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Review

Digital Interventions for People With Co-Occurring Depression and Problematic Alcohol Use: A Systematic Review and Meta-Analysis

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Abstract

Aims: This systematic review and meta-analysis assessed the effectiveness of digital interventions addressing depressive symptoms and alcohol use simultaneously among people with co-occurring depression and problematic alcohol use.

Methods: Seven databases were searched for trials evaluating digital interventions aimed at depression and alcohol use. Random-effects meta-analyses were conducted to pool effects on depressive symptoms and alcohol use up to 3-month and 6-month follow-up. Overall quality for every outcome was assessed with GRADE (Grading of Recommendations Assessment, Development and Evaluation).

Results: The pooled effect of digital interventions compared to their comparators was in favour of digital interventions. Small but significant effects on depressive symptoms at 3-month follow-up were found ($g = 0.34$, 95% confidence interval (CI): 0.06–0.62, $P = 0.02$, $k = 6$) and non-significant effects at 6-month follow-up ($g = 0.29$, 95% CI: -0.16 to 0.73, $P = 0.15$, $k = 5$). For alcohol use, the pooled effect of digital interventions was small and non-significant at 3-month follow-up ($g = 0.14$, 95% CI: -0.02 to 0.30, $P = 0.07$, $k = 6$) and significant at 6-month follow-up ($g = 0.14$, 95% CI: 0.07–0.20, $P = 0.005$, $k = 5$). Sensitivity analysis indicated the latter finding to be sensitive to statistical estimator choice. Quality of evidence was moderate, except for depressive symptoms at 6-month follow-up for which it was low.

Conclusion: Based on the literature, digital interventions are effective in reducing depressive symptoms at 3-month follow-up and alcohol use at 6-month follow-up among people with comorbid depression and problematic alcohol use. More high-quality trials are needed to confirm the current findings.

INTRODUCTION

Depressive disorders and alcohol use disorders (AUD) are common mental disorders that often co-occur (Grant *et al.*, 2015; Degenhardt *et al.*, 2018). The co-occurrence of these two conditions has been extensively studied in various epidemiological studies (Grant *et al.*, 2004; Boden and Fergusson, 2011; Lai *et al.*, 2015). A meta-analysis on epidemiological surveys conducted between 1990 and 2014 shows that people with AUD are at 2.4 times greater risk of having major depression (Lai *et al.*, 2015). Also, in alcohol users in general, higher levels of alcohol use are associated with higher levels of depressive symptoms (Horváth *et al.*, 2019). Furthermore, individuals with depressive disorders have a threefold increased risk of lifetime AUD (Boschloo *et al.*, 2011). Comorbid depression and problematic alcohol use are associated with increased risk of greater AUD severity, suicide attempts, higher disease burden and lower life satisfaction and general functioning compared to both conditions alone (Gadermann *et al.*, 2012; Briere *et al.*, 2014). In this review, we use the term 'problematic alcohol use' to refer to AUD as well as other non-clinical levels of hazardous drinking.

Psychosocial treatment of co-occurring depression and problematic alcohol use can be based on a single or dual disorder approach (Hobden *et al.*, 2018). In the latter, both comorbid conditions are treated simultaneously. This combined treatment approach has never been common practice (Riper *et al.*, 2014a). Often the comorbid disorder was either not recognized or not treated, assuming that when the primary disorder (e.g. problematic alcohol use) was treated, the other disorder (e.g. depression) would improve as well or vice versa (Schuckit, 2006; Pettinati *et al.*, 2013). Research does indeed show that depressive symptoms decrease after treatment for problematic alcohol use. However, not all individuals with comorbid problematic alcohol use and depression experience complete remission of depressive symptoms and might therefore be more prone to a relapse (Schuckit, 2006; Hobden *et al.*, 2018).

Nowadays, more combined psychological treatments are available for co-occurring depression and problematic alcohol use. These combined treatments are often based on cognitive–behavioural therapy (CBT) and motivational interviewing (MI). CBT is a common and effective treatment for depressive disorders and is aimed at changing a patient's behaviour and functioning through cognitive–behavioural restructuring of maladaptive beliefs (Beck *et al.*, 1979; Cuijpers *et al.*, 2020). MI is used to facilitate behaviour change (e.g. drinking behaviour) through enhancing motivation and commitment to change and by resolving ambivalence about change (Miller and Rollnick, 2012; Frost *et al.*, 2018). Both CBT and MI-based treatments have been proven to be effective treatments for reducing independent depression and problematic alcohol use (Vasilaki *et al.*, 2006; Kohler and Hofmann, 2015; Cuijpers *et al.*, 2020).

For co-occurring depression and problematic alcohol use, CBT/MI-based treatments also seem promising. A meta-analysis by Riper *et al.* (2014a) shows that combined CBT/MI-based treatment can be effective in reducing both depressive symptoms ($g = 0.27$) and alcohol use ($g = 0.17$) compared to treatment as usual, among people with comorbid depression and problematic alcohol use. Notably, subgroup analyses indicated that digital CBT/MI treatments had a significantly higher effect on depression outcomes compared to face-to-face treatments ($g = 0.73$ vs. $g = 0.23$) (Riper *et al.*, 2014a).

A recent systematic review also showed positive effects of digital interventions on mental health symptom severity for people with co-occurring depression and substance use disorders. Improvement in both comorbid conditions was only observed in half of the studies that were under review. However, no meta-analysis was conducted by the authors (Holmes *et al.*, 2018).

In the last decade, numerous digital interventions have been developed for either depression or problematic alcohol use. Digital interventions often include psychoeducation, CBT/MI-based support or therapy and are delivered through the Internet, computer or a mobile device. They can be self-guided or may include therapy-related feedback from a therapist or (technical) process support (Richards and Richardson, 2012; Callan *et al.*, 2017; Cuijpers *et al.*, 2017). Many reviews have already shown the effectiveness of digital interventions in reducing independent depressive symptoms and alcohol use in various settings, such as community (Deady *et al.*, 2017; Kaner *et al.*, 2017), among youth (Hollis *et al.*, 2017; Christ *et al.*, 2020), students and young adults (Davies *et al.*, 2014; Sundstrom *et al.*, 2017; Harrer *et al.*, 2019a), adults (Riper *et al.*, 2014b; Sundstrom *et al.*, 2017; Riper *et al.*, 2018) and also for guided and self-guided CBT-based interventions (Karyotaki *et al.*, 2017, 2018), although effect sizes are often in the small range.

Currently, a few combined digital interventions are available that address depressive symptoms and problematic alcohol use simultaneously. No meta-analysis has yet been conducted on the effectiveness of digital interventions for people with co-occurring depression and problematic alcohol use specifically. The present study reports the results of a systematic review that evaluated the outcomes of randomized controlled trials (RCTs) on digital interventions addressing depressive symptoms and problematic alcohol use simultaneously among adults with co-occurring depression and problematic alcohol use.

METHODS

This study was reported in accordance with the PRISMA guidelines for reporting systematic reviews and meta-analyses (Moher *et al.*, 2009). The review protocol was pre-registered in the International Prospective Register of Systematic Reviews (PROSPERO: CRD42018108299).

Search strategy

We conducted an extensive literature search from database inception to June 8th 2020. Seven electronic databases were searched: PubMed, EMBASE, PsycINFO, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science and Scopus. A research librarian assisted with developing the search string (see Supplementary Material S1). We included studies that were published in the last 15 years but did not restrict our search. We were therefore

able to identify if any eligible studies were published before this publication date, this appeared not to be the case. There were no language limitations, but studies needed to have an English abstract to be identified in the search.

The search string included MeSH (Medical Subject Headings) terms, text words and synonyms related to problematic alcohol use, depression and digital interventions and were combined with Boolean operators AND/OR. We also checked reference lists of relevant reviews and searched the WHO International Clinical Trials Registry Platform for eligible studies.

Eligibility criteria

Studies were included if they were (a) based on a RCT study design and (b) reported effects of a digital intervention that targeted both depressive symptoms and alcohol use simultaneously (c) compared to any type of control group (e.g. waitlist, active treatment, assessment only, attention control) and (d) reported both depression and alcohol use outcomes and were (e) conducted among adults with depression or elevated depressive symptoms and any form of problematic alcohol use. Digital interventions were defined as interventions including digital environments to access information, modules, feedback or assignments.

Study selection

Study selection was conducted by M.J.E.S. and C.C. and was supervised by a third senior researcher (M.B.). After every phase, any disagreements were discussed until consensus was reached. If needed, the supervising researcher was consulted. All studies identified by the search were uploaded into Rayyan Citation after duplicates were removed (Ouzzani *et al.*, 2016). M.J.E.S. and C.C. independently assessed all studies for potential eligibility based on title and abstract. After retrieving the full texts of the potentially eligible studies, M.J.E.S. and C.C. independently assessed the full texts for final inclusion.

Data extraction

Data extraction was conducted by M.J.E.S. and checked for inconsistencies by C.C. The following data were extracted: (a) study characteristics: authors, publication year, country; (b) participant characteristics: population, recruitment setting; sample size, mean age, gender; (c) intervention characteristics: intervention type, delivery mode, duration, guidance, adherence; (d) outcome measures: type of depression or alcohol-related outcomes, follow-up (e) and type of comparator. For the meta-analysis, necessary quantitative data (e.g. mean (*M*) and standard deviation (*SD*)) were extracted.

When a study had multiple comparators, we included the comparator to which the authors themselves referred to as the control condition. As indicated in our review protocol, we extracted alcohol consumption outcomes (number of standard drinks) and outcomes measuring depressive symptoms. When multiple follow-up measurements were reported, those closest to 3 and 6 months were included in the meta-analyses.

Quality assessment

All quality assessments were independently conducted by M.J.E.S. and C.C. and supervised by M.B.. Any disagreements between M.J.E.S. and C.C. were discussed until consensus was reached.

Risk of bias We used the revised Cochrane Risk of Bias tool (RoB 2.0) to assess risk of bias for every included study (Sterne *et al.*, 2019). Five domains were assessed for risk of bias: (a) randomization process, (b) deviations from intended interventions, (c) missing outcome data, (d) measurement of the outcome and (e) bias in selection of the reported result. Using the RoB 2.0 guidelines, we first came to domain-level judgements of low, some concerns or high risk of bias. Second, we used these domain-level judgements to reach an overall risk of bias judgement. If all domains were rated with low risk of bias, an overall low risk of bias was given. If at least one domain scored a judgement of some concerns and no domain was high risk of bias, then an overall judgement of some concerns was given. An overall high risk of bias was given when at least one domain was assessed as such (Sterne *et al.*, 2019).

Overall quality of evidence Grading of Recommendations Assessment, Development and Evaluation (GRADE) was used to assess the overall quality of evidence for every pooled outcome (Schünemann *et al.*, 2013). We assessed the five domains: (a) risk of bias, (b) inconsistency of results (i.e. heterogeneity), (c) indirectness of evidence, (d) imprecision of results and (c) suspected publication bias. All outcomes started as high-quality evidence, because all included studies were RCTs. We downgraded the level of evidence when limitations in any of the domains occurred. The overall quality was assessed as either high, moderate, low or very low (Schünemann *et al.*, 2013).

Meta-analysis

Main analyses All meta-analytic procedures were conducted using the *meta*, *metafor* and *dmetar* packages in R version 3.6.0 (Schwarzer, 2007; Viechtbauer, 2010; R Core Team, 2018; Harrer *et al.*, 2019b). The *esc* package was used to calculate between-group effect sizes with a small sample bias correction (Hedges' *g*) for every study; *M* and SD were used if present and otherwise the Cohen's *d* and *P* value were used using *dmetar* package (Lüdecke, 2018; Harrer *et al.*, 2019b). We used a random-effects model with the Hartung-Knapp-Sidik-Jonkman (HKSJ) estimator as the main analysis because of the small number of studies and anticipated heterogeneity (IntHout *et al.*, 2014). Simulation studies have shown that the HKSJ estimator often performs better than the frequently used DerSimonian-Laird (DL) estimator, especially when there is heterogeneity and the number of pooled studies is small (IntHout *et al.*, 2014). The random-effects model was used to pool the individual studies' effect sizes to a standardized mean difference (SMD) Hedges' *g* for both depression and alcohol use outcomes (Hedges and Olkin, 2014). A positive Hedges' *g* indicates a decrease in alcohol use or depressive symptoms. We calculated the number needed to treat (NNT) for the pooled SMDs, using the formulae by Kraemer and Kupfer (2006). The NNT indicates the number of patients needed to be treated to generate one additional positive outcome (Kraemer and Kupfer, 2006). Heterogeneity was examined by calculating the I^2 statistic and corresponding confidence intervals. T^2 and Q-statistic were calculated as additional heterogeneity measures (Borenstein *et al.*, 2017). An I^2 statistic of 25% indicates low heterogeneity and 50% and 75% indicates moderate and substantial heterogeneity, respectively (Higgins *et al.*, 2003). Prediction intervals (PI) were calculated and provide a range between which effects of future studies are expected to fall. A PI range that includes zero indicates that in some settings,
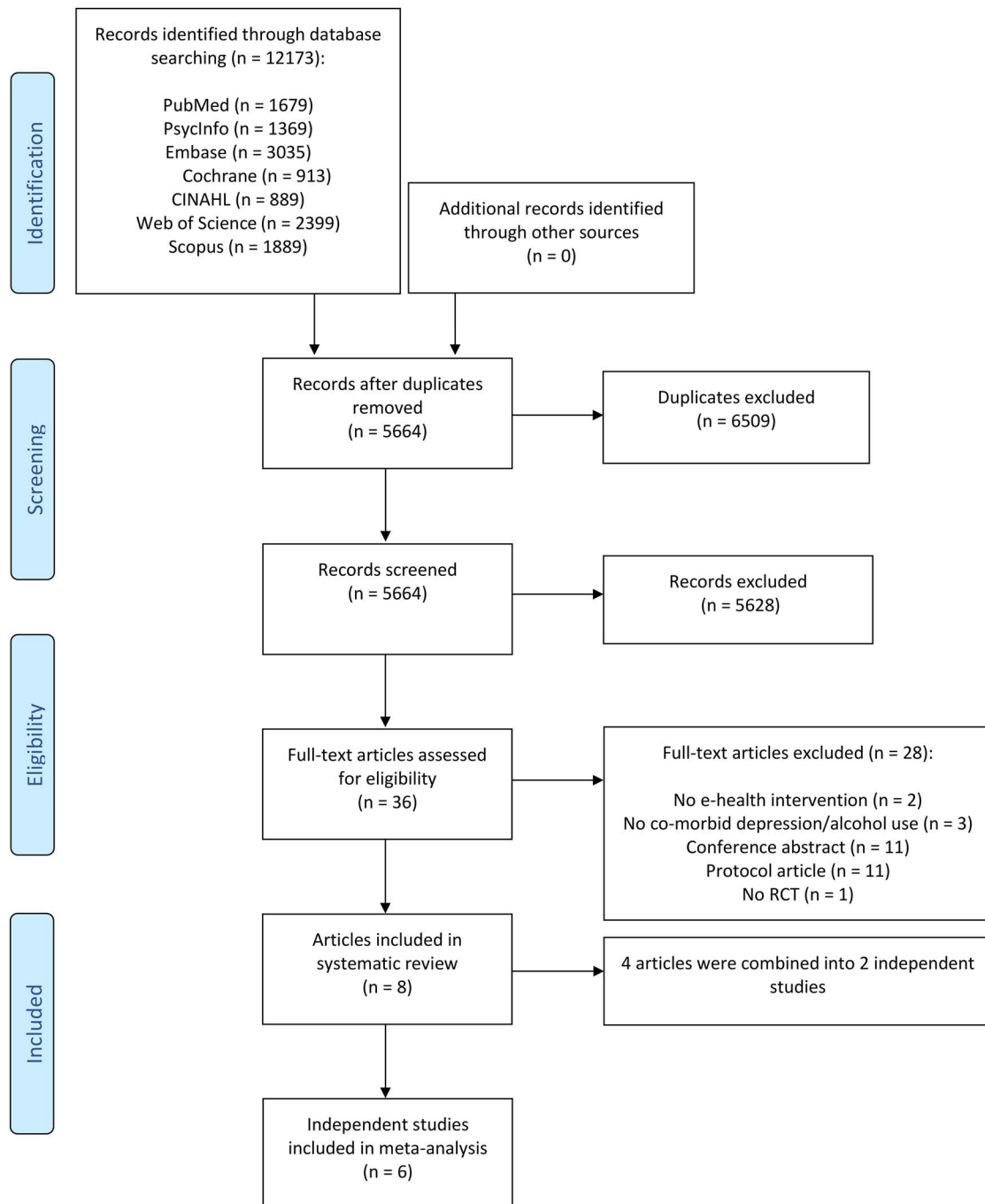
Fig. 1. Flowchart of study inclusion.

future studies on digital interventions may find no or even negative effects on depression or alcohol outcomes (IntHout *et al.*, 2016).

Additional analyses We conducted sensitivity analyses using the DL estimator to examine to what extent findings from the main analyses were sensitive to our choice to use the HKSJ estimator (Wiksten *et al.*, 2016). Influence analysis was conducted to evaluate the influence of a single study on the pooled effect size (i.e. robustness of the pooled effect size). Influential cases and outliers were examined by using the leave-one-out method, by removing the highest and lowest effect

size and outlier identification and removal (Viechtbauer and Cheung, 2010).

RESULTS

Selection and inclusion of studies

The database search resulted in a total of 12173 articles. After duplicates removal, 5664 unique articles were screened for eligibility based on title and abstract, of which 5628 articles were excluded (98% reviewers agreement). We retrieved full texts of 36 articles, and

Table 1. Study characteristics of included studies

Author, country, year	Population, alcohol/ depression criteria	Recruitment setting	Sample characteristics	Intervention description	Delivery mode	Duration intervention	Guided	Adherence intervention	Comparator	Depression/alcohol outcomes [a]	Follow-up	Analysis
Agyapong et al. (2012, 2013a) IRE	Clinical MDD (SCID) ADS/AA (SCID)	Inpatient (dual diagnosis) treatment programme	N = 54 Female = 54% Mean age = 49	Twice-daily supportive text messages after finishing inpatient treatment program in addition to usual aftercare. Text messages aimed at dealing with stress, maintaining good mental well-being, dealing with cravings, abstinence, general support	Mobile phone	3 months	No	Nr	Active: TAU (usual aftercare)	Depression symptoms (BDI-II); Units per drinking day (TLFB); Cumulative abstinence duration; Obsessive Compulsive Drinking Scale; Alcohol Abstinence Self-Efficacy Scale; Proportion of patients continuously abstinent; Days to first drink	3 months 6 months	ITT
Deady et al. (2016) AUS	Selected ≥ 7 DASS-21-Depression ≥ 8 AUDIT	Offline/online media advertisement	N = 104 Female = 60% Mean age = 22	Four weekly online CBT/MI modules (1 hour) with homework assignments	Website	10 weeks	No	Average of 1.5 modules completed[b]; 60% completed ≥1 module[b]	Passive: Attention control condition (HealthWatch)	Depression severity (PHQ-9); Drinks per week (TOT-AL); Drinking days per week	Posttreatment 3 months 6 months	ITT
Geisner et al. (2015) USA	Selected ≥ 14 BDI ≥ 4/5 (w/m) standard drinks ≥1 occasion/month and ≥ 8 AUDIT	College students	N = 170 Female = 62%[c] Mean age = 20[c]	One session of personalized feedback + psychoeducation (responses on alcohol use and consequences, protective behavioural strategies, normative perceptions and depression symptoms and coping strategies)	Computer	5 weeks	No	92% participated in intervention	Passive: Assessment only	Depression symptoms (BDI-II); Drinks per week (Daily Drinking Questionnaire); Alcohol consequences	1 month	ITT
Kay-Lambkin et al. (2009) AUS	Clinical ≥ 17 BDI-score and Lifetime MDD (SCID-RV) ≥ 2 and ≥ 4 standard drinks per day for w/m	AOD, mental health and primary healthcare settings	N depression short/long = 44[d] N alcohol short/long = 27[e]	Brief intervention (one f2f session with therapist) + 9 sessions of computer-delivered CBT/MI integrated depressive and alcohol strategies	Computer	3 months	Yes	47%[b] completed all sessions	Active: Brief intervention (one f2f session with therapist)	Depression symptoms (BDI-II); Mean number of alcohol use occasions per day (OTI-q score)	3 months 6 months 12 months	CO
Kay-Lambkin et al. (2011, 2017) AUS	Selected ≥ 17 BDI score ≥ 2 and ≥ 4 standard drinks per day for w/m	Advertisement, AOD, mental health and other primary healthcare settings	N depression short/long = 186[d] N alcohol short/long = 114[e] Female = 43%[c] Mean age = 40[c]	9 sessions of computer CBT/MI aimed at integrated depressive and alcohol-related strategies	Computer	9 weeks	Yes	30%[b] completed all sessions	Active: 9 f2f sessions person-centred therapy (supportive counselling)	Depression symptoms (BDI-II); Mean number of alcohol use occasions (OTI-q score)	3 months 6 months 12 months	ITT
O'Reilly et al. (2019) IRE	Clinical ≥ 14 BDI score MDE and AD (SCID)	Inpatient (dual diagnosis) treatment program	N alcohol short = 80 N alcohol long = 76 N depression short = 89 N depression long = 73 Female = 54%[f] Mean age = 48[f]	Twice-daily supportive text messages after discharge aimed at alcohol abstinence and depressive mood in addition to usual aftercare	Mobile phone	6 months	No	Nr	Active: TAU (usual aftercare)	Depression symptoms (BDI-II); Units of alcohol per drinking day (TLFB); Number of drinking days; Proportion of patients continuous abstinent; Time to first drink	3 months 6 months 12 months	CO

AD, alcohol dependence; AD(S)/AA, alcohol dependence (syndrome/alcohol abuse); AOD, alcohol and other drugs; AUS, Australia; BDI, Beck Depression Inventory; Clinical sample, confirmed diagnosis; CO, completers only; F2f, face-to-face; IRE, Ireland; ITT, intention to treat; MDD, major depressive disorder; MDE, major depressive episode; N, total number of participants in meta-analysis, multiple N indicates different sample sizes per timing and outcome measurement; Nr, not reported; SCID, Structured Clinical Interview for DSM-IV Axis I Disorders; Selected sample, scoring above cut-off thresholds for depressive symptoms/problematic alcohol use; PHQ-9, Patient Health Questionnaire-9; w/m, women/men.

[a]The follow-up and outcome measures in italic were included in the meta-analysis.

[b]% of all participants allocated to intervention.

[c]Total sample (including multiple comparators not all included in meta-analysis).

[d]Mixed sample and sample size estimated, number of participants in depression analysis.

[e]Mixed sample and sample size estimated, number of participants in alcohol analysis.

[f]Total sample at baseline.

8 articles met all inclusion criteria. When trial results were reported in multiple articles (e.g. when outcomes after 3- and 6-month follow-up were published in two separate articles), we combined the articles into one independent study. Six independent studies were included in the meta-analysis, see Fig. 1.

Study characteristics

Study population All studies were published between 2009 and 2019 and conducted in Australia (k = 3), Ireland (k = 2) and the United States (k = 1). Three studies were conducted on clinical depression samples and three studies on selected study samples based on elevated depressive symptoms scores, indicating moderate depression symptomology and problematic alcohol use above certain thresholds. Participants' mean age ranged from 20 to 49 years (see Table 1).

Outcomes measurements Studies reported outcomes at posttreatment (k = 1), 1-month (k = 1), 3-month (k = 5), 6-month (k = 5) and 12-month follow-up (k = 3). We pooled effects closest to 3-month (i.e. 1–3 months) and 6-month follow-up. Five studies reported depressive symptoms as scores on the Beck Depression Inventory-II questionnaire and one used the Patient Health Questionnaire-9. Alcohol use outcomes included units per drinking day (k = 2), drinks per week (k = 2) and mean number of alcohol use occasions per day (k = 2).

Comparators Four studies included active control groups, either treatment as usual (TAU) or therapist face-to-face delivered sessions. Two others included passive control groups, namely attention control condition and assessment only.

Digital interventions and adherence Two digital interventions were delivered via mobile phone and composed of receiving twice-daily supportive text messages aimed at abstinence and improvement in depressive symptoms in addition to usual aftercare, for people discharged from a dual disorder inpatient treatment programme (Agyapong *et al.*, 2012, 2013a; O'Reilly *et al.*, 2019). Four interventions were computer delivered, three of which included online CBT/MI modules aimed at reducing alcohol use and depressive symptoms (Kay-Lambkin *et al.*, 2009, 2011, 2017; Deady *et al.*, 2016). Two of these CBT/MI-based interventions included 10- to 15-minute therapist face-to-face guidance as an add-on, four digital interventions were self-guided. Lastly, one computer-delivered intervention included tailored feedback regarding alcohol use and depressive symptoms, incorporating protective behavioural strategies, coping strategies, psychoeducation and comparisons of participants' own drinking with perceived drinking norms (Geisner *et al.*, 2015).

Digital intervention adherence rates varied and were differently operationalized. One study reported that 92% of the participants participated in the intervention (Geisner *et al.*, 2015), two studies reported that 47% and 30% of the participants completed all sessions (Kay-Lambkin *et al.*, 2009, 2011, 2017) and another study reports an average of 1.5 completed modules out of a total of 4 (Deady *et al.*, 2016). Two studies did not report adherence rates (Agyapong *et al.*, 2012, 2013b; O'Reilly *et al.*, 2019).

Quality assessment

Risk of bias assessment All six studies were assessed with an overall high risk of bias, because of high-risk domain judgements on one (k = 3), two (k = 2) or three domains (k = 1) (see Fig. 2). All studies were rated high risk of bias in the measurement of the outcome, mostly because of use of self-report measurements and the inability of blinding participants. In self-report measures, the participant him- or herself is the assessor; consequently, the participants' knowledge about the received intervention (i.e. control or experimental group) could have influenced the outcome measurements and might cause bias (Sterne *et al.*, 2019). Three studies had a high risk of bias rating because of ≥5% missing data and handling of it (e.g. no sensitivity analysis or no multiple imputation). One study was rated high risk of bias for the fifth domain because of unexplained deviations from the protocol. The inability of blinding participants and use of self-report measures is common in psychological studies. If the fourth domain is omitted, three studies would still have an overall high-risk judgement and three others a some concerns judgement.

GRADE assessment The overall quality of the evidence was moderate for alcohol use at 3- and 6-month follow-up and for depressive symptoms at 3-month follow-up. We downgraded the quality of evidence for these outcomes because of the high risk of bias ratings. Overall quality for depressive symptoms at 6-month follow-up was assessed as low, because of limitations in both risk of bias and inconsistency domains (due to moderate heterogeneity). We were unable to empirically examine publication bias because of the small number of studies in this review (Higgins *et al.*, 2019) (see Table 2).

Meta-analyses

The meta-analyses on depressive symptoms at 3- and 6-month follow-up were conducted on a total sample of 647 and 461 participants, respectively. For alcohol use at 3- and 6-month follow-up, the sample included 449 and 375 participants, respectively. Sample size variation is caused by one study that only included 1-month follow-up (Geisner *et al.*, 2015). Additionally, two studies were conducted on mixed samples (Kay-Lambkin *et al.*, 2009, 2011, 2017).

Depressive symptoms In the main-analysis, the overall pooled effect size of digital interventions on depressive symptoms at 3-month follow-up was small but significant, with g = 0.34 (P = 0.02, 95% confidence interval (CI): 0.06–0.62, k = 6), which corresponds with an NNT of 5.26 (see Table 2 and Fig. 3). Heterogeneity was low to moderate (I^2 27%, 95% CI: 0–70%). The PI ranged from g − 0.30 to 0.98, indicating that in future similar studies, the effect could as well be either positive or negative on depressive symptoms. The additional analyses showed similar results: sensitivity analysis resulted in g = 0.32 (P = 0.0014), no outliers were detected and influence analyses showed significant but somewhat fluctuating small effects (g = 0.25, P = 0.02 and g = 0.41, P = 0.02), which means findings are sufficiently robust and do not heavily depend on an individual study.

In the main analysis, the pooled effect size for depressive symptoms at 6-month follow-up was small and non-significant with g = 0.29 (P = 0.15, 95% CI: −0.16 to 0.73, k = 5). Heterogeneity was moderate (I^2 48%, 95% CI: 0%–81%), and PI ranged from −0.75 to 1.32. Additional analyses showed similar non-significant effects, with g = 0.27 (P = 0.08) in sensitivity analyses and effect sizes ranging from g = 0.11 to 0.40 (P = 0.22 and 0.11, respectively) in influence analysis.

Alcohol use In the main analysis, the overall pooled effect size for digital interventions compared to control groups on alcohol
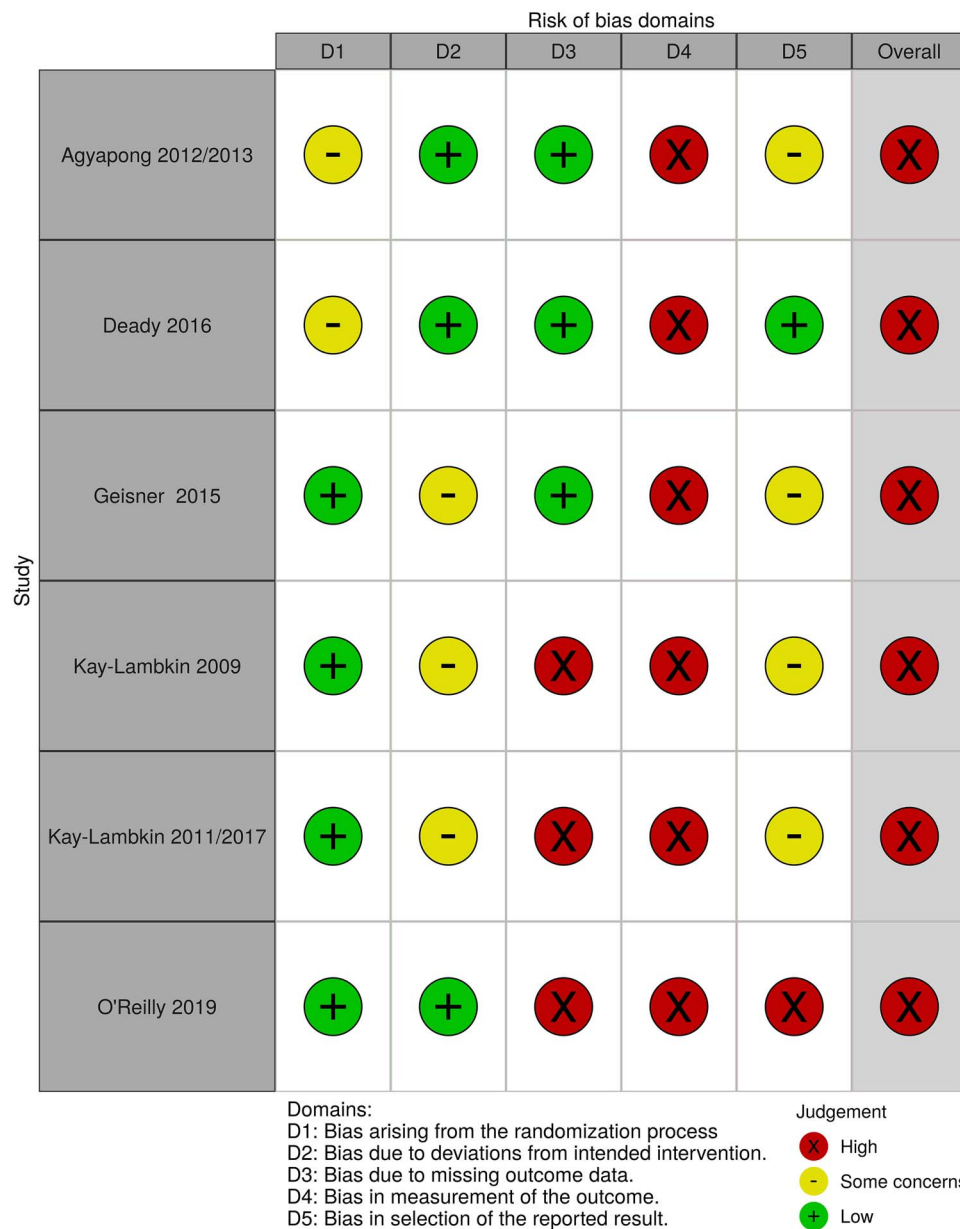
Fig. 2. Risk of bias assessment.

use at 3-month follow-up was small and non-significant, with $g = 0.14$ ($P = 0.07$, 95% CI: -0.02 to 0.30, $k = 6$). Heterogeneity was low (I^2 0%, 95% CI: 0%–51%). The PI ranged from -0.16 to 0.44. Sensitivity analysis resulted in a similar non-significant effect ($g = 0.13$, $P = 0.12$). Influence analysis in which the highest effect size was removed, resulted in a non-significant effect ($g = 0.10$, $P = 0.09$) and removal of lowest effect size resulted in a significant effect size ($g = 0.20$, $P = 0.03$). No outliers were detected.

In the main analysis, the pooled effect size for alcohol use at 6-month follow-up was small and significant with $g = 0.14$ ($P = 0.005$, 95% CI: 0.07–0.20, NNT = 13.05, $k = 5$). Heterogeneity was low (I^2 0%, 95% CI: 0%–0%), and the PI ranged from 0.05 to 0.22. The sensitivity analysis resulted in $g = 0.14$ ($P = 0.27$); consequently, the confidence interval but not the effect size estimate is sensitive to

statistical estimator choice. The influence analyses yielded effect sizes ranging from $g = 0.11$ to 0.15 ($P = 0.03$ and $P = 0.0007$, respectively), and no outliers were detected.

DISCUSSION

This study aimed to evaluate the effectiveness of digital interventions compared to any control group on depressive symptoms and alcohol use at different follow-up periods among people with co-occurring depression and problematic alcohol use. We found a small but significant effect in favour of digital interventions on depressive symptoms at 3-month follow-up and a non-significant effect for depressive symptoms at 6-month follow-up ($g = 0.34$ and 0.29, respectively). In addition, a non-significant effect ($g = 0.14$) was found on alcohol use

Table 2. Pooled effect sizes of digital interventions on alcohol use and depressive symptoms at 3- and 6-month follow-up

Outcome	Nc	Effect size			Heterogeneity estimators				NNT
		g	95% CI	P	I² (95% CI)	T²	Q (P)	95% PI	
Depressive symptoms at 3-month follow-up									
Main analysis[a]	6	0.34	0.06 to 0.62	0.02	27 (0–70)	0.042	6.84 (0.23)	−0.30 to 0.98	5.26
Additional analyses									
Highest ES removed[b]	5	0.25	0.06 to 0.45	0.02	0 (0–66)	0.009	2.46 (0.65)	−0.12 to 0.63	7.00
Lowest ES removed[c]	5	0.41	0.10 to 0.73	0.02	8 (0–81)	0.04	4.34 (0.36)	−0.29 to 1.11	4.38
Sensitivity analysis[d]	6	0.32	0.12 to 0.52	0.0014	27 (0–70)	0.02	6.84 (0.23)	−0.13 to 0.77	5.56
Depressive symptoms at 6-month follow-up									
Main analysis[a]	5	0.29	−0.16 to 0.73	0.15	48 (0–81)	0.08	7.64 (0.11)	−0.75 to 1.32	6.25
Additional analyses									
Highest ES removed[e]	4	0.11	−0.12 to 0.34	0.22	0 (0–63)	0.006	1.24 (0.74)	−0.33 to 0.56	16.13
Lowest ES removed[f]	4	0.40	−0.18 to 0.98	0.11	32 (0–76)	0.07	4.43 (0.22)	−0.98 to 1.78	4.49
Sensitivity analysis[d]	5	0.27	−0.58 to 0.04	0.08	48 (0–81)	0.06	7.64 (0.11)	−1.18 to 0.64	6.52
Alcohol use at 3-month follow-up									
Main analysis[a]	6	0.14	−0.02 to 0.30	0.07	0 (0–51)	0.008	2.58 (0.77)	−0.16 to 0.44	12.70
Additional analyses									
Highest ES removed[b]	5	0.10	−0.02 to 0.22	0.09	0 (0–14)	0.001	0.97 (0.91)	−0.08 to 0.28	17.74
Lowest ES removed[c]	5	0.20	0.03 to 0.37	0.03	0 (0–37)	0.005	1.33 (0.86)	−0.09 to 0.49	8.89
Sensitivity analysis[d]	6	0.13	−0.04 to 0.30	0.12	0 (0–51)	0	2.58 (0.77)	−0.11 to 0.37	13.44
Alcohol use at 6-month follow-up									
Main analysis[a]	5	0.14	0.07 to 0.20	0.005	0 (0–0)	0.0001	0.15 (0.997)	0.05 to 0.22	13.05
Additional analyses									
Highest ES removed[f]	4	0.11	0.02 to 0.20	0.03	0 (0–0)	<0.0001	0.10 (0.99)	−0.02 to 0.24	15.83
Lowest ES removed[e]	4	0.15	0.12 to 0.18	0.0007	0 (0–0)	<0.0001	0.10 (0.99)	0.10 to 0.20	11.79
Sensitivity analysis[d]	5	0.14	−0.10 to 0.38	0.27	0 (0–0)	0	0.15 (0.997)	−0.25 to 0.53	13.04

Quality assessment — GRADE domains (RCTs)

Domain	Depressive symptoms 3-month	Depressive symptoms 6-month	Alcohol use 3-month	Alcohol use 6-month
Study design	RCTs	RCTs	RCTs	RCTs
Risk of bias	X	X	X	X
Inconsistency	✓	X	✓	✓
Directness	✓	✓	✓	✓
Imprecision	✓	✓	✓	✓
Publication bias	N.a.	N.a.	N.a.	N.a.
Overall quality rating	+++	++	+++	+++

95% PI, prediction interval; additional analyses, influence analyses (leave-one-out analysis); ES, effect size; g, Hedges' g; GRADE = very low, +; low, ++; moderate, +++; high, ++++; x, limitations in domain; ✓, not limitations in domain; Long-term, 6-month follow-up; N.a., not applicable, we were not able to asses publication bias; Nc, number of comparisons; Short-term, 1- to 3-month follow-up; T², Tau²; Q, Q-statistic.

[a]HKSJ estimator.
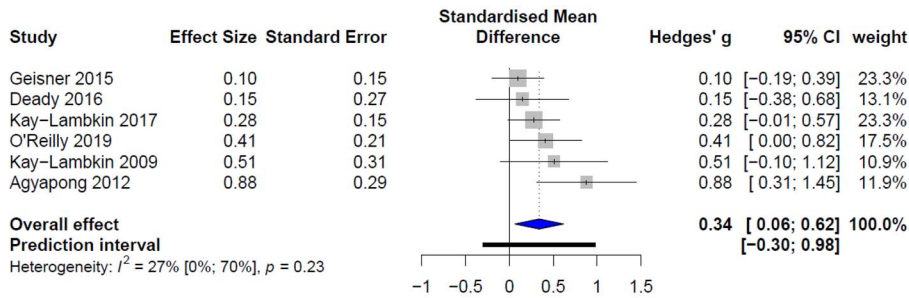[b]Omitting Agyapong *et al.* (2012).
[c]Omitting Geisner *et al.* (2015).
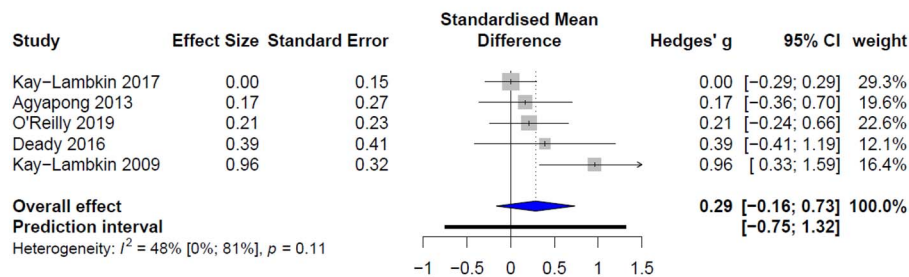[d]DL estimator.
[e]Omitting Kay-Lambkin et al. (2009).
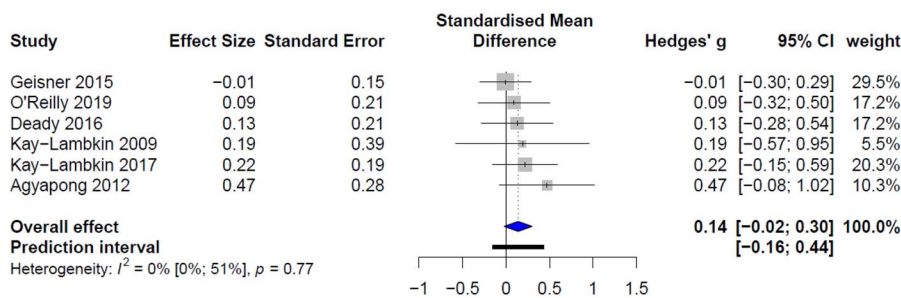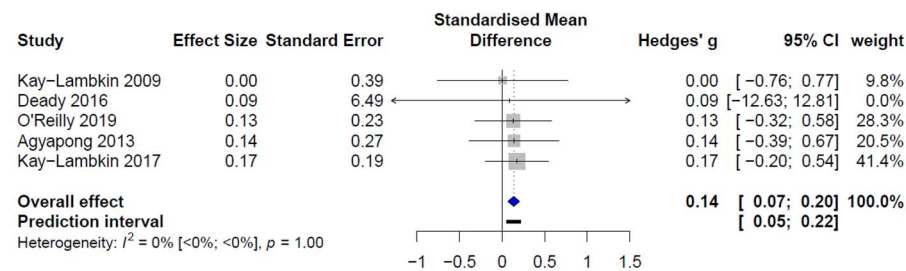[f]Omitting Kay-Lambkin et al. (2011, 2017).

Fig. 3. Main meta-analyses on depressive symptoms and alcohol use at 3- and 6-month follow-up. Note: Wide 95% CI calculated on exact data as published in Deady *et al.* (2016).

at 3-month follow-up and a small but significant effect ($g = 0.14$) on alcohol use at 6-month follow-up. Sensitivity analysis indicated the confidence interval of the latter finding to be sensitive to statistical estimator choice. Statistical heterogeneity was low to moderate for both depression outcomes and low for alcohol use outcomes. The quality of evidence was moderate, except for depressive symptoms at 6-month follow-up for which evidence was low. Both GRADE ratings indicate that future research is likely to have an important impact on the confidence in the current findings and possibly change the estimates of the effects (Atkins et al., 2004). This uncertainty is also reflected in the PIs, which indicate that similar future studies could as well find positive or negative effects of digital interventions.

The current meta-analysis shows the preliminary beneficial effects of digital interventions in reducing depressive symptoms at 3-month follow-up and possibly alcohol use after 6-month follow-up. This observed effect on depressive symptoms ($g = 0.34$) is above the threshold for a clinically relevant effect for depression treatment (i.e. $g = 0.24$) (Cuijpers et al., 2014). Our findings seem partly in line with an older subgroup meta-analysis in which digital interventions were compared with face-to-face interventions, including 2 and 13 comparisons, respectively (Riper et al., 2014a). The authors found digital, exclusively CBT/MI-based interventions, for co-occurring depression and problematic drinking to outperform face-to-face CBT/MI in reducing depressive symptoms ($g = 0.73$ and $g = 0.23$, $P = 0.030$) but not for alcohol use ($g = 0.39$ and $g = 0.16$, $P = 0.346$) (Riper et al., 2014a). Effect size differences might be caused by differences in follow-up, comparators and included studies, as our review was not restricted to only CBT/MI-based interventions. Furthermore, we included mostly trials that compared self-guided digital interventions with active control groups. This often leads to small differential effect sizes. However, in our analyses, we found that studies with passive comparators did not have the largest effect sizes compared to active comparators. We hypothesise that this might have been caused by other factors such as intervention characteristics (e.g. mode of delivery, intensity, adherence) or participant characteristics.

Despite the fact that positive effects of digital interventions were not consistently found for both comorbid conditions, combined digital interventions might still have potential. First, for people who otherwise not seek professional care, digital treatment might be a suitable alternative (Schmidt, 2016; Kaner et al., 2017; Riper et al., 2018). Second, depression treatment alone is not always effective in reducing problematic alcohol use. A recent study showed that despite clinically relevant effects of both digital and regular depression treatment, alcohol use among depressed hazardous drinkers remained unchanged (Strid et al., 2019). Additionally, digital interventions for comorbid depression and problematic alcohol use are well-received by both professionals and patients (Deady et al., 2014). The majority of patients believed digital interventions (i.e. either supportive text messages or online CBT/MI modules) to be supportive and applicable in improving their mental well-being and controlling their alcohol use (Agyapong et al., 2013b; Deady et al., 2014). All in all, this shows that combined digital interventions have potential to be of value.

The fact that we only identified six RCTs and four protocol papers of ongoing trials on digital interventions for comorbid depression and problematic alcohol use shows that this is an emerging field. These ongoing trials can provide an important contribution to the field and possibly reduce inconsistencies regarding the current meta-analyses findings (Kay-Lambkin et al., 2015; Schaub et al., 2016; Cunningham et al., 2018; Frohlich et al., 2018). However, participant recruitment in previous studies has proven difficult and this may hinder fast progression in the field (Deady et al., 2016; Krause et al., 2019; O'Reilly et al., 2019). Clinical heterogeneity among included

interventions was present due to differences in settings, duration, guidance and delivery-mode, but statistical heterogeneity was low to moderate. This might indicate that despite variations in interventions and populations, effects of the individual studies, although not all statistically significant, are quite homogeneous and often favour digital interventions over control conditions.

Limitations

Our findings should be interpreted in context of some limitations, such as the small number of included studies with sometimes small samples, which limits the power of the current study, and the inconsistencies in findings of the sensitivity analysis on alcohol use at 6-month follow-up. Furthermore, all studies had a high risk of bias and publication bias could not be assessed. Studies needed to have an abstract written in English in order to be identified in our search, which might have introduced language bias. Clinical heterogeneity was present among the included studies in terms of differences in intervention and population characteristics. Two studies were conducted on a mixed sample of depressed patients using cannabis and/or alcohol use in hazardous levels, for which we calculated the sample sizes for our comparison.

Future research

Future research is needed to replicate the current findings and to make the findings more robust. We did not observe consistent significant effects of digital interventions on both comorbid conditions at 6-month follow-up; more research is warranted that addresses this issue further and the possibility of lagged effects after this 6-month time point. To increase the quality of RCTs, researchers could consider including larger sample sizes, blinded clinician-rated outcomes in addition to self-report measures, pre-register trial protocols, adequate handling of missing data (e.g. multiple imputation) and uniform measurement and operationalization of alcohol use outcomes, for example by using outcomes included in the brief alcohol intervention core outcome set (Shorter et al., 2019). It would be of interest to report intervention adherence rates and include 12-month follow-up measurements and evaluate cost-effectiveness. Researchers could consider developing interventions that are accessible on smartphones or smartphone app-based and evaluate in what type of setting and for what type of clients digital interventions are especially beneficial. In this way, more efficient use of digital interventions might be accomplished, which could benefit intervention implementation in practice. Lastly, an individual patient data meta-analysis could possibly resolve some of the current shortcomings (e.g. increase in power, reliability and standardisation in analysis) of this traditional meta-analysis (Riley et al., 2010).

CONCLUSION

Despite its limitations, this meta-analysis provides evidence of the effectiveness of digital interventions for people with co-occurring depression and problematic alcohol use. Our findings indicate that digital interventions can have a positive effect on depressive symptoms at 3-month follow-up and alcohol use at 6-month follow-up. More research is needed to corroborate the current findings and enhance evidence-based treatment options for people with comorbid depression and problematic alcohol use.

SUPPLEMENTARY MATERIAL

Supplementary material is available at Alcohol and Alcoholism online.

DATA AVAILABILITY

The data underlying this article are available in DANS EASY, at https://doi.org/10.17026/dans-xfm-g98b.

CONFLICT OF INTEREST STATEMENT

None declared.

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