 drinks on one occasion for women in the past 30 days. At the 6-month follow-up, participants in the

brief intervention condition had rates of binge drinking (23%) similar to those in the treatment-as-usual condition (25%). The other study reporting binge drinking outcomes in adults compared an online PNF intervention to a no-intervention control group.[53] Binge drinking was defined as drinking ≥5 drinks on one occasion. At the 6-month follow-up, the binge drinking rate in the online PNF condition (47%) was similar to that of the non-intervention control condition (45%).

Consequences of Drinking—Social Problems

One trial, conducted in Veterans, reported intervention effects on the negative social consequences of drinking at 6-month follow-up.[50] This study is also described immediately above, under "Binge Drinking." This study measured negative social consequences of drinking with the Short Inventory of Problems, a 15-item measure on which higher scores indicate more social problems. In this study, the brief online alcohol intervention had a mean score on the self-report measure of social problems (mean 5.9, SD 10.2) that was similar to that observed in the treatment-as-usual-only group (mean 6.5, SD 9.3). No 12-month data were available.

Other Outcomes

In addition to the outcomes described above, we examined trials for analyses of HRQOL, alcohol-related health problems, medical utilization, and adverse effects from treatment. No trials with adults reported these outcomes with sufficient data to analyze.

Results from Studies of College Students

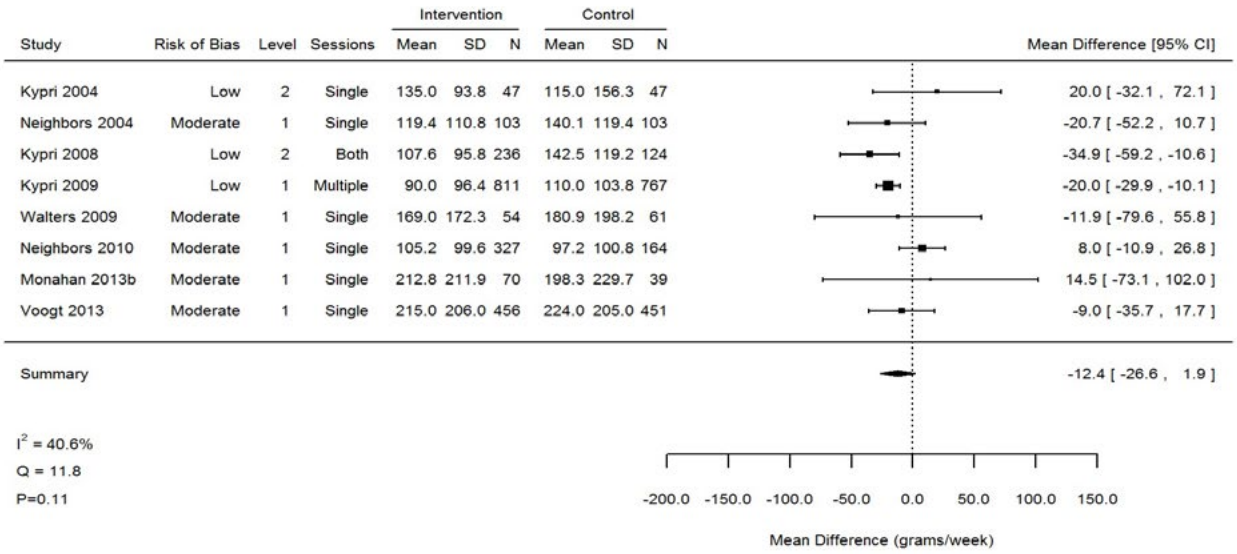
Ten trials were conducted in college student samples.[34-36,45,56-59,61,66] Due to theorized potential differences in sample characteristics and responsiveness to treatments, we analyzed these samples separately from the adult samples. Of the 10 trials conducted in college student samples, 8 provided mean age (median of means 19.9 years, range 18.2 to 20.9 years). The proportion of females ranged from 38% to 64%, with a median of 55%. In the 4 trials reporting race/ethnicity, the proportion of participants of non-Caucasian race/ethnicity ranged from 15% to 43%, with a median of 28%. The location of the e-interventions varied considerably, as the 6 studies reporting location included college health services, college classrooms, research labs, and home-based e-interventions. The programs used also varied, and no one program was used in more than 2 studies. E-interventions were primarily delivered online (n=8 studies). Treatment was not intensive, as the modal number of e-intervention sessions was 1 (n=8 studies). Half of the studies used waitlist comparison groups, but more active comparison groups were included, as 3 studies used attention/information comparisons, and one used face-to-face therapy as a comparison. A total of 9 studies provided data on alcohol consumption (either g/week, binge drinking episodes, or meeting alcohol limit guidelines). Eight studies provided data on negative social and/or legal consequences of drinking. No data on HRQOL were provided. Regarding the level of supplementary human support provided, 7 trials had minimal support, and 3 trials had low support. Of the 8 trials that provided baseline alcohol consumption data, baseline means were lower than in adult studies, ranging from 85 g/week to 291 g/week (median 183 g/week).

Alcohol Consumption

Figure 6 shows a forest plot of MDs for the 8 studies conducted in college students that had sufficient data at 6-month follow-up assessment to analyze alcohol consumption.[34-36,45,57,58,61,66] In

these studies, e-interventions were associated with a small, statistically insignificant reduction in alcohol consumption (MD -12.4 g/week; 95% CI, -26.6 to 1.9). There was moderate heterogeneity in treatment effects (Q=11.8; p=0.11; I^2=41%).

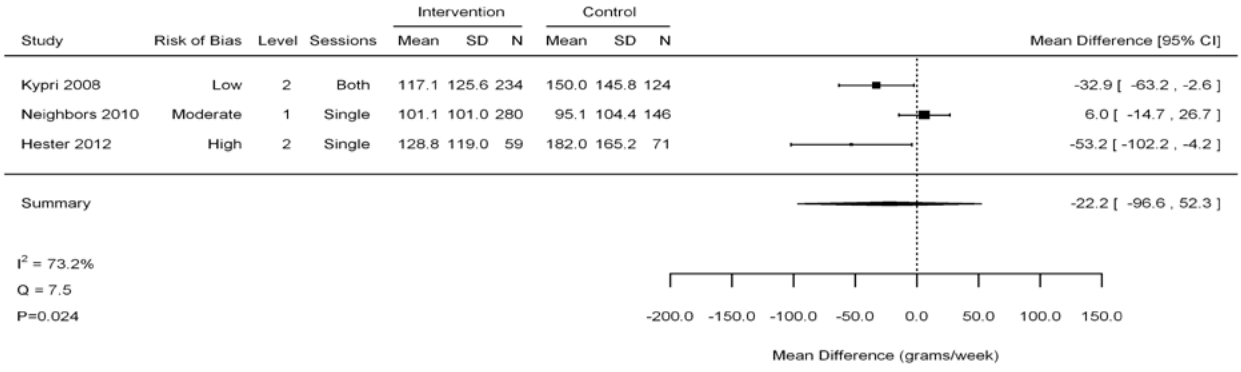
Figure 6. Alcohol Consumption at 6 Months in Studies of College Students



Abbreviations: CI=confidence interval; N=number of participants; SD=standard deviation

There were also 3 studies with sufficient data to analyze 12-month follow-up assessments of alcohol consumption.[34,35,56] A forest plot for these studies is shown in Figure 7. In these studies, e-interventions were associated with a small, statistically insignificant reduction in alcohol consumption. (MD -22.2 g/week; 95% CI, -96.6 to 52.3). There was substantial heterogeneity in treatment effects (Q=7.5; p=0.024; I^2=73%).

Figure 7. Alcohol Consumption at 12 Months in Studies of College Students



Abbreviations: CI=confidence interval; N=number of participants; SD=standard deviation

Alcohol Reduction to Meet Drinking Limits

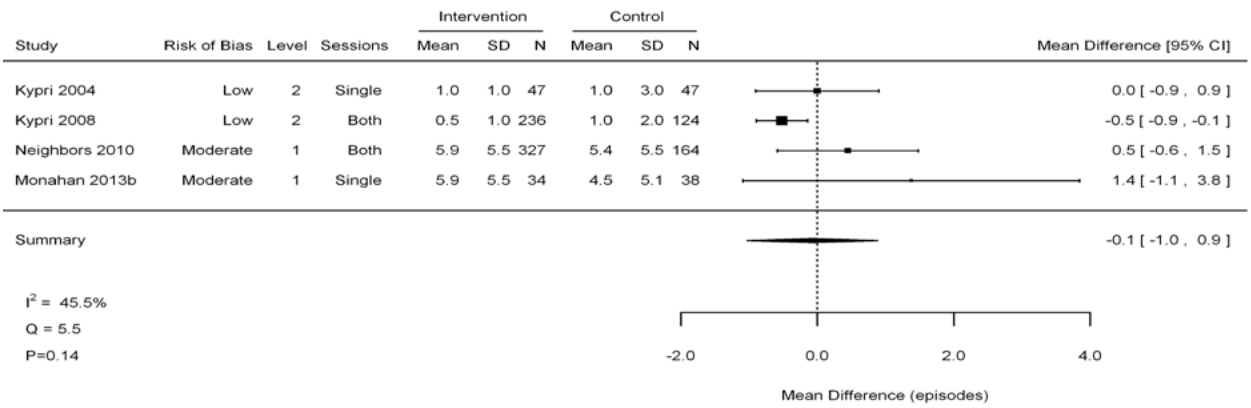
One study with college students had data on 6-month outcomes for meeting drinking limit guidelines.[57] In this study, drinking guidelines were defined as a limit of 14 drinks per week for women and 28 drinks per week for men. The e-intervention consisted of psychoeducation about

negative consequences of current alcohol consumption level, including health, financial, and motor vehicle accident risks. In addition, the e-intervention provided normative comparisons and information on treatment resources. Relative to an assessment-only comparison group, the e-intervention resulted in an elevated probability of meeting drinking limits at 6 months (OR 1.53; 95% CI, 1.09 to 2.17).

Binge Drinking

Figure 8 shows a forest plot of MDs for the 4 trials conducted with college students that had sufficient data at 6-month follow-up assessment to analyze effects of e-interventions on binge drinking episodes.[34,35,45,58] In these studies, e-interventions were associated with a very small, statistically insignificant reduction in binge drinking (MD -0.1 episodes; 95% CI, -1.0 to 0.9), with low to moderate evidence of heterogeneity in effect sizes (Q=5.5; p=0.14; I^2=46%).

Figure 8. Episodes of Binge Drinking at 6 Months in Studies of College Students



Abbreviations: CI=confidence interval; N=number of participants; SD=standard deviation

There were no trials with sufficient data to analyze 12-month follow-up assessments of binge drinking episodes.

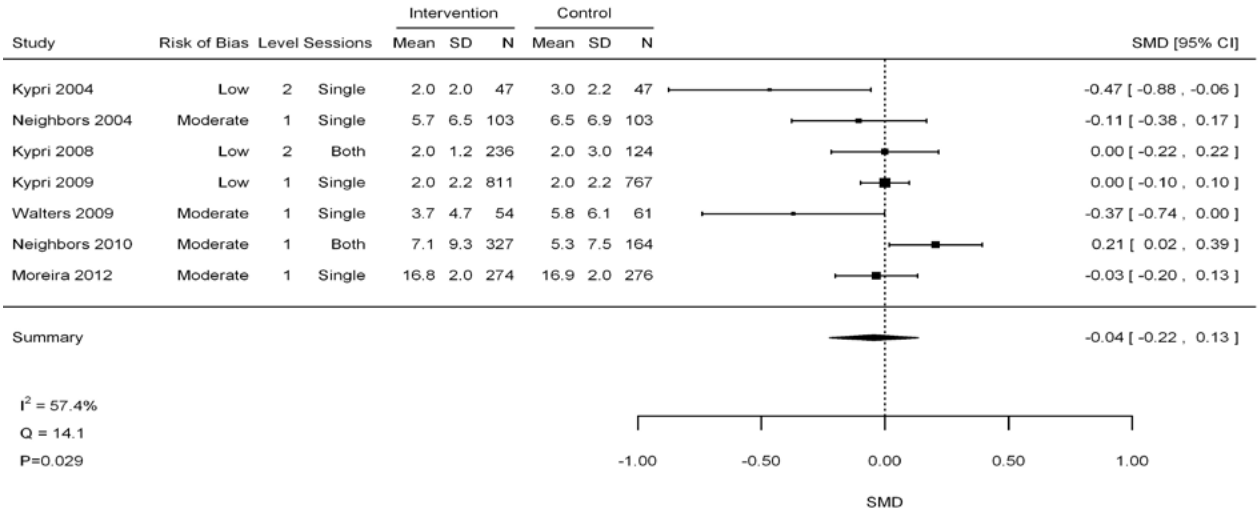
Two additional trials reported the proportion of subjects with binge drinking, but these outcomes could not be combined with the mean episodes of binge drinking and thus these studies were excluded from the meta-analysis.[57,66] One study compared a brief online e-intervention to a no-intervention comparison group.[66] At the 6-month follow-up, the proportion of participants reporting binge drinking in the e-intervention group (68%) was similar to that in the control group (66%). Another trial compared a brief online e-intervention to an informational leaflet intervention.[57] Binge drinking was defined as >120 g for males and >80 g for females during one episode in the last 2 weeks. The median number of binge drinking episodes was the same for both groups (median=1). These findings of no intervention effect on episodes of binge drinking are consistent with the finding of no effect on mean number of binge drinking episodes for the studies included in the meta-analysis.

Consequences of Drinking—Social Problems

Figure 9 shows a forest plot of SMDs for the 7 trials conducted in college students that had sufficient data at 6-month follow-up assessment to analyze the effects of e-interventions on

negative social consequences of drinking.[34-36,57-59,61] In these trials, e-interventions were associated with a very small, statistically insignificant reduction in the negative social consequences of drinking (SMD -0.04; 95% CI, -0.22 to 0.13), with moderate heterogeneity in treatment effects (Q=14.1; p=0.029; I^2=57%).

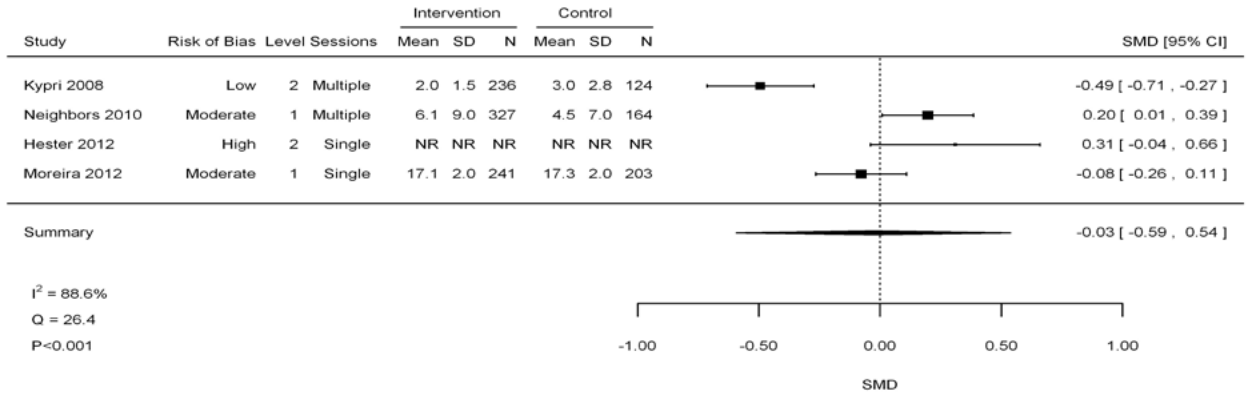
Figure 9. Negative Social Consequences of Drinking at 6 Months in Studies of College Students



Abbreviations: CI=confidence interval; N=number of participants; SD=standard deviation; SMD=standardized mean difference

Figure 10 shows a forest plot of SMDs for the 4 trials with sufficient data at 12-month follow-up for assessment of negative social consequences of drinking.[34,35,56,59] Similar to results observed in the 6-month data, e-interventions were associated with a very small, statistically insignificant reduction in negative social consequences of drinking at 12-month follow-up (SMD -0.03; 95% CI, -0.59 to 0.54); there was substantial heterogeneity in treatment effects (Q=26.4; p<0.001; I^2=89%). A sensitivity analysis that removed the one study at high risk of bias was consistent with the primary analysis (MD -0.12 g/week; 95% CI, -0.98 to 0.74; I^2=90.9%).

Figure 10. Negative Social Consequences of Drinking at 12 Months in Studies of College Students*



*Hester 2012 did not report mean and SD. The estimate of treatment effect was derived from other statistics.
Abbreviations: CI=confidence interval; N=number of participants; SD=standard deviation; SMD=standardized mean difference

Other Outcomes

No trials in college students reported HRQOL, alcohol-related health problems, medical utilization, or adverse effects from treatment with sufficient data to analyze.

Summary of Findings

We reviewed a total of 22 studies that compared e-interventions with inactive controls in participants with varying degrees of alcohol misuse. Most interventions were accessed online, used a single session, and had minimal to low levels of supplementary human support. While most studies provided data on alcohol consumption outcomes, other important outcomes were reported infrequently. Treatment effects on weekly alcohol consumption were relatively small and statistically insignificant, and varied importantly across trials. Fewer studies provided data on meeting drinking limit guidelines at the end of the study, reducing binge-drinking episodes, and decreasing social problems related to alcohol. Moderately strong evidence showed no effects on binge drinking or alcohol-related social problems, but these outcomes were reported primarily in student samples. The strength of the current evidence for the longer-term (≥6 months) benefits of e-interventions on alcohol consumption and its associated effects on health and well-being is low.

Quality of Evidence for KQ 2

Of the 22 trials relevant to this question, 7 were judged to be at low risk of bias, 12 at moderate risk of bias, and 3 at high risk of bias (Appendix C). We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to rate the overall strength of evidence (SOE) for outcomes that addressed alcohol consumption and social problems related to alcohol use. For 2 of the alcohol consumption outcomes (weekly consumption and meeting alcohol limits), we judged the SOE as low. The SOE was downgraded for inconsistent and imprecise treatment effects and, for the weekly consumption outcome, moderate risk of bias. Moderately strong evidence showed no effects on binge drinking or alcohol-related social problems, but these outcomes were reported primarily in student samples. These outcomes were downgraded for some important inconsistency in treatment effects and indirectness, since most of the studies involved student samples with lower baseline alcohol consumption than the adult samples.

KEY QUESTION 3: For adults at high risk of AUD (*eg*, audit-C ≥8), or who have a diagnosis of AUD, what are the effects of e-interventions compared with inactive controls?

Key Points

- Only 3 studies compared e-interventions with no-intervention controls in participants with AUD (n=533).
- In a single trial, a multi-component smartphone program used to support recovery following residential treatment increased abstinence (OR 1.94; 95% CI, 1.14 to 3.31) and decreased risky drinking days at 12-month follow-up (SOE=low).
- A computerized feedback system coupled with telephonic counseling in participants recruited from primary care did not reduce alcohol consumption. An IVR system used

for participants discharged from residential treatment did not decrease the risk of relapse (SOE=insufficient).

Study Characteristics and Treatment Effects

We identified 3 trials (Table 6) involving 533 participants that met inclusion criteria for KQ 3.[33,52,60] All studies were conducted in adult, non-student samples and were judged to be at moderate[33,52] or high[60] risk of bias (Appendix C). None of the e-interventions was identified as a commercial product. Because these studies varied considerably in participants enrolled, interventions, and outcomes reported, we describe each separately below.

Table 6. Study Characteristics (KQ 3)

Study	Setting	Mean Age (SD)	N	Inclusion Criteria	E-Intervention	Control	Follow-up Interval	Outcomes	Overall Risk of Bias
Bischof, 2008[33]	Primary care	36.5 (13.5)	408 (124 AUD subgroup)	AUDIT ≥5 and ≥2 binge episodes in past 4 weeks or >20 g (F) or 30 g (M) daily	Computerized feedback on alcohol use and 1-4 telephonic MI sessions	Waitlist	12 months	Alcohol consumption	Moderate
Gustafson, 2014[52]	Residential care facilities	38.4 (10.4)	349	Completing residential treatment program for DSM-IV alcohol dependence	Multicomponent smartphone application offered for 8 months	Treatment as usual	12 months	Alcohol consumption Social effects	Moderate
Mundt, 2006[60]	Residential facility	41.9 (9.2)	60	Completing residential treatment program for AUD	IVR prompted or ad lib	No IVR	6 months	Alcohol consumption HRQOL Social effects	High

Abbreviations: AUD=alcohol use disorder; AUDIT=Alcohol Use Disorders Identification Test; DSM-IV=*Diagnostic and Statistical Manual of Mental Disorders,* 4th edition; E-Intervention=electronic intervention; F=female; HRQOL=health-related quality of life; IVR=interactive voice response; KQ=key question; M=male; MI=motivational interviewing; N=number of participants; SD=standard deviation

Gustafson and colleagues[52] recruited 349 participants from 5 U.S. residential treatment facilities who were completing treatment for alcohol dependence. The average age was 38.4 (SD 10.4) years old, 39% were women, 80% were white, and mean years of education were not reported. At discharge from residential treatment, participants were randomized to: 1) the multicomponent Addiction-Comprehensive Health Enhancement Support System (A-CHESS) for 8 months; or 2) treatment as usual. Intervention participants received a smartphone with the A-CHESS application, which included both static and interactive features, mobile phone service, and a data plan. Two hundred and eighty-six (286) smartphones were given to the 170 intervention participants due to malfunctioning, lost, stolen, and damaged phones. Participants could elect to share data from the A-CHESS application with their counselors: 93.5% shared data from the weekly Brief Addiction Monitor, and 41.9% shared data about alcohol relapse. At 12-month follow-up, the intervention group had higher rates of abstinence (OR 1.94; 95% CI, 1.14 to 3.31) and fewer risky drinking days per 30-day period (MD -1.47; 95% CI, -0.13 to -2.81). There were no significant effects on any of the 8 items measuring negative consequences of drinking.

Bischof and colleagues[33] recruited 408 participants from German primary care practices with alcohol problems ranging from a positive alcohol screen to alcohol dependence established by a criterion-based structured interview. Average age was 36.5 (SD 13.5) years old, 32% were women, race was not reported, and mean years of education were 10.5 (2.5). We report on the subgroup (n=124) with alcohol dependence. Participants were randomized to: 1) a no-intervention control; 2) computerized feedback plus 4 brief counseling sessions of 30 minutes each delivered by telephone; or 3) computerized feedback and 1 to 4 brief counseling sessions of 30 minutes each delivered by telephone. For the latter group, counseling sessions were discontinued when the patient met criteria for a reduction in alcohol consumption and indicated high self-efficacy to maintain the reduction in alcohol consumption. The computerized feedback was based on the transtheoretical model of behavior change, and telephonic counseling was based on motivational interviewing and delivered by a trained psychologist. At 12-month follow-up, the intervention groups did not differ from the control group in alcohol consumption (p=0.62) or in the proportion meeting criteria for binge drinking (54.5% intervention vs 50% control; p=0.69). Other outcomes prioritized for this review were not reported.

Mundt et al[60] evaluated the effect of an IVR system in 60 participants treated for alcohol dependence at a Wisconsin residential treatment facility. Average age was 41.9 (SD 9.1) years, 45% were women, 95% were white race, and mean years of education were not reported. At discharge from residential treatment, participants were randomized to: 1) a no-intervention control; 2) prompted use of the IVR system; or 3) ad libitum use of the IVR system. The prompted group was called and encouraged to use the system if they failed to make a daily call to the IVR system for 2 consecutive days. The IVR system included assessments of drinking status, alcohol cravings, self-efficacy, difficulty coping, and risk of relapse. Participants were directed to modules that incorporated tailored feedback based on patterns of alcohol consumption: resolve not to drink module, drinking reasons module, and cognitive behavioral advice module. The system included voice mail capability and allowed participants to request a personal phone call from the coordinator. At 6-month follow-up, intervention subjects had placed a mean of 51.4 (SD 22.6) IVR calls; mean calls were higher (p=not statistically significant [NS]) in the ad

libitum group. Self-reported abstinence was reported in 20 of 30 intervention subjects (67%) and 13 of 18 control subjects (72%; p=not reported [NR]). There were no statistically significant intervention effects on functional status, or work and social adjustment.

Summary of Findings

Three trials conducted in participants with alcohol used disorders found positive effects from a multicomponent smartphone application, but no intervention effects from a computerized feedback system coupled with telephonic counseling or an IVR system.

Quality of Evidence for KQ 3

The 3 trials were judged to be at moderate[33,52] or high[60] risk of bias (Appendix C). Using the GRADE framework,[69] the SOE is low (moderate risk of bias, imprecise effects) that a multicomponent smartphone intervention decreases alcohol use in adults with alcohol use disorders. The SOE is insufficient for the effects of IVR and computerized feedback couple with brief telephone counseling.

KEY QUESTION 4: For adults who misuse alcohol, are at high risk of AUD, or have a diagnosis of AUD, what are the effects of e-interventions alone or used in combination with face-to-face therapy compared with face-to-face therapy alone?

Key Points

- Six trials (1090 participants) compared e-interventions alone or in combination with face-to-face brief motivational interviewing (BMI) to BMI alone. All studies enrolled individuals with alcohol misuse, but varied markedly with regard to setting and subject and intervention characteristics.
- Combination of e-interventions plus BMI versus BMI alone: Two studies in adults compared BMI plus IVR to BMI alone and found no improvement in primary drinking outcomes with the addition of IVR. A subgroup analysis found benefit with combined IVR and BMI for HIV-positive adults who met DSM-IV criteria for alcohol dependence. In a study of college students, the addition of an e-intervention utilizing 1 to 2 sessions of personalized normative feedback (PNF) plus psychoeducation to BMI versus BMI alone showed no improvement in 12-month drinking outcomes.
- E-interventions alone versus BMI alone: In 3 head-to-head comparisons, all involving college students, e-interventions were associated with significantly heavier alcohol intake at follow-up (ranging from 50 to 81 g greater weekly consumption) compared with BMI. Binge drinking frequency was higher in e-intervention participants than in BMI participants (MD 2 to 2.5 more episodes per month).
- This diverse group of studies did not find a benefit of e-interventions alone or as an adjunct to face-to-face BMI, compared with face-to-face BMI alone for college students or midlife primary care patients who misuse alcohol.

Study Characteristics

Six trials (Table 7), described in 5 papers and involving 1090 participants, compared e-interventions alone or used in combination with face-to-face BMI to face-to-face BMI alone.[36,45,48,54,55] The paper by Monahan and colleagues[45] reported results from 2 separate trials. Two trials (508 participants), conducted with midlife patients in primary care settings, compared the combination of IVR plus face-to-face BMI to face-to-face BMI alone.[54,55] Four trials (582 participants) focused on college students in their late teens.[36,45,48] Three of these compared e-interventions to BMI.[36,45] The fourth compared the combination of an e-intervention plus BMI to BMI alone.[48] All studies enrolled subjects based on recent alcohol misuse (*eg*, ≥1 episode of heavy drinking in the past 14 or 30 days, acute intoxication, or alcohol policy violation) rather than specific evidence of a diagnosable AUD. Thus, subject inclusion criteria in these studies are similar to those used in the studies described in KQ 2. One study used DSM-IV criteria to assess enrolled subjects, allowing subgroup analysis for those with a diagnosis of alcohol dependence.[54] Two studies[48,54] were judged to be at low risk of bias, and 4 studies were assessed as being at moderate risk of bias.[36,45,55]

Table 7. Study Characteristics (KQ 4)

Author	Setting	Mean Age	N	Inclusion Criteria (M/F)	e-Intervention	Control	Follow-up Interval	Outcomes	Overall Risk of Bias
Barnett 2007[48]	College health service	18.8	225	Referred due to intoxication or violation	Alcohol 101 + BMI	BMI ± 25-min booster	12 months	Alcohol consumption Social effects	Low
Hasin, 2013[54]	HIV primary care	46	170	>3 drinks once in 30 days	IVR daily x 60 days + BMI	BMI, 20-25 min	12 months	Alcohol consumption	Low
Helzer, 2008[55]	Primary care	45	338	>NIAAA drinking limits or CAGE 1+	IVR daily x 6 months + BMI ± PNF	BMI ± mailed PNF	6 months	Alcohol consumption	Moderate
Monahan, 2013a=Study 1[45]	College health service	21.2	73	>4/3 drinks once in past 30 days	Alcohol 101	BMI 1 x 50-min session	6 months	Alcohol consumption	Moderate
Monahan, 2013b=Study 2[45]	College course	18.6	91	>4/3 drinks once in past 30 days	e-CHUG	BMI	6 months	Alcohol consumption	Moderate
Walters, 2009[36]	College campus	19.8	193	>4/3 drinks once in past 14 days	e-CHUG	BMI ± PNF	6 months	Alcohol consumption Social effects	Moderate

Abbreviations: BMI=brief motivational interviewing; CAGE=Cut down/Annoyed/Guilty/Eye-opener; e-CHUG=Electronic Check-Up to Go; F=female; IVR=interactive voice response; KQ=key question; M=male; min=minute(s); NIAA=National Institutes of Alcoholism and Alcohol Abuse; PNF=personalized normative feedback

E-Intervention Characteristics

E-interventions studied were daily IVR calls for periods of 60 days[54] or 6 months;[55] Alcohol 101 interactive CD-ROM;[45,48] and e-CHUG, a web-based interactive program.[36,45] Comparator face-to-face counseling consisted of single-session of BMI; 2 studies included a brief booster or follow-up counseling sessions. The extent of counselor experience, training, supervision, and fidelity monitoring varied across the 6 studies. Characteristics of the e-interventions evaluated are summarized in Table 8.

Table 8. Characteristics of E-Interventions (KQ 4)

Characteristic	Adult studies (n=2; 508 participants)	Student studies (n=4; 582 participants)
Delivery location:		
Primary care	2	0
College health services	0	2
College campus	0	2
Intervention design:		
BMI plus e-intervention	2	1
e-intervention alone	0	3
Intervention name:		
Alcohol 101	0	2
e-CHUG	0	2
Not named	2	0
Delivery Mode:		
IVR	2	0
Accessed online	0	2
Accessed on desktop computer	0	2
Number of e-intervention sessions:		
1	0	3
>1	2 (IVR daily)	1
In-person BMI sessions:		
1	1	3
>1	1	1
Outcomes:		
Alcohol consumption	2	4
HRQOL	0	0
Social/legal effects	0	2
Risk of bias:		
Low	1	1
Moderate	1	3

Abbreviations: BMI=brief motivational interviewing; e-CHUG=Electronic Check-Up to Go; HRQOL=health-related quality of life; IVR=interactive voice response; KQ=key question

Alcohol Consumption

E-intervention Alone versus Face-to-Face Counseling (3 Trials)

E-interventions were compared with face-to-face interventions only in college student populations. In all 3 head-to-head comparisons of e-interventions versus face-to-face

BMI, e-interventions were associated with poorer alcohol outcomes than was face-to-face counseling.[36,45]

Monahan et al[45] reported 2 trials comparing e-interventions to BMI in college students recruited in a campus health service. The entry criterion for both studies was at least one episode of consuming >5 drinks (males) or >4 drinks (females) in the past month. In Study 1, 60 subjects were randomized to the Alcohol 101 CD-ROM or face-to-face BMI. In Study 2, 68 subjects were randomized to an interactive, web-based program that included personalized feedback (e-CHUG) or face-to-face BMI. At 6-month follow-up in Study 1, participants receiving the e-intervention were consuming more alcohol per week than those assigned to face-to-face BMI, but results were statistically insignificant (MD 52.2 g/week; 95% CI, -35.7 to 140.1). A similar difference was found in Study 2 (MD 50.1 g/week; 95% CI, -52.6 to 152.8). In both studies, the frequency of binge drinking at 6 months was higher in those receiving the e-intervention, but results were statistically significant only in Study 2. Study 1 e-intervention participants reported 5.5 (SD 6.7) past-month binge episodes versus 3.5 (SD 3.3) for BMI participants (MD 2.0; 95% CI, -0.57 to 4.7). In Study 2, e-intervention participants reported 5.8 (SD 5.5) past-month binge episodes versus 3.3 (SD 4.9) with BMI (MD 2.5; 95% CI, 0.14 to 5.01).

Walters et al[36] studied college students (average age 19.8 years) reporting at least one episode of consuming ≥5 drinks (males) or ≥4 drinks (females) in the past 2 weeks. Two hundred and seventy-nine subjects were randomized to one of 4 conditions: 1) assessment only; 2) e-CHUG; 3) BMI without structured assessment feedback; 4) BMI that incorporated PNF derived from a structured assessment. The assessment-only group is not relevant to this KQ. At 6-month follow-up, e-intervention participants were consuming 168.9 g of alcohol per week (SD 172.3) versus 162.3 (SD 295.9) for BMI only and 142.7 (SD 133.7) for BMI with feedback. In an analysis that adjusted for differences in baseline values, participants assigned to the e-intervention reported significantly higher alcohol consumption compared with those receiving BMI with feedback (5.79 drinks per week, standard error of the mean [SEM] 2.05, p=0.005).

E-intervention Plus Face-to-Face Counseling versus Face-to-Face Counseling Alone (3 Trials)

In the 3 trials comparing e-interventions plus face-to-face counseling versus face-to-face counseling alone, the addition of an e-intervention was not associated with decreased alcohol consumption.[48,54,55] Two studies enrolled midlife adult patients recruited from primary care settings,[54,55] and one recruited participants from a college health service.[48]

Helzer et al[55] studied adult primary care patients (mean age 45) whose average alcohol consumption exceeded NIAAA recommended drinking limits or who scored >1 positive on the Cut down/Annoyed/Guilty/Eye-opener (CAGE) questionnaire. The study was conducted across 15 primary care clinics, involving 112 providers who were trained in conducting brief intervention for excessive alcohol use. All potential subjects received a face-to-face brief intervention delivered by their primary care provider and were then invited to participate in the study, in which 338 subjects were randomized to: 1) face-to-face brief intervention only; 2) face-to-face brief intervention plus 6 months of daily IVR follow-up; or 3) face-to-face brief intervention plus 6 months of daily IVR follow-up plus feedback. Feedback consisted of a mailed, printed graph showing daily consumption as reported via IVR in comparison with

the participant's stated drinking goal, accompanied by a personalized note from Dr. Helzer highlighting the importance of the information. Two hundred and seventy-three subjects (81%) completed the 6-month follow-up interview, with no significant differences in follow-up rate between treatment groups. At 6-month follow-up, mean weekly drinking levels were 25.0 standard drinks (SEM 1.3) in subjects randomized to IVR; 22.4 (SEM 1.4) standard drinks in subjects assigned to IVR plus feedback; and 18.3 (SEM 1.3) for those assigned to brief intervention alone. In a preplanned comparison of all IVR participants (combining those with and without feedback) versus brief intervention-only participants, IVR was associated with significantly heavier weekly drinking (22.6 drinks per week, SEM 0.8) compared with brief intervention only (18.3 drinks, SEM 1.3; p=0.01).

Hasin et al[54] compared BMI plus IVR to BMI alone in a primary care clinic serving HIV-positive individuals (mean age 46). The inclusion criterion was consumption of >4 standard drinks on one occasion within the past 30 days. One-hundred and seventy subjects were randomized to a 20- to 25-minute BMI session only versus BMI plus daily IVR for 60 days (BMI+IVR). At 12-month follow-up, there was no difference between groups for the primary outcome measure, number of drinks per drinking day. In subgroup analysis, subjects who met criteria for a DSM-IV diagnosis of alcohol dependence, drinks per drinking day were lower in the BMI+IVR than the BMI-only group ($p<0.03$).

Barnett et al[48] compared the combination of BMI plus the Alcohol 101 CD-ROM program with BMI alone in college students (n=225) who were referred to campus health service due to an episode of acute intoxication or violation of campus alcohol policy. At 12-month follow-up, there were no between-group differences in alcohol consumption or alcohol related social or legal problems.

Other Outcomes

Other outcomes were reported infrequently. Two studies conducted in college students reported the effects of e-interventions on social outcomes at 6[36] or 12 months.[48] Neither study found a differential effect between BMI and the e-intervention for this outcome. No study reported effects on HRQOL, alcohol-related health problems, medical utilization, or adverse effects of treatment.

Summary of Findings

Six trials (1090 participants) compared e-interventions alone or in combination with face-to-face BMI to BMI alone. Studies were too diverse to compute summary estimates of effect. IVR in combination with BMI was the only e-intervention compared to face-to-face treatment in non-collegiate populations. The addition of IVR did not decrease alcohol consumption in 2 trials that enrolled midlife primary care patients with alcohol misuse. In collegiate populations, BMI was generally more effective than e-interventions alone in decreasing alcohol consumption.

Quality of Evidence for KQ 4

Two trials were judged to be at low risk of bias and 4 at moderate risk (Appendix C). For e-interventions compared with face-to-face treatment, we judged the SOE as low. These studies had moderate risk of bias, were conducted in collegiate populations, and effect estimates did

not exclude a difference of 3 standard drinks per week or a SMD of ≤0.4, the thresholds we set for a precise estimate of effect. When evaluating the overall SOE, we considered a difference of 3 standard U.S. drinks/week or an SMD ≥0.4 as clinically significant and defined precise effects as those with 95% CIs that excluded smaller effects. For combined e-interventions plus face-to- face treatment versus face-to-face alone, we judged the SOE to be low for effects on alcohol consumption, and insufficient for effects on social and legal outcomes. These studies had moderate risk of bias and primarily used IVR interventions, which have important differences from other e-interventions because the interface is through a telephone or analog line.

SUMMARY AND DISCUSSION

Substance use disorders, including alcohol use disorder (AUD), are among the most common and costly conditions among Veterans presenting for treatment in the Veterans Health Administration (VHA) system.[12,13] A recent systematic review[8] found moderately strong evidence that in-person, multi-contact, brief behavioral interventions decreased alcohol consumption in primary care patients who screened positive for alcohol misuse. Electronic interventions (e-interventions) for alcohol misuse have been proposed as a useful way to extend the reach of initial intervention and relapse prevention to maintain treatment gains for alcohol misuse.

We identified 26 randomized controlled trials (RCTs) involving 14,497 total participants that were relevant to our key questions (KQs). Participants were selected for these trials based on one or more alcohol consumption criteria, but only 3 studies based inclusion on an assessment of AUD. Most trials compared e-interventions with inactive controls. E-interventions were typically accessed online and consisted of one session completed without supplementary human support; personalized normative feedback (PNF) was the predominant strategy. Studies and participants were roughly equally divided between college students and other groups of adults. Adult participants were typically midlife, the majority of whom had at least some college education, with baseline alcohol consumption in excess of 14 drinks per week.

We assessed the strength of evidence (SOE) for the highest priority outcomes—alcohol consumption and alcohol-related social problems. Overall, there was low SOE that e-interventions compared with inactive controls did not decrease alcohol consumption outcomes in participants with alcohol misuse. In patients with AUD, a multicomponent smartphone application decreased the risk of relapse after residential treatment (SOE=low). In the few studies using face-to-face treatment as the comparator, e-interventions alone or in combination with face-to-face treatment were not associated with decreased alcohol use, but these studies were conducted exclusively in student populations. Interactive voice response (IVR) e-interventions may be less effective than face-to-face treatment. Table 9 details SOE ratings for the highest priority outcomes by KQ.

Table 9. Detailed SOE Ratings

Outcome	SOE Domains				Effect Estimate (95% CI)	SOE
	Number of Studies (Participants)*	Study Design/ Risk of Bias	Consistency Directness	Precision Publication Bias		
KQ 2: E-intervention vs control in individuals who screen positive for alcohol misuse						
Alcohol consumption (weekly)	17 (10,122)	RCT/Moderate	Inconsistent Direct	Imprecise None detected	MD -25.0 g/week (-59.3 to 9.3) Adults, n=6 studies MD -12.4 g/week (-26.6 to 1.9) Students, n=8 studies	Low Low
Met alcohol consumption limits	6 (4932)	RCT/Low	Some inconsistency Direct	Imprecise None detected	RR 1.22 (0.79 to 1.89) Adults, n=4 studies OR 1.53 (1.09 to 2.17) Students, n=1 study	Low Low
Alcohol consumption (binge drinking)	8 (5043)	RCT/Low	Some inconsistency Some indirectness	Precise None detected	MD 2% with binge Adults, n=2 studies MD -0.01 episodes (-1.0 to 0.9) Students, n=4 studies	Moderate Moderate
Alcohol-related social problems	8 (5765)	RCT/Low	Some inconsistency Some indirectness	Precise None detected	No difference Adults, n=1 study SMD -0.04 (-0.22 to 0.13) Students, n=7 studies	Low Moderate

Outcome	SOE Domains				Effect Estimate (95% CI)	SOE
	Number of Studies (Participants)*	Study Design/ Risk of Bias	Consistency Directness	Precision Publication Bias		
KQ 3: E-intervention vs control in individuals with AUD						
Alcohol consumption (maintain abstinence)	3 (533)	RCT/Moderate	Consistent Direct	Imprecise None detected	Increase in abstinence for adults with smartphone e-intervention: OR 1.94 (1.14 to 3.31) No difference with IVR or computerized feedback	Low Insufficient
Alcohol-related social problems	2 (409)	RCT/Moderate	NA Direct	Imprecise None detected	No difference in adults	Low
KQ 4: E-intervention vs face-to-face counseling						
Alcohol consumption†	3 (438)	RCT/Moderate	Consistent Some indirectness	Imprecise None detected	Ranged from 50 to 80 g/week higher with e-intervention Students, n=3 studies	Low
Alcohol-related social problems	1 (210)	RCT/Moderate	NA Some indirectness	Imprecise None detected	SMD -0.16 (-0.76 to 0.43) Students, n=1 study	Insufficient
KQ 4: Combined e-intervention + face-to-face counseling vs face-to-face counseling alone						
Alcohol consumption	3 (668)	RCT/ Moderate	Consistent Some indirectness	Imprecise None detected	Adults: No difference in 1 study; higher in 1 study Students: No difference in 1 study	Low Low
Alcohol-related social problems	0	NA	NA NA	NA NA	No studies	Insufficient

*Numbers given here are for the total number studies/participants considered in the SOE ratings. Numbers included in the summary effect estimates may vary.
†One standard drink in the U.S contains 14 grams of alcohol (*eg*, one 12-ounce beer that is 5% alcohol by volume).

Abbreviations: AUD=alcohol use disorder; CI=confidence interval; e-intervention=electronic intervention; g=grams; IVR=interactive voice response; KQ=key question; MD=mean difference; n=number; NA=not applicable; OR=odds ratio; RCT=randomized controlled trial; RR=risk ratio; SMD=standardized mean difference; SOE=strength of evidence

SUMMARY OF EVIDENCE BY KEY QUESTION

KQ 1. Characteristics of and User Support for E-Interventions

The e-interventions for alcohol misuse were typically brief, consisting of one session lasting 30 minutes or less. Intervention content was often focused on psychoeducation, PNF, and negative consequences expected from continuation of the participant's current level of alcohol consumption. Interventions including more complex psychotherapy content typically utilized a motivational interviewing approach, with relatively little cognitive-behavioral intervention beyond psychoeducation. Overall, the majority of e-interventions did not utilize supplementary human support. Even when such support was provided, it rarely included counseling beyond brief advice to reduce alcohol consumption levels. Only a single study meeting inclusion criteria used a smartphone as the delivery platform.

KQ 2. Effects of E-Interventions Compared with Inactive Controls in Adults who Misuse Alcohol

We found low SOE that e-interventions relative to inactive controls (usual care, waitlist, or attention controls) decreased weekly alcohol consumption (n=17 studies) or increased the proportion meeting drinking limits (n=6 studies) in participants with alcohol misuse. Treatment effects varied importantly across studies, and we were unable to definitively explain this variability. Qualitative analyses suggested that studies using more intensive treatment were associated with greater reductions in alcohol consumption. This observation is consistent with a previous systematic review that found short-term effects of single-session PNF interventions were inferior to e-interventions with longer duration.[27] Relative to the variability in the observed effects, the summary effects were modest, ranging from 1 to 2 fewer drinks per week, suggesting a modest long-term (≥6 months) effect of e-interventions on alcohol misuse outcomes. These estimates of treatment effect could be biased toward the null because control participants' behaviors may have been affected by assessments of alcohol misuse—similar to a placebo effect in drug studies.

While most studies provided data on the weekly volume of alcohol consumption, other important outcomes targeted in this review, such as effects on alcohol-related health and social or legal consequences, were reported infrequently. Moderately strong evidence showed no effects on binge drinking or alcohol-related social problems, but these outcomes were reported primarily in student samples. The SOE for the longer term (≥6 months) benefits of e-interventions on alcohol consumption and its associated effects on health and well-being is low. However, due to the small number of studies evaluating several of the relevant outcomes, the brevity and limited scope of the e-interventions, and the lack of supplementary human support for these interventions, further research is warranted.

KQ 3. Effects of E-Interventions Compared with Inactive Controls in Adults at High Risk of AUD (*eg*, AUDIT-C ≥8) or with a Diagnosis of AUD

Three studies compared e-interventions with inactive controls or treatment as usual in participants with AUD. One study[33] randomized participants to one of 2 groups utilizing computerized feedback with up to 4 phone counseling sessions lasting 30 minutes each or

a control group receiving no intervention. This study is relatively novel in providing such extensive counseling, but data from the study did not provide evidence of long-term effects on alcohol outcomes. A second study evaluated a multicomponent smartphone application in patients completing residential treatment and found higher rates of abstinence and fewer risky drinking days.[52] The final study[60] recruited inpatients who were randomized at discharge to one of 2 groups using IVR assessments of drinking-related variables and tailored treatment modules with an option to request a counseling phone contact or a control group receiving no intervention. There was no significant effect of the e-intervention on reported alcohol outcomes. Thus, with widely varying interventions, there are conflicting findings on the efficacy of e-interventions for long-term alcohol consumption in participants with AUD. We found low SOE that a smartphone intervention decreased risk of relapse, but the evidence was insufficient for other e-interventions. There was insufficient evidence for evaluating other alcohol-related outcomes.

KQ 4. Effects of E-Interventions Alone or Used in Combination with Face-to-Face Therapy Compared with Face-to-Face Therapy Alone in Adults who Misuse Alcohol

Six studies compared e-interventions, used either independently or in conjunction with face-to-face counseling, to treatment consisting of face-to-face counseling alone. Three of the 6 studies combined e-interventions with face-to-face treatment. Those studies utilized IVR as the e-intervention and brief motivational interviewing (BMI) as the counseling component.

In collegiate populations, BMI delivered face-to-face was generally more effective than e-interventions alone in decreasing alcohol consumption. No studies compared these interventions in non-college samples. Although the available evidence suggests that e-interventions alone are inferior to face-to-face BMI, the small number of trials and the use of college student samples result in a low SOE. In studies using combined e-intervention and face-to-face counseling, 2 studies found no difference and one study found higher reported alcohol consumption with the combined intervention relative to face-to-face counseling alone. We judged the SOE for combined IVR and BMI interviewing as low. Other types of combined e-interventions have not been researched.

CLINICAL AND POLICY IMPLICATIONS

Though prior systematic reviews have found positive short-term effects on alcohol consumption in students, those effects have generally not been maintained at longer term follow-up.[24] This is consistent with the results of our review, which examined trials reporting alcohol-related outcomes at ≥6 months and found absent to modest effects. In addition, the few available trials suggested that e-interventions might be less effective than face-to-face counseling, a finding also supported by prior reviews in student samples.[24] Prior syntheses that evaluated studies in adults have found few studies. Khadjesari and colleagues[26]concluded that "computer-based interventions may reduce alcohol consumption compared with assessment-only," but only 6 of the 24 studies included in this review were conducted in non-student samples, and only 2 of those reported outcomes at ≥6 months. Riper and colleagues concluded that "E-self-help interventions without professional contact are effective in curbing adult problem drinking in high-income countries."[27] However, 4 of the 9 studies assessed outcomes at ≤3 months, and 8

studies included in our review were not evaluated in the Riper review, primarily because they were published after the search date.

The presence of systematic annual screening for alcohol misuse in primary care using the Alcohol Use Disorders Identification Test for Clinicians (AUDIT-C) provides a good means of identifying patients who would be candidates for e-interventions if they decline specialty clinic treatment. However, the evidence in favor of existing e-interventions is low, suggesting that further work is needed to develop effective e-interventions for alcohol misuse. Further, it is not clear whether brief intervention for alcohol is effective for AUD specifically, as the majority of studies target alcohol misuse. This is problematic, as previous reviews of brief alcohol interventions have commented that they do not seem to be as effective in people with AUD.[8,70] Limited data from adult studies suggests a possible benefit of increasing the intensity of e-interventions by extending treatment duration, adding phone counseling, or utilizing mobile applications. More intensive supplementary human support might also improve participant engagement and the effectiveness of e-interventions. More research is needed to determine whether this is effective, as there were not enough e-interventions incorporating a human support component for us to carry out quantitative analyses that resulted in reliable estimates of effect modifiers.

If effective e-interventions can be developed and tested, they have the potential to address many of the barriers to face-to-face treatment of alcohol misuse. For example, some data suggest that Veterans would prefer the convenience of e-interventions[71] as opposed to negotiating the latency to treatment initiation, time investment, and travel barriers to attending clinic visits. In addition, health care providers cite barriers to addressing alcohol misuse at clinic visits that could be circumvented by utilizing e-interventions. The barriers for health care professionals include perceived inadequate training and treatment resources,[72] time constraints,[73] and concerns about negative effects on the doctor-patient relationship.[74]

There are also methods by which e-interventions could be designed to prevent relapse after the termination of intensive face-to-face counseling to achieve initial abstinence from alcohol. The continuing utilization of e-interventions could provide an accessible way for individuals to utilize treatment components originally introduced during face-to-face counseling. New programs could be tailored to a Veteran sample and could incorporate recent developments in treatment as well as be adapted for increasingly prevalent technologies such as smartphones. VHA has introduced some smartphone applications that offer assessment, basic coping tools, and referral to treatment resources. Designing e-intervention materials specifically for mobile devices could be accomplished by translating the content generated in counseling sessions for the patient to carry with them throughout the day, including high-risk situations. Clinicians and patients could also tailor e-intervention content to incorporate personalized motivations to stop drinking, avoid situations that increase the risk of relapse, and use coping strategies. The trial by Gustafson and colleagues[52] incorporated these principles and demonstrated benefit in maintaining abstinence in patients completing treatment for AUD.

Many of the e-interventions we reviewed were focused on psychoeducation and PNF, with relatively few data available on e-interventions incorporating treatment components that are a standard part of psychotherapy for alcohol misuse. Studies including a broader range of treatment

techniques typically reported application of motivational interviewing components. Given the central importance of relational components such as partnership and empathy in conventional face-to-face motivational interviewing, it is unclear the degree to which e-interventions actually replicate the core processes of motivational interviewing. Interventions may be enhanced by faithfully replicating core components of motivational interviewing, incorporating other proven therapies such as cognitive-behavioral techniques or pairing e-interventions with pharmacotherapy for alcohol misuse.

One recent example is a trial by Brief and colleagues[75] that was ineligible for inclusion in our quantitative analyses because the final follow-up assessment was at 3 months post-randomization. However, it is relevant to this review because it was conducted with Veterans and included coping skills for the common comorbidity of alcohol misuse. The e-intervention used 8 online modules lasting approximately 20 minutes each to provide personalized feedback, facilitate decisional balance, set drinking goals, and receive feedback on progress toward goals. Veterans also received information on skills for coping with trigger situations including PTSD-related symptoms (stress, mood, and anger management) and practices to promote normal night-time sleep. Relative to waitlist, participants receiving the e-intervention significantly reduced alcohol consumption, binge drinking episodes, and alcohol-related problems. The median drinks per day decreased from 24 to 6 at 3-month follow-up. Results suggest the potential utility of e-interventions that are more intensive and broaden their strategies to address related problems that could be contributing to drinking behavior.

One expected contribution of e-interventions is the provision of low-cost clinical services to treat chronic problems such as alcohol misuse over a long period of time without utilizing a great deal of clinical resources. This efficient use of Veterans Affairs (VA) resources to improve the reach and long-term efficacy of alcohol treatment could provide valuable information to determine the value of e-interventions to the VA system. Consequently, clinical researchers could provide important contributions by including measures of cost-effectiveness in trials, especially when comparing e-interventions to traditional, clinic-based, face-to-face treatment.

The use of e-interventions for alcohol misuse will ultimately require attention to privacy and information security risks. Researchers must address these risks, eliminating them when possible and, if not possible, attending to the need to effectively communicate risks to Veterans using the technology. This includes the risk of information being intercepted during transmission to the study site, as well as breaches in the information stored at the study site and on computers and phones accessing the e-intervention.

LIMITATIONS

Our review builds upon and extends prior reviews by following a protocol-based, transparent process that engaged relevant VA policy makers; including recently published studies; and taking an inclusive approach to electronic interventions. Another strength is the focus on sustained effects of e-interventions, prioritized as clinically important by our research team and technical expert panel. Our review has limitations as well. These include statistical assumptions in transforming data reported in many different formats into a common metric (*eg*, grams of alcohol per week), and judgments about when to combine multiple e-interventions tested in a single

trial for meta-analyses. We also made the judgment not to conduct subgroup analyses, having specified in advance that these analyses would be conducted only if subgroups contained at least 4 studies per group. Other research teams may have made different decisions.

The literature also had important limitations. Because outcomes were self-reported, daily IVR interventions may have "trained" participants to report more alcohol consumption more accurately, biasing these studies against an intervention effect. Others have found that assessment itself has been associated with reduced alcohol consumption,[8] so alcohol consumption reductions in the e-intervention groups could have been concealed by concurrent reductions in inactive control groups. The relatively low intensity of the interventions in the available literature on e-intervention for alcohol misuse limits the reliability of conclusions drawn about e-interventions as a general approach. In particular, the lack of data on the incremental efficacy of including various levels of supplementary human support prevents evaluation of potential applications of e-interventions for alcohol misuse. The small number of studies or subgroup analyses reporting on effects in participants with AUD limits interpretation for specialty clinic-based clinicians who typically treat patients with AUD specifically, as opposed to alcohol misuse generally. Other study limitations are described below.

Publication Bias

To assess for publication bias, we searched ClinicalTrials.gov to identify completed but unpublished studies that would likely meet our eligibility criteria. Two such trials were identified from this search. The small number of trials reporting given outcomes prevented reliable quantitative evaluation of publication bias. Funnel plots were not used because analyses did not meet the minimum threshold of at least 10 studies for meaningful analysis.

Study Quality

We assessed study quality by having 2 independent investigators provide a rating of risk of bias. Most trials were judged to be at moderate risk of bias (n=14); 5 were at low risk, and 7 were at high risk of bias. In this literature, the most common study limitations increasing risk of bias were lack of participant blinding to study condition and incomplete or perceived potential for selective reporting of outcome data.

Heterogeneity

For effects on alcohol consumption, treatment effects varied from moderate to substantial. Variability in treatment effects were observed despite separate analyses for college samples and other adults. The variability in treatment effects on alcohol consumption limits the conclusions that can be drawn.

Applicability of Findings to the VA Population

In VHA, Veterans are screened annually for alcohol misuse using the AUDIT-C; approximately 15% screen positive. Among those who screen positive, >80% screen positive for alcohol misuse, with <20% screening positive at a threshold (*eg*, AUDIT-C ≥8) suggesting probable AUD. The majority of trials in this review used similar methods to enroll participants, and exclusion criteria were relatively few. In other aspects, these trials may have limited applicability

to VA. Only one trial[50] was conducted in a VA sample, half the trials were conducted in college students, and over half were conducted outside the United States. In the non-college samples, midlife adults, the majority of whom were college educated, participated; this is in contrast to the predominantly older population currently served by VA. Co-existing mental illness is common with alcohol misuse, but other mental illness diagnoses were not reported in these studies, introducing uncertainty about the applicability of these findings to Veterans with alcohol misuse and coexisting depression or anxiety disorders.

RESEARCH GAPS/FUTURE RESEARCH

Although the current state of the evidence does not strongly support long-term benefit from e-interventions for alcohol misuse, the evidence for short-term effects from low-intensity interventions and longer-term effects from higher intensity interventions suggests the potential for benefit. Table 10 identifies gaps in evidence and study designs that could address these gaps. Although it would be possible to generate an extensive list of gaps in evidence, we restricted this list to the areas judged to be highest priority, given the current state of evidence. To facilitate future literature syntheses, we encourage investigators conducting clinical trials to include these studies in trial registries.

Table 10. Highest Priority Evidence Gaps

Evidence Gap	Study Designs
Uncertainty about effects in adults with varying educational levels and co-occurring mental and physical illness	RCTs in well-described samples with analyses for interaction effects by education and other mental or physical illness
Uncertain effects in older adults	Observational studies to evaluate interest, user interface issues, and barriers to e-interventions in older adults
Uncertainty about the effects of multi-session, multi-component interventions	RCTs
Uncertainty about whether effects found in alcohol misuse generally are applicable to individuals meeting criteria for an AUD	RCTs requiring AUD for inclusion or reporting AUD as a subgroup analysis
Uncertainty about effects of robust e-interventions used in combination with face-to-face therapy.	RCTs of combined treatments that include economic outcomes
Uncertainty about the validity of self-reported outcomes for alcohol consumption	Bioverification measures, the use of collateral informants to provide independent reports of drinking behavior, or mobile monitoring that would allow frequent breath alcohol assessments in participants' naturalistic environments

Abbreviations: AUD=alcohol use disorder; RCTs=randomized controlled trials

CONCLUSIONS

The limited evidence from trials of e-interventions compared with controls on long-term (≥6 months) alcohol outcomes in participants who screened positive for alcohol misuse suggests that effects are small or absent. The available data were even more limited for participants

with AUD or comparisons of e-interventions with face-to-face treatment. Further research is needed to determine with higher confidence whether e-interventions can produce long-term benefits for alcohol-related outcomes. In particular, given the limited number and duration of intervention episodes in the studies reviewed, it is possible that these e-interventions were simply not designed to produce enduring effects on alcohol misuse. As reported in previous reviews, brief, in-person interventions can produce sustained reductions in alcohol consumption in those with hazardous drinking who do not meet criteria for AUD, which likely provides benefits at the public health level, and that could be the primary value of these low-intensity interventions. At this time, the evidence does not support substitution of e-interventions for brief, in-person treatment. Future research on e-interventions should include evaluations of more intensive or longer duration alcohol e-interventions.

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APPENDIX A. SEARCH STRATEGIES

SEARCH STRATEGIES BY DATABASE

Database: PubMed

Search date: 8/18/14

Set #		Results
1	"Behavior Therapy"[Mesh:NoExp] OR ((behavior[tiab] OR behaviour[tiab]) AND (therapy [tiab] OR therapies[tiab])) OR "Cognitive Therapy"[Mesh] OR ((cognitive[tiab] OR cognition[tiab]) AND (therapy[tiab] OR therapies[tiab])) OR "Psychotherapy, Brief"[Mesh] OR ((brief[tiab] OR short-term[tiab]) AND (psychotherapy[tiab] OR psychotherapies[tiab])) OR "brief counseling"[tiab] OR intervention[tiab] OR interventions[tiab] OR "Health Education"[Mesh]	668012
2	"Alcoholism"[Mesh] OR "Alcohol Drinking"[Mesh] OR ((heavy[tiab] OR hazardous[tiab] OR harmful[tiab] OR excessive[tiab] OR problem[tiab] OR binge[tiab] OR controlled[tiab] OR risky[tiab] OR "at risk"[tiab] OR "at-risk"[tiab] OR use[tiab]) AND drink*[tiab] AND (Alcohol[tiab] OR "Alcoholic Beverages"[Mesh]))	107410
3	"Therapy, Computer-Assisted"[Mesh] OR "Internet"[Mesh] OR "Cellular Phone"[Mesh] OR "Computers"[Mesh] OR "Computer-assisted"[tiab] OR computerized[tiab] OR "low intensity"[tiab] OR internet[tiab] OR web[tiab] OR "social media"[tiab] OR online[tiab] OR computer[tiab] OR computers[tiab] OR electronic[tiab] OR mobile[tiab] OR smartphone[tiab] OR smartphones[tiab] OR tablet[tiab] OR tablets[tiab] OR self-paced[tiab] OR "health buddy"[tiab] OR e-health[tiab] OR ehealth[tiab] OR m-health [tiab] OR mhealth[tiab]	584939
4	#1 AND #2 AND #3	746
5	((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT (animals[mh] NOT humans[mh]) NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp]))	2446984
6	#4 AND #5; limit to English, 2000 - present	364

Database: Embase

Search date: 8/18/2014

Set #		Results
1	'cognitive therapy'/exp OR 'behavior therapy'/exp OR 'behavior modification'/exp OR 'health education'/exp OR (('psychotherapy'/exp OR psychotherapy:ab,ti OR psychotherapies:ab,ti) AND (brief:ab,ti OR 'short term':ab,ti)) OR ((behavior:ab,ti OR behaviour:ab,ti) AND (therapy:ab,ti OR therapies:ab,ti)) OR ((cognitive:ab,ti OR cognition:ab,ti) AND (therapy:ab,ti OR therapies:ab,ti)) OR 'brief counseling':ab,ti OR intervention:ab,ti OR interventions:ab,ti	932809
2	'alcoholism'/exp OR 'drinking behavior'/exp OR ((heavy:ab,ti OR hazardous:ab,ti OR harmful:ab,ti OR excessive:ab,ti OR problem:ab,ti OR binge:ab,ti OR controlled:ab,ti OR risky:ab,ti OR "at risk":ab,ti OR "at-risk":ab,ti OR use:ab,ti) AND drink*:ab,ti AND (Alcohol:ab,ti OR 'alcoholic beverage'/exp))	147931

Set #		Results
3	'computer assisted therapy'/exp OR 'mobile phone'/exp OR 'Internet'/exp OR 'computer'/exp OR 'Computer assisted':ab,ti OR computerized:ab,ti OR 'low intensity':ab,ti OR internet:ab,ti OR web:ab,ti OR "social media":ab,ti OR online:ab,ti OR computer:ab,ti OR computers:ab,ti OR electronic:ab,ti OR mobile:ab,ti OR smartphone:ab,ti OR smartphones:ab,ti OR tablet:ab,ti OR tablets:ab,ti OR self-paced:ab,ti OR 'health buddy':ab,ti OR e-health:ab,ti OR ehealth:ab,ti OR m-health:ab,ti OR mhealth:ab,ti	1496238
4	#1 AND #2 AND #3	1352
5	('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR random*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR (cross NEAR/1 over*):ab,ti OR placebo*:ab,ti OR (doubl* NEAR/1 blind*):ab,ti OR (singl* NEAR/1 blind*):ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti) NOT ('case report'/exp OR 'case study'/exp OR 'editorial'/exp OR 'letter'/exp OR 'note'/exp)	1334623
6	#4 AND #5	435
7	#6 AND [embase]/lim NOT [medline]/lim	153
8	#7, 2000 – present, English	165

Database: PsycINFO

Search date: 8/18/2014

Set #		Results
1	((DE "Behavior Therapy") OR (DE "Cognitive Behavior Therapy")) OR (DE "Cognitive Therapy") OR (DE "Brief Psychotherapy") OR (DE "Health Education") OR TI (((behavior OR behaviour) AND (therapy OR therapies[tiab)) OR ((cognitive OR cognition) AND (therapy OR therapies)) OR ((brief OR short-term) AND (psychotherapy OR psychotherapies)) OR "brief counseling" OR intervention OR interventions) OR AB (((behavior OR behaviour) AND (therapy OR therapies[tiab)) OR ((cognitive OR cognition) AND (therapy OR therapies)) OR ((brief OR short-term) AND (psychotherapy OR psychotherapies)) OR "brief counseling" OR intervention OR interventions)	276210
2	(DE "Alcoholism") OR (DE "Alcohol Drinking Patterns" OR DE "Alcohol Abuse" OR DE "Alcohol Intoxication" OR DE "Social Drinking") OR ((TI (heavy OR hazardous OR harmful OR excessive OR problem OR binge OR controlled OR risky OR "at risk" OR "at-risk" OR use) OR AB (heavy OR hazardous OR harmful OR excessive OR problem OR binge OR controlled OR risky OR "at risk" OR "at-risk" OR use)) AND (TI (drink*) OR AB (drink*)) AND (TI Alcohol OR AB Alcohol OR (DE "Alcoholic Beverages")))	53853

Set #		Results
3	(((DE “Computer Assisted Therapy”) OR (DE “Internet”)) OR (DE “Cellular Phones”)) OR (DE “Computers” OR DE “Analog Computers” OR DE “Computer Games” OR DE “Digital Computers” OR DE “Microcomputers”) OR TI (“Computer-assisted” OR computerized OR “low intensity” OR internet OR web OR “social media” OR online OR computer OR computers OR electronic OR mobile OR smartphone OR smartphones OR tablet OR tablets OR self-paced OR “health buddy” OR e-health OR ehealth OR m-health OR mhealth) OR AB (“Computer-assisted” OR computerized OR “low intensity” OR internet OR web OR “social media” OR online OR computer OR computers OR electronic OR mobile OR smartphone OR smartphones OR tablet OR tablets OR self-paced OR “health buddy” OR e-health OR ehealth OR m-health OR mhealth)	140406
4	S1 AND S2 AND S3	561
5	#4 AND #5; Limiters - Publication Year: 2000-; English; Methodology: TREATMENT OUTCOME/CLINICAL TRIAL	58

Database: The Cochrane Library

Search date: 8/18/2014

Set #		Results
1	MeSH descriptor: [Behavior Therapy] explode all trees OR MeSH descriptor: [Cognitive Therapy] explode all trees OR MeSH descriptor: [Psychotherapy, Brief] explode all trees OR MeSH descriptor: [Health Education] explode all trees OR ((behavior:ab,ti OR behaviour:ab,ti) AND (therapy :ab,ti OR therapies:ab,ti)) OR ((cognitive:ab,ti OR cognition:ab,ti) AND (therapy:ab,ti OR therapies:ab,ti)) OR ((brief:ab,ti OR short-term:ab,ti) AND (psychotherapy:ab,ti OR psychotherapies:ab,ti)) OR “brief counseling”:ab,ti OR intervention:ab,ti OR interventions:ab,ti	83540
2	MeSH descriptor: [Alcoholism] explode all trees OR MeSH descriptor: [Alcohol Drinking] explode all trees OR ((heavy:ab,ti OR hazardous:ab,ti OR harmful:ab,ti OR excessive:ab,ti OR problem:ab,ti OR binge:ab,ti OR controlled:ab,ti OR risky:ab,ti OR “at risk”:ab,ti OR “at-risk”:ab,ti OR use:ab,ti) AND drink*:ab,ti AND (Alcohol:ab,ti OR MeSH descriptor: [Alcoholic Beverages] explode all trees	4523
3	MeSH descriptor: [Therapy, Computer-Assisted] explode all trees OR MeSH descriptor: [Internet] explode all trees OR MeSH descriptor: [Cellular Phone] explode all trees OR MeSH descriptor: [Computers] explode all trees OR “Computer-assisted”:ab,ti OR computerized:ab,ti OR “low intensity”:ab,ti OR internet:ab,ti OR web:ab,ti OR “social media”:ab,ti OR online:ab,ti OR computer:ab,ti OR computers:ab,ti OR electronic:ab,ti OR mobile:ab,ti OR smartphone:ab,ti OR smartphones:ab,ti OR tablet:ab,ti OR tablets:ab,ti OR self-paced:ab,ti OR “health buddy”:ab,ti OR e-health:ab,ti OR ehealth:ab,ti OR m-health :ab,ti OR mhealth:ab,ti	31584
4	#1 AND #2 AND #3 (not limited by date)	197

APPENDIX B. CRITERIA USED IN QUALITY (RISK OF BIAS) ASSESSMENT OF RCTs

General Instructions: Rate each risk of bias item listed below as **Low risk/High risk/Unclear risk** (see Cochrane guidance to inform judgements). Add comments to justify ratings. After considering each of the quality items, give the study an overall rating of "**Low risk**," "**Moderate risk**," or "**High risk**" (see below).

Rating of individual items:

1. **Selection bias:**
   a. **Randomization adequate* (Adequate methods include: random number table, computer-generated randomization, minimization w/o a random element) **Low risk/High risk/ Unclear risk**
   b. **Allocation concealment* (Adequate methods include: pharmacy-controlled randomization, numbered sealed envelopes, central allocation) **Low risk/High risk/Unclear risk**
   c. *Baseline characteristics* (Consider whether there were systematic differences observed in baseline characteristics and prognostic factors between groups, and if important differences were observed, if the analyses controlled for these differences) **Low risk/ High risk/Unclear risk**
2. **Performance bias:**
   a. **Concurrent interventions or unintended exposures:* (Consider concurrent intervention or an unintended exposure [*eg*, crossovers; contamination – some control group gets the intervention] that might bias results) **Low risk/High risk/Unclear risk**
   b. *Protocol variation:* (Consider whether variation from the protocol compromised the conclusions of the study) **Low risk/High risk/Unclear risk**
3. **Detection bias:**
   a. **Subjects Blinded?:* (Consider measures used to blind subjects to treatment assignment and any data presented on effectiveness of these measures) **Low risk/High risk/Unclear risk**
   b. **Outcome assessors blinded (hard outcomes):* (Outcome assessors blind to treatment assignment for "hard outcomes" such as mortality) **Low risk/High risk/Unclear risk**
   c. **Outcome assessors blinded (soft outcomes):* (Outcome assessors blind to treatment assignment for "soft outcomes" such as symptoms) **Low risk/High risk/Unclear risk**
   d. *Measurement bias:* (Reliability and validity of measures used) **Low risk/High risk/ Unclear risk**
4. **Attrition bias:**
   a. **Incomplete outcome data:* (Consider whether incomplete outcome data were adequately addressed, including: systematic differences in attrition between groups [differential

attrition]; overall loss to follow-up [overall attrition]; and whether an "intention-to-treat" [ITT; all eligible patients that were randomized are included in analysis] analysis was performed) (Note – mixed models and survival analyses are in general ITT) **Low risk/ High risk/Unclear risk**

5. **Reporting bias:**

   a. **Selective outcomes reporting:* (Consider whether there is any suggestion of selective outcome reporting (*eg*, systematic differences between planned and reported findings)? **Low risk/High risk/Unclear risk**

*Items contained in Cochrane Risk of Bias Tool

Overall study rating:

Please assign each study an overall quality rating of "Low risk," "High risk," or "Unclear risk" based on the following definitions:

A "**Low risk**" study has the least bias, and results are considered valid. A low risk study uses a valid approach to allocate patients to alternative treatments; has a low dropout rate; and uses appropriate means to prevent bias, measure outcomes, and analyze and report results. [Items 1a and 1c; 2a; 3b and 3c; and 4a are all rated low risk]

A "**Moderate risk**" study is susceptible to some bias but probably not enough to invalidate the results. The study may be missing information, making it difficult to assess limitations and potential problems (unclear risk). As the moderate risk category is broad, studies with this rating vary in their strengths and weaknesses. [Most, but not all of the following items are rated low risk: Items 1a and 1c; 2a; 3b and 3c; and 4a]

A "**High risk**" rating indicates significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; have large amounts of missing information; or have discrepancies in reporting. The results of a high risk study are at least as likely to reflect flaws in the study design as to indicate true differences between the compared interventions. [At least one-half of the individual quality items are rated high risk or unclear risk]

Conflict of interest: (Record but not used as part of Risk of Bias Assessment)

   a. *Was there the absence of potential important conflict of interest?:* The focus here is financial conflict of interest. If no financial conflict of interest (*eg*, if funded by government or foundation and authors do not have financial relationships with drug/ device manufacturer), then answer "Yes." **Yes/No/Unclear**

APPENDIX C. QUALITY OF INCLUDED STUDIES

Study	Individual Quality Assessment Criteria Ratings											Overall Rating	COI Absent?
	1a	1b	1c	2a	2b	3a	3b	3c	3d	4	5		
Barnett, 2007[1]	Low	Low	Low	Low	Low	High	Low	Low	Low	Low	Low	**Low**	Yes
Bischof, 2008[2]	UNCL	Low	Low	Low	Low	High	UNCL	UNCL	Low	Low	Low	**Moderate**	Yes
Boon, 2011[3]	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	UNCL	**Low**	Yes
Cucciare, 2013[4]	Low	UNCL	Low	Low	Low	UNCL	Low	Low	Low	Low	Low	**Low**	No
Cunningham, 2009[5]	Low	UNCL	Low	Low	Low	UNCL	UNCL	UNCL	Low	Low	Low	**Moderate**	Yes
Gustafson, 2014[6]	Low	UNCL	Low	UNCL	Low	High	NA	High	Low	Low	Low	**Moderate**	Yes
Hansen, 2012[7]	Low	Low	Low	Low	Low	UNCL	UNCL	UNCL	UNCL	UNCL	Low	**Moderate**	Yes
Hasin, 2013[8]	Low	Low	Low	Low	Low	High	Low	Low	Low	Low	Low	**Low**	Yes
Helzer, 2008[9]	UNCL	UNCL	High	Low	Low	High	Low	Low	UNCL	Low	Low	**Moderate**	Yes
Hester, 2012[10]	UNCL	UNCL	Low	Low	Low	High	UNCL	UNCL	Low	UNCL	Low	**High**	Yes
Kypri, 2009[11]	Low	Low	UNCL	Low	Low	UNCL	Low	Low	Low	Low	Low	**Low**	Yes
Kypri, 2008[12]	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	**Low**	Yes
Kypri, 2004[13]	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	**Low**	Yes
Monahan, 2013a[14]	Low	UNCL	Low	Low	Low	High	Low	Low	Low	UNCL	UNCL	**Moderate**	Yes
Monahan, 2013b[14]	Low	UNCL	Low	Low	Low	High	Low	Low	Low	UNCL	UNCL	**Moderate**	Yes
Moreira, 2012[15]	Low	Low	Low	Low	Low	Low	Low	Low	Low	High	Low	**Moderate**	Yes
Mundt, 2006[16]	UNCL	UNCL	Low	Low	Low	High	UNCL	High	Low	UNCL	UNCL	**High**	No
Neighbors, 2010[17]	Low	Low	UNCL	UNCL	Low	UNCL	Low	Low	Low	Low	Low	**Moderate**	Yes
Neighbors, 2004[18]	UNCL	High	UNCL	Low	Low	UNCL	Low	Low	Low	Low	Low	**Moderate**	Yes
Neumann, 2006[19]	UNCL	UNCL	Low	UNCL	Low	High	UNCL	UNCL	Low	High	UNCL	**High**	Yes
Riper, 2008[20]	UNCL	UNCL	Low	UNCL	High	High	UNCL	UNCL	Low	High	Low	**High**	Yes
Schulz, 2013[21]	Low	UNCL	Low	Low	Low	High	NA	Low	Low	Low	Low	**Moderate**	Yes
Sinadinovic, 2012[22]	UNCL	UNCL	High	UNCL	High	High	UNCL	UNCL	Low	High	Low	**High**	Yes
Voogt, 2013[23]	Low	UNCL	Low	UNCL	Low	Low	UNCL	UNCL	Low	Low	Low	**Moderate**	Yes
Wallace, 2011[24]	Low	Low	Low	Low	Low	Low	Low	Low	Low	High	Low	**Moderate**	Yes
Walters, 2009[25]	UNCL	UNCL	Low	Low	Low	High	Low	High	Low	Low	Low	**Moderate**	Yes

Abbreviations: COI=(financial) conflict of interest; NA=not applicable; UNCL=unclear

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APPENDIX D. PEER REVIEW COMMENTS/AUTHOR RESPONSES

Reviewer	Comment	Response
Question 1: Are the objectives, scope, and methods for this review clearly described?		
1	Yes. No comments	Acknowledged
2	Yes. Very well done. A few suggestions below related to the methods.	Acknowledged
3	Yes. Excellent description of objectives, scope and methods. I would welcome the chance to have this experienced team involved in SR's for the revision of the VA/DoD CPG on SUD that is scheduled to begin in FY15. No scoping has been initiated and there are existing contracts with Lewin and ECRI that are involved with other CPGs, but perhaps there are opportunities to explore?	Thank you. We will forward this request to the VA ESP Coordinating Center to explore participation in the CPG.
4	Yes. More information could be provided early on about the specific studies selected for review. The report is difficult to read and follow as written. I realize there is probably a format for these reviews, but given there is only a relatively limited number of studies, I would rather see a brief synopsis of the studies first.	The report adheres to the VA ESP standard template. We agree that the length and format of the report draft can make it difficult to follow. In the version of the report that will be disseminated, the main report will be preceded by a brief executive summary that serves as a synopsis for the report.
5	Yes. The objectives, scope, and methods for this review are clearly described. This is a thorough and robust report on the use of e-interventions for alcohol misuse.	Thank you.
5	Table 2. I don't quite understand why pregnant women would have been excluded from the studies you examined. It is a group with potential for alcohol abuse and there are increasingly more women veterans. I'm sure there is a reason, but a rationale would be useful.	E-interventions for alcohol misuse in pregnant women are a worthy topic of research, but we reasoned that the processes and outcomes for pregnant women would be too different from the general population. Nevertheless, we retained information on how many studies were available so additional work could be completed on this topic. We found 16 studies whose abstracts suggested they could be trials focused on pregnant women, but did not conduct full-text reviews to evaluate their inclusion. We revised the discussion to note this limitation of the literature and highlight the need for future research.
6	Yes. The objectives and scope of this review are clearly and concisely described. Detailed description of methods including data abstraction and quality assessment, as well as data synthesis makes process completely transparent.	Acknowledged
Question 2: Is there any indication of bias in our synthesis of the evidence?		
1	No. No comments.	Acknowledged
2	No. No comments.	Acknowledged
3	No. No comments.	Acknowledged
4	No. The report does not appear biased.	Acknowledged
5	No. No comments.	Acknowledged

Reviewer	Comment	Response
6	No. None whatsoever.	Acknowledged
Question 3: Are there any published or unpublished studies that we may have overlooked?		
1	Yes. 1. Screening and Behavioral Counseling Interventions in Primary Care to Reduce Alcohol Misuse: USPSTF Recommendation Statement. Ann Intern Med. 2013; 159(3):210-218. Link: http://www.uspreventiveservicestaskforce.org/uspstf12/alcmisuse/alcmisusefinalrs.htm 2. . Jonas et al Comparative Effectiveness Review: Screening, Behavioral Counseling, and Referral in Primary Care to Reduce Alcohol Misuse. AHRQ. July 2012. Link: http://www.ncbi.nlm.nih.gov/books/NBK99199/	The cited publications were reviewed and are not trials evaluating e-interventions for alcohol misuse. However, these are relevant publications that have been integrated into the background literature review and discussion.
2	No. Not that I am aware of.	Acknowledged
3	Yes. There should be some explicit attention to the omission of the Brief et al trial from the review. Also note that p 20 indicates there would be an update beyond 11/19/13 that should include this study? It was published very close to the search deadline, and perhaps that's why it got missed? I don't find it at clinicaltrials.gov. At least some discussion of the findings is warranted, especially given the sample. **Web intervention for OEF/OIF veterans with problem drinking and PTSD symptoms: a randomized clinical trial.** Brief DJ, Rubin A, Keane TM, Enggasser JL, Roy M, Helmuth E, Hermos J, Lachowicz M, Rybin D, Rosenbloom D. J Consult Clin Psychol. 2013 Oct;81(5):890-900	The study by Brief et al was identified in our updated literature search but was excluded because outcomes were not reported at ≥6 weeks. However, because this study uses a more robust intervention than included studies and was conducted in Veterans, we discuss it briefly in the report's discussion.
3	The SR found no rcts of smartphone applications, but the following was in progress and listed in clinicaltrials.gov at http://www.clinicaltrials.gov/ct2/show/NCT01003119?term=gustafson&rank=9 This is an important study that warrants discussion (e.g., p 53) and perhaps even acknowledgement in the ES that addresses smartphone apps in para 2 p 8. The intervention incorporates many of the features identified in the Discussion (p 53) for future evaluation. Might also add specifically to Table 10 (or use as e.g. for multi-component interventions – p 56 row 1). The smartphone app is under active consideration by the Connected Health Office in VHA and perhaps Kathy Frisbee should be contacted for her input on the status (very preliminary from what I understand) **A smartphone application to support recovery from alcoholism: a randomized clinical trial.** Gustafson DH, McTavish FM, Chih MY, Atwood AK, Johnson RA, Boyle MG, Levy MS, Driscoll H, Chisholm SM, Dillenburg L, Isham A, Shah D. JAMA Psychiatry. 2014 May;71(5):566-72. doi: 10.1001/jamapsychiatry.2013.4642	The study identified from ClinicalTrials.gov has been completed and published (Gustafson, 2014; cited by the reviewer). This study was identified in our updated literature search and is included in the final report.
4	Not to my knowledge as relates specifically to alcohol.	Acknowledged

Reviewer	Comment	Response
5	No. No comments.	Acknowledged
6	Randomized controlled trial of two brief alcohol interventions for OEF/OIF veterans. McDevitt-Murphy, Meghan E.; Murphy, James G.; Williams, Joah L.; Monahan, Christopher J.; Bracken-Minor, Katherine L.; Fields, Jordan A. Journal of Consulting and Clinical Psychology, Vol 82(4), Aug 2014,	The McDevitt-Murphy et al trial is relevant to alcohol research in Veterans, but was excluded because the intervention was face-to-face, as opposed to including an e-intervention, which is the focus of the current review.
6	A Smartphone Application to Support Recovery From Alcoholism: A Randomized Clinical Trial David H. Gustafson, PhD1; Fiona M. McTavish, MS1; Ming-Yuan Chih, PhD1; Amy K. Atwood, PhD1; Roberta A. Johnson, MA, MEd1; Michael G. Boyle, MA1; Michael S. Levy, PhD2; Hilary Driscoll, MA3; Steven M. Chisholm, MA4; Lisa Dillenburg, MSW1; Andrew Isham, MS1; Dhavan Shah, PhD5 JAMA Psychiatry. 2014;71(5):566-572. doi:10.1001/jamapsychiatry.2013.4642	Thank you for noting the trial by Gustafson et al. As indicated above, this was identified in our updated literature search and is included in the final report.
Question 4: Please write additional suggestions or comments below. If applicable, please indicate the page and line numbers from the draft report.		
1	No comments	Acknowledged
2	Thank you for the opportunity to review this report. Drs. Williams and Dedert and their team have done an excellent job synthesizing this literature. I hope that my suggestions and comments will help to improve what is already an outstanding report. **Main comments:** 1. Methods. The authors should provide justification for using odds ratios for dichotomous outcomes, or they should consider using RRs or RDs. Most methodological guidance documents provide rationale that suggests using RRs for most situations similar to what is synthesized in this report. For some situations, risk differences might be appropriate (but rationale for choosing them should be provided). Most methodologists do not think that ORs should be used for this type of analysis.	Thank you for this observation that a RR is a more appropriate summary statistic for a dichotomous outcome. We agree and have substituted a RR in the analyses of the dichotomous outcome “met drinking limits.”

Reviewer	Comment	Response
2	2. Results. Exec Sum pg 4, lines 32-35, and ES pg 5, lines 1-3 (and many other locations in tables and text throughout the report). This comment is about how to describe results of the meta-analyses that were not statistically significant. This issue comes up in several places in the Exec Sum and in the full report. For example, for the MD -29.9 (95% CI, -78.2 to 18.3), many would describe that data simply as finding "no statistically significant difference" or even just "no significant difference". The authors have described it as finding "a small reduction in alcohol consumption, but the 95% CI was wide and included no effect". I think wording it this way is confusing and makes it sound like the authors are more confident that there is truly an effect (and it makes readers wonder why some results are described in this manner, but others were not). I would argue that that data show that there is no significant effect or that the existing data don't provide the power to find anything less than a moderate to large effect. The SOE for that finding was low, indicating that we have low confidence in the effect estimate (i.e., the effect might be anywhere in that very wide CI, and we're not at all confident that it's 29.9).	We have edited the report to provide consistency in how statistically insignificant results are described. We were aiming for a non-technical way to express the results, but have modified the text to use more traditional language and be more consistent in our description of the findings.
2	2. Results (continued). Also, a reduction of 29.9 grams/week is a little more than 2 drinks/week, and many clinicians would not consider that to be a clinically significant reduction, especially considering the average drinks/week that the subjects were consuming at baseline.	Thank you. We agree. In the final report, we have stated: "When evaluating the overall SOE, we considered a difference of 3 standard U.S. drinks/week or an SMD ≥0.4 as clinically significant and defined precise effects as those with 95% confidence intervals (CIs) that excluded smaller effects."
2	2. Results (continued). Further, I have some concern that the estimates of effect are overestimates because they include the studies rated as high risk of bias (and it appears that those studies often found larger estimates of effect)—see my comment #4, and others, below.	Although the value of subgroup analyses by risk of bias ratings is controversial, we conducted sensitivity analyses in the limited instances where there were sufficient studies to support these analyses. These results have been added to the report, but were similar to the original analyses and so did not change the conclusions.
2	2. Results (continued). In other places, the authors have described results of meta-analyses that were not statistically significant simply as "no difference" or similar (which seems more appropriate, given the data). It's not clear why certain instances took the other approach (of describing the finding as a small or modest effect, but with the follow-up line that the CI included no effect).	As indicated above, we have edited the report to provide consistency in how statistically insignificant results are described.
2	3. Methods and Results. This applies to several places, related to interpretation of the data. Many readers will not be familiar with grams/week of alcohol. Since most of the data was for that outcome, it would be helpful to provide readers with some interpretation that allows them to understand the findings in terms of drinks per week—either just giving the conversion in 1 or 2 places (usually it's 13.7 grams = 1 standard drink) or else explaining how many drinks per week it is for the various main findings.	To provide the reader with a more accessible way of interpreting the results, we have added the definition for a U.S. standard drink (including grams of alcohol) to an inset box in the Executive Summary.

Reviewer	Comment	Response
2	4. Methods and Results. The risk of bias ratings seem to be ignored when conducting the quantitative syntheses. The ROB ratings were used to prioritize and interpret findings when conducting qualitative syntheses, appropriately. But, why were they ignored in the quantitative synthesis? I would suggest that more attention should be given to them in the quantitative syntheses. It seems that there are 2 approaches commonly used to do this in the most rigorous meta-analyses—either include all the studies in the main analysis and remove the high ROB studies as a sensitivity analysis (or this can be shown in a single plot that includes an overall pooled estimate and stratifies by high vs. low/mod ROB), or include only low/mod ROB studies in the main analysis and add the high ROB studies as a sensitivity analysis.	Although the value of subgroup analyses by risk of bias ratings is controversial, we conducted sensitivity analyses in the limited instances where there were sufficient studies to support these analyses. These results have been added to the report, but were similar to the original analyses and so did not change the conclusions.
2	5. Discussion. ES pg 8 under Clinical and Policy Implications, Lines 4-5. And pg 9 under Conclusions (and similar material in several places in the full report). Regarding claims about small positive effects and short-term benefits. I'm not convinced that the review found "positive effects of e-interventions on alcohol consumption over the short-term". This is perhaps related to my comment #2 above, and how to interpret the data. Looking at the meta-analyses, there were no statistically significant findings for consumption outcomes. Further, those estimates include the studies rated as high risk of bias that appear to have higher estimates of effect than studies with low/mod ROB.	Thank you for identifying this point of confusion. Our review did not examine short-term outcomes, and the places in the report in which we discuss short-term outcomes are references to prior work. We have rephrased these statements to prevent confusion about our findings. The revised report more clearly indicates our findings of absent or modest effects, which are contrasted with some previous evidence of small benefits of brief alcohol interventions.
2	6. Discussion. ES pg 8 under Clinical and Policy Implications. Lines 7-8. (and similar material in the full report). It is great to see this part about more intensive interventions, and the possibility that more intense e-interventions might be effective. I think this is a key issue, and maybe it deserves even more attention. It has been shown that very brief single contact face-to-face interventions are typically not effective. So, it is not surprising that single session, brief e-interventions are not effective. It's nice to have some qualitative approach for assessing differences in effect by intensity, but it seems possible to also conduct quantitative analyses to address this issue—at a minimum, the authors could stratify meta-analyses by intensity or just add columns to the forest plots so that readers can quickly align/see various intensities and the associated effects (right now, the report requires readers to look back and forth at many places to piece it all together when looking at the forest plots).	While the limited number of trials on the topic of e-interventions for alcohol prevented us from conducting more quantitative analyses, we agree that the qualitative relationships are difficult to follow in this extensive report. To facilitate comprehension of this important issue, we have inserted information on the risk of bias, level of supplemental human support, and intervention dose (single vs multiple sessions) into the figures. We have also added a brief discussion of a study (Brief, 2013) of a more intensive intervention in Veterans with alcohol misuse to the report's Discussion. This study was not included in the Results section because outcomes were not reported at ≥6 months.
2	7. Forest plots. Related to issues raised in my previous comments: throughout the report, it would help to have a few more columns added to the plots. Specifically, showing the following for each study: risk of bias, level (1, 2, or 3), and whether the intervention was a single contact or multiple contacts.	See response to immediately preceding comment.

Reviewer	Comment	Response
2	8. Table 1. Pg 11. a. Suggest indicating somehow that "unhealthy alcohol use" is synonymous with alcohol misuse because it shows up in the literature a lot and sometimes people are confused about how those terms compare. b. Suggest adding "alcohol use disorder" to the Table and perhaps adding some information to the left column to indicate DSM IV (alcohol abuse and alcohol dependence) or DSM-5 (AUD) under the terms associated with the different versions of DSM. c. For risky or hazardous use, there are also per occasion amounts (as well as weekly) – they are typically 4 or more per occasion for adult women and anyone older than 65 years, and 5 or for younger men. d. Table 1 footnote. Related to the DSM-IV part of the footnote. Only alcohol abuse and alcohol dependence are DSM-IV terms. Risky or hazardous use terms were developed from other sources (mainly through the prevention literature). Harmful use is an ICD-10 term.	This table has been modified in several places to add the suggested information.
2	9. Heterogeneity. The authors could perhaps do more to explore and explain heterogeneity. Stratifying forest plots by risk of bias might provide/show an explanation for it in some of the plots. For example, when looking at Figure 3 (I squared was 62%), I would bet that the heterogeneity among the low/mod ROB studies was 0% and that the high ROB studies (really it's just 1 of them, Riper) account for the statistical heterogeneity. I didn't try to look into this level of detail for all of the meta-analyses, but I wonder if the issue is similar in the other analyses with moderate or high statistical heterogeneity.	Thank you for the suggestion. We have reformatted the forest plots to show risk of bias. Where feasible, we have conducted and reported results from sensitivity analyses that exclude studies at high risk of bias.
2	10. pg 31. Figure 3. It is interesting that only the 2 studies rated high ROB (Neumann and Riper) found a statistically significant effect (within the study). Reading the report, it was not so easy to piece that information together, as I had to look back and forth between the Appendices and the Figure. Those were also the only 2 "level 2" studies in that forest plot. So, it may not be so simple as to say that we have the (common) situation of high ROB studies overestimating effects, because the levels (and maybe other things) also differ. Regardless, it would be helpful to show more columns within the plot so that readers don't have to look back and forth at so many places, by indicating the ROB, the Level, and whether they were a single or multi-contact intervention within the Figure.	We have added information to the figures to draw attention to key variables and allow readers to more easily examine qualitative patterns in the data.
2	11. pg 41. Line 37. Says that evidence is insufficient…There seems to be a discrepancy with the SOE table (Table 7) – it has low SOE for alcohol consumption outcomes. I didn't cross-check other places in the report to see whether they matched the text here or the SOE table.	We have verified that the "insufficient" rating was correct and have updated the SOE table to match the table.

Reviewer	Comment	Response
2	12. pg 46. Lines 36-37. I think this is the first mention of the thresholds used to determine precision, and they're only mentioned here for KQ 4. Suggest that these should be in the Methods section also (especially if they also apply to other KQs). The thresholds used for other outcomes should also be reported.	We have added this information to the "Data Synthesis" section so that readers could consider the threshold for precision while reading the results.
2	13. Table 9. The SOE table. a. Suggest separating the SOE grades for adults and students. It doesn't seem to make sense to combine the SOE grades for those 2 groups when all of the evidence was separated for those populations throughout the report. Further, I see some rows where it seems that some domain ratings should perhaps differ for the adult data and the student data -- e.g., I wonder if the authors would keep the same ratings for aggregate risk of bias and for precision in some of these rows if they separated SOE grades for adults and students. b. Transparency of the SOE grades could be improved. GRADE recommends providing footnotes to make the rationale clear, when needed. For example, for adults, for meeting limits, there were 3 RCTs, and 2 of those 3 were rated high ROB. Yet, aggregate ROB was rated as low in the SOE table. I would suggest that the authors provide some rationale for this rating. Another example, for many of the rows the thresholds for when the evidence was precise or imprecise is unclear. Another example, the entry "some indirectness" is used in a couple of places, and some rationale for what that means and how it was factored into the overall grade would help with transparency of the SOE grades.	We understand the concern and have given separate SOE ratings when ratings diverged importantly for adult and student populations. We kept detailed records of the SOE ratings but do not think most readers will want this detail. Cochrane readers have specifically described excessive footnotes as a barrier to understanding. Our overall judgment about the risk of bias is not based on a simple count of studies but is informed by contribution of low risk of bias studies to the summary estimate (study weights). In the example cited, low risk of bias studies contributed 64% of the study weight to the summary estimate.
2	14. pg 54. Limitations. Lines 17-19. Regarding judgment not to conduct subgroup analyses, and specifying the need for 4 studies per group. I think this is the first time this shows up in the report. If this was an a priori decision, it should be described in the Methods section. More importantly, the authors should provide rationale for this decision, with references supporting its validity.	We have added this criterion to the Methods section under "Data Synthesis and Analysis," along with a reference to: Fu R, Gartlehner G, Grant M, et al. Conducting Quantitative Synthesis When Comparing Medical Interventions: AHRQ and the Effective Health Care Program. In: Agency for Healthcare Research and Quality. Methods Guide for Comparative Effectiveness Reviews [posted October 2010]. Rockville, MD. Available at: http://effectivehealthcare.ahrq.gov/.

Reviewer	Comment	Response
2	**Minor comments:** 1. page 2 of Exec Sum. Lines 2-4 (and maybe also in later parts of the report that invoke the PRISMA statement). I think the PRISMA standards are not quite described/invoked appropriately. PRISMA only provides preferred reporting standards (telling us what should be reported in systematic reviews and meta-analyses), it does not provide methodological guidance for how to actually conduct systematic reviews. So, reviews are not actually "conducted" according to PRISMA standards; rather, they are reported according to PRISMA standards—and other methodological manuals or publications guide how reviews are conducted (such as the EPC methods manual that the authors reference in other places). 2. pg 4 of Exec Sum. Line 5. Delete only 3. pg 4 of Exec Sum. Lines 6, 13, and 19-21. It would help to provide the n after "Most". 4. pg 4 of Exec Sum. Line 16. It might help to describe/define PNF here. 5. pg 6 of Exec Sum. Line 12. End the sentence after "misuse". Start next sentence with "They varied…" (deleting ", but"). 6. pg 7 of Exec Sum. Line 7. This bullet about SOE for KQ 4 was not included for the earlier KQs. For consistency, either delete it here or include bullets/info about SOE for the other/earlier KQs also.	Most of the suggested edits have been made as suggested. We did not add the "n's" after "most" (comment 3 at left), as the intention for the Executive Summary is to provide a high-level summary without all the details contained in the main report.
2	7. pg 7 of ES. Line 14. "midlife" is unclear. Suggest providing mean age that is intended or similar. .	We clarified "midlife" by adding the median age.
2	8. pg 7-8 of ES. Table ES-1. Related to main comment #2. For the first 3 rows, why not just put in "No statistically significant difference" and then the data in parentheses in the "Effect Estimate" column? Same for the 3rd row up from the bottom that has "small, statistically insignificant difference". (The Table seems to be inconsistent across outcomes for how/when to determine that there was "no difference" vs. saying something about a small difference that was not statistically significant)	We were attempting to enhance clarity through a less technical presentation. We have modified the presentation to use clearer language when summarizing results qualitatively, and to include 95% CIs for outcomes with summary effect estimates.
2	9. pg 9 of ES. Line 17. It might help to describe what the only VA study found here in the Executive Summary, given the audience	We describe that only a single study was conducted in a VA population and that this affects applicability. We did not think that emphasizing the results from this one trial (given 26 trials overall) would be informative.
2	10. page 12. Line 26. Add "s" to adverse effect	Thank you. We have edited as suggested.

Reviewer	Comment	Response
2	11. pg 15. Table 2. Publications, last row. "Western Europe" is an unclear region that has evolved in the fairly recent past. Also, it is unclear if the intention here was to consider Europe as having 4 regions (western, eastern, northern, southern) or as having 2 regions (just eastern and western). Both geographic divisions are used in various places. The former approach would lead to the exclusion of studies from Sweden and Italy, for example. There is not general agreement about which countries to consider as western, eastern, northern, and southern Europe. I'm not disagreeing with limiting the eligibility as the authors have, but the specific eligible countries should be listed. Also, the issue of which country the studies were conducted in seems more appropriately listed in the Setting row, rather than the Publications row of Table 2.	"Western Europe" refers to Countries of the European Union. We have modified the text to clarify this.
2	12. pg 21. Figure 1. The typical flow diagram recommended by PRISMA specifies (at the bottom of the figure) both the total number included for any evaluation (which you have) and the number included in quantitative analyses (which is missing)	Thank you for the suggestion. In general, we agree with this approach, but in this specific instance we have not included the number included in quantitative syntheses, since the number varied widely by outcome and population.
2	13. pg 27. Figure 2. This may show up OK on a computer screen, but I can't tell the difference between the 2 colors used in the bar graph when printing the document in black and white. Consider using a larger contrast between the 2 colors.	We have changed the color contrast in this figure and also made one category diagonally striped rather than solid.
2	14. pg 32. Lines 11 and 13. Why did it drop from 4 to 3 studies?	This inconsistency has been corrected.
2	15. Several of the Figures include Kypri 2008 (as well as a Kypri 2009 study). The ROB appendix has 2 Kypri 2009 studies, but no Kypri 2008 study.	There are 3 Kypri studies (2004, 2008, and 2009). We have carefully reviewed the report, the risk of bias table, and the appendices. All 3 Kypri studies are referenced correctly.
2	16. p 49. Table 9. The row for Alcohol Social Problems, Effect estimate column. I think a negative sign is missing for the 95% CI for the SMD data.	Thank you. The negative sign has been added.
2	17. p 50. Table 9. For KQ 4. Effect estimate of 50 to 80g/wk. What was the CI? If not available, a footnote explaining the data more would help	There was no summary estimate for this outcome. The range of effects is presented. We have modified the text to clarify that this is a range.
2	18. pg 51. Lines 28-29. The way the 1st and 2nd sentences are worded, it sounds like the 2nd sentence will be about "other" outcomes (i.e., non-alcohol consumption outcomes). But, then the 2nd sentence starts with a point about binge drinking, which is an alcohol consumption outcome.	This sentence was edited for clarity. The intent was to convey that the most data are available for the volume of alcohol consumed, while other outcomes were reported in comparatively fewer studies, including those outcomes we targeted in the review (*eg*, binge drinking episodes).
2	19. pg 54. Line 34. Delete the underscore after ClinicalTrials.gov	Thank you. We have edited as suggested.

Reviewer	Comment	Response
2	20. Methods. Risk of bias. The official documents referenced by the authors use low, medium (not moderate), and high ROB ratings. Moderate is used in grading the SOE, but medium is used when rating ROB. I'm not sure why high and low were the same in both systems, but the middle categories differed (and I'm not sure that it really matters enough to change it throughout the report)	Acknowledged
3	I appreciated attention to clinically meaningful change vs. statistically reliable change elsewhere in the document, but might add a comment to TABLE ES-1. Might also indicate the threshold set for a "precise estimate of effect" from p 46 line 37.	We have added detail to our definition of clinically significant effects and precise effects to the Executive Summary Methods section.
3	Throughout the document, assure accurate distinction of AUDIT-C > 8 from AUDIT-C >=8 (e.g., p 55 line 15 that is accurate; elsewhere there is sometimes mention of AUDIT-C >8)	The change from AUDIT-C>8 to AUDIT-C $\geq$8 has been made throughout the document.
3	P 11 para 1 last sent – reference 14 for personal communication misspells source	Thank you. This has been corrected.
3	P 14 Table 2 last row – may be worth mentioning the number of trials excluded based solely on n<50, however the rationale for design decision is persuasive.	We did not track the number of trials excluded due to n<50.
3	P 28 last sent – the potential for selective reporting is well taken in this literature. I encourage some statement about the importance of trial registration and analyses consistent with original analytic plan. Also curious what percent of selected trials appeared in clinicaltrials.gov	We have added a statement supporting trials registries in the Future Research section. Although we searched ClinicalTrials.gov for completed but unpublished studies, we did not evaluate whether published trials had been included in ClinicalTrials.gov.
3	Table 9 data row 1 – convert g/week to standard US drinks/week, consistent with TableES-1	We retained the g/week units in this table so that it would correspond directly to the forest plots. We have added a footnote that gives the grams of alcohol in 1 standard U.S drink and we describe the results in the text using the number of standard U.S. drinks.
4	I agree with the overall conclusions drawn, but the organization of the report makes it cumbersome to follow as noted above. It's unclear why all the studies related to college students are included or relevant to veterans. Their inclusion does make it more comprehensive, but a shorter report of more direct relevance to veterans may be preferable in this context.	Studies conducted in college populations were included after discussion with our stakeholders and technical expert panel. Although these studies were considered less applicable to Veterans, they form a large proportion of the extant literature, and our study team thought these studies could contribute to a better understanding of the e-intervention effects.

Reviewer	Comment	Response
5	1. Background: The Pew Foundation's January 2014 report states that 87% of American adults ages 18 and older use the internet: http://www.pewinternet.org/fact-sheets/health-fact-sheet/ Your source says 79%. But Pew is cited often, is well-respected, and it helps strengthen the argument to potentially use e-interventions and to fund research in the future	Thank you for this suggestion. We have updated the description and citation as recommended.
5	2. Please define IVR for the reader in the background instead of waiting to the results.	We now define the "IVR" abbreviation earlier in the report and provide an explanation of how it differs from other e-interventions.
5	3. Data abstraction: The word ethanol is all of a sudden used in the data abstraction but nowhere else. Through the rest of the paper the word alcohol is used.	Thank you. "Ethanol" has been replaced with "alcohol."
5	4. Summary and Discussion: Because this is a VA report, readers will likely want to know how many trials were conducted in VA samples. While you provide this information it is buried. I would put this more towards the beginning of your summary and discussion perhaps in the second paragraph where you first mention that "Studies were equally divided between college students and other groups of adults."	Thank you for the suggestion. This detail has been added the Results sections of the Executive Summary and main report.
6	Separate analyses and reporting for college students and adults was very helpful.	Thank you.
6	P. 27 Figure 2. Strategies Used in E-Interventions – increase contrast between bars in graph.	The figure has been revised to increase the contrast.
6	It would be helpful to know more about the source of the normative data used to generate PNF in each study, given that it is the modal intervention- i.e. is normative feedback based on a sample of other college students at the same university, a representative national sample, such as NHSDUH, or some other data set.	The comparison sample has been further described in KQ 1.
6	KQ2 Key points (p.28) and summary of findings (p.38) focus on low strength of evidence supporting longer-term (>6 mo) benefits of e-Interventions in adults, and conclude that available data on long-term effects is modest or absent. It appears that the strength of evidence for short-term effects seems is similarly low (Fig 3, page 31). If that is the case, key points and summary should reference lack of both short and long-term benefit.	Our review included only studies that reported outcomes at ≥6 months. Therefore, our SOE ratings are limited to these outcomes. However, in the Discussion, we discuss other reviews that include trials with shorter duration outcomes.
6	What general conclusions (if any) can be drawn by comparing the studies conducted with adult and student samples (e.g. comparing Figures 3 and 6)? Is it accurate to say that there is a higher strength of evidence for certain short-term effects of e-interventions in college students? P.52 lines 24-25 seems to support this conclusion.	We assessed the SOE for student and adult populations separately. We have updated the SOE ratings for alcohol-related social problems showing low SOE in adults and moderate SOE in students.

Reviewer	Comment	Response
6	p. 42, lines 18-25. It would seem that combining e-interventions with BMI could actually be iatrogenic, at least in the college student population, with regard to binge drinking outcomes. Does the last bullet need to be strengthened to reflect his finding – i.e. not only do these interventions not have a benefit, but they may be harmful?	The single study in college students of combined e-intervention plus BMI did not show any difference from the e-intervention alone. Our bullet accurately summarizes this finding. BMI compared directly to e-interventions alone resulted in greater reduction in alcohol consumption, and this is reflected in the bullet summarizing this finding.
6	Clinical and Policy Implications section provides thoughtful synthesis and helpful recommendations. Hopefully this report will help move the field beyond its focus on single session PNF interventions, to developing and evaluating more robust, intensive interventions that draw upon evidence-based psychotherapies, and perhaps focus on relapse prevention.	Thank you.
Question 5: Are there any clinical performance measures, programs, quality improvement measures, patient care services, or conferences that will be directly affected by this report? If so, please provide detail.		
1	HPDP Staff, including Health Behavior Coordinators, HPDP Program Managers, and Veterans Health Education Coordinators will all benefit from this information. NCP staff will appreciate the thorough review and thoughtful recommendations, which will help inform guidance in the Limit Alcohol Healthy Living message materials, the Veterans Health Library, and, potentially, the Healthy Living Assessment. It certainly suggests the need to support additional research on more robust e-interventions. Additional counseling pairing or comparison intervention might include Telephone Lifestyle Coaching.	Thank you. We will forward the recommendation for target audiences to the ESP coordinating center and the CIDER dissemination center.
2	No comments	Acknowledged
3	There is potential applicability to newly established Joint Commission ORYX measures on SUB. They rely on documentation that could be informed by e-interventions; however the metrics are focused in inpatients plus some follow-up after discharge. As noted PCS is considering adaptation of the Gustafson et al ACHESS smartphone app for VHA use.	Acknowledged
4	No comments.	Acknowledged
5	No comments.	Acknowledged
6	Findings are highly relevant to VHA Mental Health Services, including the MIRECCs, and the National Center for PTSD. Also relevant to VA HSR&D research audience, particularly the Mental Health QUERI.	Thank you. We will forward the recommendation for target audiences to the ESP coordinating center and the CIDER dissemination center.
Question 6: Please provide any recommendations on how this report can be revised to more directly address or assist implementation needs.		
1	No comments.	Acknowledged
2	No comments.	Acknowledged

Reviewer	Comment	Response
3	Given the findings, implementation of reviewed interventions is premature and the report seems appropriately cautious.	Thank you.
4	It would seem inappropriate to recommend implementation of these approaches given the modest findings of their efficacy. The report adequately addresses these concerns.	Acknowledged
5	No comments.	Acknowledged
6	None.	Acknowledged
Question 7: Please provide us with contact details of any additional individuals/stakeholders who should be made aware of this report.		
1	OMHS leadership (Harold Kudler, Lisa Kearney, Andy Pomerantz…), CIH Executive Director, Steve Maisto (sto.Maisto@va.gov), Dave Oslin (Dave.Oslin@va.gov)	Thank you. We will forward the recommendation for target audiences to the ESP coordinating center and the CIDER dissemination center.
2	No comments	Acknowledged
3	Kathy Frisbee in Connected Health	Thank you. We will forward the recommendation for target audiences to the ESP coordinating center and the CIDER dissemination center.
4	No comments.	Acknowledged
5	I would recommend sending this report to the National Institute on Drug Abuse (NIDA) since they fund research on substance abuse in military life and this report will also be useful for non-VA populations as well.	Thank you. We will forward the recommendation for target audiences to the ESP coordinating center and the CIDER dissemination center.
6	None.	Acknowledged

APPENDIX E. STUDY CHARACTERISTICS

Study; **No. of participants randomized;** **No. of treatment arms**	**Intervention Type**	**Control Type**	**Age (Mean [SD]); % Female; % White**	**Location; Setting; VA? (Yes/No)**	**Education (by Category or Mean Years [SD])**	**Baseline Alcohol Intake (g/wk)**	**Baseline Alcohol Score (Instrument)**
Barnett, 2007[1] 225 2	Electronic intervention (e-Intv)	Face-to-face	18.8 (0.9) 51 76	USA University No	Total population: ≥college: 100%	92.15	NR
Bischof, 2008[2] 408 3	e-Intv + phone (full) e-Intv + phone (stepped)	Waitlist (WL)	36.5 (13.5) 32 NR	Europe NR No	Mean years(SD): e-Intv (full): 10.3 (2.7) e-Intv (stepped): 10.4 (2.7) WL: 10.4(2.1)	253.90	NR
Boon, 2011[3] 450 2	e-Intv	Information control (IC)	40.5 (15.2) 0 NR	Europe Web access No	e-Intv: <college: 46.1% ≥college: 53.9% IC: <college: 47.7% ≥college: 52.3%	312.91	NR
Cucciare, 2013[4] 167 2	e-Intv	Treatment as usual (TAU)	59.3 (15.0) 12 69	USA Clinic Yes	NR	336.11	AUDIT-C Overall: 6.4 (2.50) e-Intv : 6.3 (2.5) TAU :6.5 (2.5)
Cunningham, 2009[5] 185 2	e-Intv	IC	40.20 (13.45) 47 NR	Canada NR No	e-Intv: ≥college: 78.3% IC: ≥college: 77.4%	180.52	AUDIT-C Overall: 6.7 (2.10) e-Intv : 7.0 (2.1) IC: 6.4 (2.1)
Gustafson, 2014[6] 349 2	e-Intv + TAU	TAU	38.0 (10.0) 39.3 80.2	USA Smartphone No	Total population: <college: 92.0% ≥college: 8.0%	NR	NR
Hansen, 2012[7] 1380 3	e-Intv (PNF) e-Intv (personalized brief advice)	WL	44-65 (range) 45 NR	Europe Web access No	Total population: 15+ years of education: 51.7%	271.87	NR

Study; No. of participants randomized; No. of treatment arms	Intervention Type	Control Type	Age (Mean [SD]); % Female; % White	Location; Setting; VA? (Yes/No)	Education (by Category or Mean Years [SD])	Baseline Alcohol Intake (g/wk)	Baseline Alcohol Score (Instrument)
Hasin, 2013[8] 258 3	Motivational interviewing (MI) + interactive voice response (IVR)	MI IC	45.70 (8.10) 22 None (100% African-American)	USA NR (primary diagnosis is HIV) No	NR	NR	NR
Helzer, 2008[9] 273 3	Brief intervention from primary care physician (PCP-BI) + IVR PCP-BI + IVR + PNF	PCP-BI	45.10 (12.00) 38 NR	Europe NR (IVR study) No	Mean (SD): years PCP-BI + IVR: 14.8 (3.1) PCP-BI + IVR + PNF: 15.0 (2.7) PCP-BI (control): 14.9 (2.8)	430.48	NR
Hester, 2012[10] 144 2	e-Intv	TAU	20.40 (2.0) 38 57	USA University clinic No	Total population: ≥college: 100%	290.75	NR
Kypri, 2009[11] 2435 2	e-Intv	WL	19.70 (2.0) 45 NR	New Zealand Web access No	e-Intv: ≥college: 100% WL: ≥college: 100%	85.00	Instrument NR Overall: 14.2 (5.10) e-Intv : 14.2 (5.1) WL: 14.3 (5.1)
Kypri, 2008[12] 429 2	e-Intv	IC	20.1 (2.00) 52 NR	New Zealand NR No	e-Intv: ≥college: 100% IC: ≥college: 100%	NR	AUDIT Overall: 14.9 (5.10) e-Intv: 14.9 (5.1) IC: 15.1 (5.5)
Kypri, 2004[13] 104 2	e-Intv	IC	20.20 (1.62) NR NR	New Zealand University clinic No	e-Intv: ≥college: 100% IC: ≥college: 100%	NR	AUDIT Overall: 16.6 (5.85) e-Intv: 16.6 (5.7) IC: 16.6 (6.0)
Monahan, 2013a[14] 74 2	e-Intv (Alcohol 101)	MI (BASICS)	18-26 (range) 59 73	USA University research lab No	Total population: ≥college: 100%	176.83	NR
Monahan, 2013b[14] 133 3	e-Intv (e-CHUG)	MI (BASICS) WL	18-26 (range) 50 65.4	USA University research lab No	Total population: ≥college: 100%	205.18	NR

Study; No. of participants randomized; No. of treatment arms	Intervention Type	Control Type	Age (Mean [SD]); % Female; % White	Location; Setting; VA? (Yes/No)	Education (by Category or Mean Years [SD])	Baseline Alcohol Intake (g/wk)	Baseline Alcohol Score (Instrument)
Moreira, 2012[15] 1751 2	e-Intv	WL	17-19: 59.6% 20-24: 34.3% >25: 6.1% OR <25: 93.7% 62 NR	Europe NR No	Total population: ≥college: 100%	140.61	AUDIT Overall: 11.10 (7.01) e-Intv : 11.25 (7.15) WL: 11 (6.86)
Mundt, 2006[16] 60 3	IVR IVR + follow-up For relapse prevention	WL	41.9 (9.20) 45 95	USA NR (IVR) No	NR	NA (relapse prevention)	NR
Neighbors, 2010[17] 491 3	e-Intv (gender-specific feedback [GSF]) multi-dose (GSF2+)	Attention control (AC)	18.2 (0.60) 57.6 65.3	USA NR No	Total population: ≥college: 100%	159.12	NR
Neighbors, 2004[18] 252 2	e-Intv	WL	18.50 (1.2) 59 79.5	USA University No	Total population: ≥college: 100%	161.35	ACI (alcohol consumption inventory) Overall: 1.95 (1.35) e-Intv:2.03 (1.35) WL: 1.86 (1.35)
Neumann, 2006[19] 1136 2	e-Intv	WL	Median (range): 30.5 (24-29) 21 NR	Europe Clinic No	NR	188.91	AUDIT (median [IQR]) e-Intv: 7 (6-11) WL: 8 (6-11)
Riper, 2008[20] 261 2	e-Intv	IC	46.1 (9.1) 49 NR	Europe NR No	e-Intv: <college: 31.5% ≥college: 68.5% IC: <college: 29 ≥college: 71	436.00	NR
Schulz, 2013[21] 448 2	e-Intv	WL	41.72 (NR) 43.5 NR	Europe Web access No	Total population: ≥college: 34%	129.4	AUDIT≥ 8 Overall: 80%

Study; No. of participants randomized; No. of treatment arms	Intervention Type	Control Type	Age (Mean [SD]); % Female; % White	Location; Setting; VA? (Yes/No)	Education (by Category or Mean Years [SD])	Baseline Alcohol Intake (g/wk)	Baseline Alcohol Score (Instrument)
Sinadinovic, 2012[22] 202 2	e-Intv	TAU	32.5 (NR) 45 NR	Europe NR Dual diagnosis: ETOH + drug No	NR	NR	AUDIT-C Overall: 7.60 (2.85) e-Intv: 7.8 (2.7) TAU: 7.3 (3.0)
Voogt, 2013[23] 913 2	e-Intv	WL	20.9 (1.70) 40 NR	Europe NR No	Total population: ≥college: 100%	218.01	NR
Wallace, 2011[24] 2652 2	e-Intv	IC	38.0 (11.0) 57 NR	Europe NR No	e-Intv: ≥college: 52% IC: ≥college: 51%	368.00	AUDIT-C Overall: 8.5 (2.02)
Walters, 2009[25] 279 4	e-Intv (web FB only)	MI MI + FB WL	19.80 (NR) 64.2 84.6	USA University No	Total population: ≥college: 100%	206.95	Other RAPI alcohol-related problems Overall: 6.35 (6.45) e-Intv: 5.99 (6.01) MI: 6.37 (6.50) MI + FB: 6.67 (6.92) WL: 6.38 (6.35)

Abbreviations: AC=attention control; AUDIT=Alcohol Use Disorders Identification Test; AUDIT-C=Alcohol Use Disorders Identification Test-Consumption; e-Intv=electronic intervention; ETOH=alcohol; FB=feedback; g=grams; GSF=gender-specific feedback; GSF2+=multi-dose gender-specific feedback; HIV=human immunodeficiency virus; IC=information control; IQR=interquartile range; IVR= interactive voice response; MI=motivational interviewing; NA=not applicable; NR=not reported; PCP-BI=brief intervention from primary care physician; PNF=personalized normative feedback; RAPI=Rutgers Alcohol Problem Index; SD=standard deviation; TAU=treatment as usual; VA=Veterans Administration; wk=week; WL=waitlist

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APPENDIX F. E-INTERVENTION CHARACTERISTICS

Study	Population	e-Intv	Support Level	Computer Type	Computer Location	Security/ PHI?	e-Program Name	GS-PNF? Comparison	Treatment Technique	Face-to-face in e-Intv?	Live Therapy Sessions?	Computer Sessions (Number, Length)
Barnett, 2007[1]	Students	e-Intv	2	Software program on a PC (desk or laptop)	NR	NR	Alcohol 101	Yes; student peers	PsyEdu, AEdu	Yes, for intake only; F2F control	1 x 45 min individual session; 2nd, 25 min session 1 mo later in half of each arm if randomized to booster	1 x 20-25 min; 2nd x 20-25 min if randomized to booster
Bischof, 2008[2]	Adults	e-Intv + phone (full, stepped)	3	NR	NR	NR	NR	No	SBI, TF	Yes, with the e-Intv	4 scheduled calls, each 30-40 min	1, length NR
Boon, 2011[3]	Adults	e-Intv	2	Accessed via Web	University	NR	www.drinktest.nl	Yes; age-matched adults	SBI, NC, goals	RA for screening only	NA	1 x 10 min
Cucciare, 2013[4]	Adults	e-Intv	1	Accessed via Web	PC in clinic	NR	NR	Yes; age-matched adults	PsyEdu, NC	No	NA	1 x 10-15 min
Cunning-ham, 2009[5]	Adults	e-Intv	1	Accessed via Web	NR	Secure; no PHI	Check Your Drinking	Yes: age-matched adults	PsyEdu, NC, SBI	No	NA	1 x <10 min
Gustafson, 2014[6]	Adults	e-Intv after residen-tial treat-ment	2	Smartphone	Mobile	Secure; NR	A-CHESS	No	AS-Edu, CBT, email, GPS, peer, RP, S-M, text	No	No	41% used some features daily; weekly check-in
Hansen, 2012[7]	Adults	e-Intv PFI & PNF	1	Accessed via Web	NR	Secure; NR	NR	Yes; municipality residents	SBI, NC, PsyEdu	No	NA	1, length NR
Hasin, 2013[8]	Adult-HIV patients	IVR+MI	3	NA: IVR	NA	NR	NR	NA (IVR)	PsyEdu, SBI, S-M, goals	Yes, MI with PhD; F2F control	3 in-person sessions 1st: 20-25 min; 2nd/3rd: 10-15 min	IVR, 60 days, 1-3 min per day
Helzer, 2008[9]	Adults	IVR	3	NA: IVR (PCP-BI+IVR; PCP-BI+IVR+PNF)	IVR on phone	NR	NR	NA (IVR)	SBI, S-M, goals	Yes, for intake only; F2F control	NR	Daily IVR x 6 mo; Monthly group; length NR

Study	Population	e-Intv	Support Level	Computer Type	Computer Location	Security/ PHI?	e-Program Name	GS-PNF? Comparison	Treatment Technique	Face-to-face in e-Intv?	Live Therapy Sessions?	Computer Sessions (Number, Length)
Hester, 2012[10]	Students	e-Intv	2	Software program on a PC (desktop or laptop)	Student health clinic	Secure; no PHI	College Drinker's Checkup	Yes; student peers	SBI, NC, goals, DBE	RA for screening only	NA	1 x 35 min
Kypri, 2009[11]	Students	e-Intv	1	Accessed via Web	Home	NR	THRIVE	Yes: age-matched, New Zealand population	PsyEdu, NC, Hwk, TF	No	(Extensive assessment)	2 (1 + "booster" at 1 mo); length NR
Kypri, 2008[12]	Students	e-Intv x 1 (multi-dose x 3)	2	Accessed via Web	NR	NR	NR	NR	SBI, AS-Edu	RA for screening only	NA	1 or 3 SBI sessions; median length 9.3 min
Kypri, 2004[13]	Students	e-Intv	2	Accessed via Web	Student Health Clinic	NR	NR	NR	SBI, NC, AS-Edu, CMN	RA for screening only	Technical aid plus gave leaflet	1, average length 11.2 min
Monahan, 2013a[14]	Students	e-Intv	1	Software program on a PC (desktop or laptop)	Research lab	NR	Alcohol 101	No	PsyEdu	Yes, graduate student for intake; F2F control	1 individual session, 50-60 min	1 x 30+ min
Monahan, 2013b[14]	Students	e-Intv	1	Software program on a PC (desktop or laptop)	Research lab	NR	e-CHUG	Yes; student peers	PsyEdu	Yes, graduate student for intake; F2F control	1 individual session, 50-60 min	1 x 30+ min
Moreira, 2012[15]	Students	e-Intv	1	Accessed via Web	NR	NR	NR	Yes, but not GS; student peers	SBI, AS-Edu	No	NA	1, length NR
Mundt, 2006[16]	Adults: Relapse prevention	IVR IVR + FU	3	NA: IVR	NA	Secure; no PHI	NR	NA (IVR)	PsyEdu, SBI, S-M, goals	Yes, with study coordinator	4 calls; option to receive and/ or leave phone messages	IVR, 90 days, <5 min each day
Neighbors, 2010[17]	Students	e-Intv GSF, GSF2+	1	Accessed via Web	NR	Secure; NR	BASICS	Yes: student peers	SBI	No	NA	GSF: 1 GSF2+: 2-5 based on adherence (each 50 min long)
Neighbors, 2004[18]	Students	e-Intv	1	Accessed via Web	College classroom	NR	BASICS	Yes, but NR if GS; student peers	PsyEdu, SBI	No	NA but extensive assessment	1, length NR

Study	Population	e-Intv	Support Level	Computer Type	Computer Location	Security/ PHI?	e-Program Name	GS-PNF? Comparison	Treatment Technique	Face-to-face in e-Intv?	Live Therapy Sessions?	Computer Sessions (Number, Length)
Neumann, 2006[19]	Adults	e-Intv	2	Software program on a PC (desk or laptop)	Clinic	NR	FRAMES	Yes, but GS NA (all men)	PsyEdu, SBI, goals, TPR	RA for screening only	NA	1 x 90 min
Riper, 2008[20]	Adults	e-Intv	2	Accessed via Web	NR	Secure; no PHI	minderdrinken.nl	No	S-M, ST, goals	Moderated peer-to-peer discussion forum	6 wk	NR
Schulz 2013[21]	Adults	e-Intv	1	Accessed via Web	NA	NR	Alcohol-Everything Within Limits	Yes, but NR if GS; NR	AS-Edu, NC, PNF, PsyEdu, TF	No	No	3, length NR
Sinadinovic, 2012[22]	Adults: alcohol &drug	e-Intv	1	Accessed via Web	NR	NR	eScreen.se	Yes, but NR if GS; Swedish population	SBI, S-M, MI	No	NA	Unlimited; mean (SD) = 2.66 (4.31), length NR
Voogt, 2013[23]	Students	e-Intv	1	Accessed via Web	NR	NR	What Do You Drink (WDYD)	Yes; student peers	PsyEdu	No	NA	1 x 20 min
Wallace, 2011[24]	Adults	e-Intv	1	Accessed via Web	NR	Secure; no PHI	Down Your Drink	Yes; UK population	SBI, S-M, ST, goals, VC, RP	No	NA	Unlimited, length NR
Walters, 2009[25]	Students	e-Intv	1	Accessed via Web	Home	NR	e-CHUG (modified)	Yes: U.S. student norms	SBI, NC	No; F2F control	NA	1 x 30 min

Abbreviations: A-CHESS=Addiction-Comprehensive Health Enhancement Support System; AEdu=alcohol education through "virtual party," taking personal responsibility; AS-Edu=alcohol-specific education; BASICS=Brief Alcohol Screening and Intervention for College Students; CBT=computerized cognitive-behavioral therapy program; CMN=correction of misperceived norms; DBE=decisional balance exercise; e-CHUG=Electronic Check-Up to Go; e-Intv=electronic intervention; email=email response from counselor; F2F=face-to-face; FRAMES=feedback, responsibility, advice, menu of options, empathy, self-efficacy; FU=follow-up; goals=goal-setting; GPS=global position monitoring of high-risk locations; GS=gender-specific; GSF=gender-specific feedback; GSF2+=multi-dose gender-specific feedback; GS-PNF=gender-specific personalized normative feedback; HIV=human immunodeficiency virus; Hwk=homework; IVR= interactive voice response; MI=motivational interviewing; min=minute(s); mo=month(s); NA=not applicable; NC=negative consequences; NR=not reported; PC=personal computer; PCP-BI=brief intervention from primary care physician; peer=online peer support; PFI=personalized feedback intervention; PHI=protected health information; PNF=personalized normative feedback; PsyEdu=psychoeducation; RA=research assistant; RP=relapse prevention; SBI=screening and brief intervention; SD=standard deviation; S-M=self-monitoring; ST=skills training; text=motivational quotes via text message; TF=tailored feedback (blood level); THRIVE=Tertiary Health Research Intervention Via Email; TPR=taking personal responsibility; VC=values clarification; WDYD=What Do You Drink; wk=weeks

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