

**Are Computer-Based Treatment Programs Effective at Reducing Symptoms of Substance Misuse and Mental Health Difficulties Within Adults? A Systematic Review**

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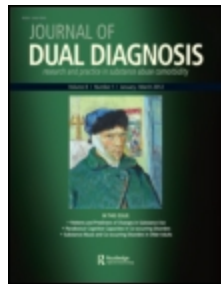
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**Are computer-based treatment programs effective at reducing symptoms of substance misuse and mental health difficulties within adults?: A systematic review**

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Keywords:	substance misuse, mental health, computer, treatment
Abstract:	<p><b>Objective</b> Comorbid substance misuse and mental health difficulties are recognized as a leading contributor to disease burden worldwide. Amidst cuts to healthcare services, computer-based interventions may provide support for patients experiencing these difficulties. The aims of this systematic review were to identify and investigate the efficacy of these computer-based interventions at improving substance misuse and mental health outcomes.</p> <p><b>Methods</b> A systematic search was conducted of CINAHL Plus, PsycARTICLES, PsycINFO, MEDLINE, Web of Science, and the Cochrane library. Grey literature was also searched for relevant papers. Data were extracted from 33 papers, which met eligibility criteria by reporting a computer-based intervention designed to treat substance misuse and mental health in adults. Quality assessments were conducted on these papers.</p> <p><b>Results</b> Computer-based interventions generally led to an improvement of substance misuse and mental health outcomes within groups and when compared against waitlist control and psychoeducation. Computer-based interventions were effective at improving dual diagnosis outcomes, and improvements to mental health outcomes specifically were maintained for up to nine months. However, the combined effect of computer-based interventions and therapist support was found to be more effective than the effects of computer-based interventions alone.</p>

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	<p>Conclusions</p> <p>Many papers were limited by high attrition rates commonly attributed to 'digital' interventions. Future research should consider systematically recruiting a range of participants, including those potentially affected by the digital divide, and incorporating methods within research to maintain engagement. This review was also limited by the heterogeneity of the papers reported, many of which differed between targeting dual diagnosis and targeting either substance misuse or mental health respectively, with outcomes investigating other difficulties out of curiosity.</p>

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7 ***Are computer-based treatment programs effective at reducing symptoms of***  
8 ***substance misuse and mental health difficulties within adults?: A systematic***  
9 ***review***  
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15 **Short title:** Computer interventions for dual diagnosis  
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**Abstract****Objective**

Comorbid substance misuse and mental health difficulties are recognized as a leading contributor to disease burden worldwide. Amidst cuts to healthcare services, computer-based interventions may provide support for patients experiencing these difficulties. The aims of this systematic review were to identify and investigate the efficacy of these computer-based interventions at improving substance misuse and mental health outcomes.

**Methods**

A systematic search was conducted of CINAHL Plus, PsycARTICLES, PsycINFO, MEDLINE, Web of Science, and the Cochrane library. Grey literature was also searched for relevant papers. Data were extracted from 33 papers, which met eligibility criteria by reporting a computer-based intervention designed to treat substance misuse and mental health in adults. Quality assessments were conducted on these papers.

**Results**

Computer-based interventions generally led to an improvement of substance misuse and mental health outcomes within groups and when compared against waitlist control and psychoeducation. Computer-based interventions were effective at improving dual diagnosis outcomes, and improvements to mental health outcomes specifically were maintained for up to nine months. However, the combined effect of computer-based interventions and therapist support was found to be more effective than the effects of computer-based interventions alone.

**Conclusions**

Many papers were limited by high attrition rates commonly attributed to 'digital' interventions. Future research should consider systematically recruiting a range of participants, including those potentially affected by the digital divide, and incorporating methods within research to maintain engagement. This review was also limited by the heterogeneity of the papers reported, many of which differed between targeting dual diagnosis and targeting either substance misuse or mental health respectively, with outcomes investigating other difficulties out of curiosity.

**Keywords:** substance misuse, mental health, computer, treatment

## Introduction

Epidemiological evidence suggests that between 75-85% of service users attending substance misuse treatment services also experience mental health difficulties (Weaver et al., 2003). Additionally, between 20-56% of services users being treated for mental health difficulties also identify as having dual diagnosis (Strathdee et al., 2002). Dual diagnosis here refers to this co-occurrence of mental health difficulties and substance misuse (Kessler, 2004). Regarding treatment and diagnosis of these co-morbid difficulties, each may impact on the other. Those seeking support for mental health difficulties may deny substance use due to the legality of this, and some symptoms of substance misuse may share symptomology with other mental health issues, meaning that comorbidity may be missed (Mueser et al., 2016). Additionally, substances may impact the effectiveness of some mental health medications, further exacerbating problems with treatment (ibid.). Furthermore, these comorbid difficulties may increase risk of relapse, infections and other complications, and social deprivation (Baingana et al., 2015). It is unsurprising therefore that dual diagnosis is classed as one of the leading contributors of disease burden globally (Buckley, 2006; Whiteford et al., 2013), and comorbid mental health and substance misuse difficulties comprise 22.7% of global years lived with a disability (Vos et al., 2012). Alongside this increasing burden to healthcare systems, it is recommended that health services need to respond with evidence-based treatment programs and interventions to prevent and treat comorbid mental health difficulties and substance misuse difficulties (Whiteford et al., 2015).

There is currently no standardized treatment for comorbid mental health and substance misuse difficulties. Although guidelines recommend an integrated treatment approach (Morisano et al., 2014), there are still substantial barriers to accessing combined service support, including a lack of dedicated services (Priester et al., 2016), knowledge of evidence-based treatment and specialist staff training (Clark et al., 2008). Furthermore, with social care services experiencing financial cuts amidst austerity measures (Glasby, 2017), computer-based interventions (CBIs) may provide cost-effective solutions to care (Olmstead et al., 2010). Here, CBIs refer to digital and online interventions. As the digital world increases, and more interventions are developed across these platforms, CBIs are substantial enough to review independent of mobile applications (Taylor & Luce, 2003). Programs can have a large outreach with minimal staff needed to facilitate support (Griffiths et al., 2006) and may increase engagement with treatment through reducing stigma for service users (Dixon et al., 2016). Also, as substance misuse or mental health difficulties may be triggered at any time of day, digital health offers further benefits such as the ability to access support in any place and at any time. This allows the user to take control over their specific difficulty, without being

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3 constrained to typical office hours to receive treatment nor having to travel to services for support  
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5 (Dugdale et al., 2016; Eysenbach, 2001; Griffiths et al., 2006).  
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8 Despite potential practical benefits to the application of CBIs compared to face-to-face  
9 support, it is important to understand the clinical effects of CBIs, to determine their therapeutic  
10 suitability for treating co-morbid mental health difficulties and substance misuse difficulties.  
11 Although there is available evidence researching the use of CBIs for mental health difficulties and  
12 substance misuse, to our knowledge, there are currently no reviews summarizing these to explore  
13 the overall effectiveness of CBIs and inform practical decisions around intervention design.  
14 Therefore, the aim of this paper is to determine whether computer-based treatment programs are  
15 effective at reducing symptoms of substance misuse and mental health difficulties within adults.  
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## 23 **Methods**

24 This systematic review was conducted following the guidelines set out by Preferred Reporting Items  
25 for Systematic Reviews and Meta-Analyses (PRISMA: Liberati et al., 2009). The research protocol for  
26 this review has been submitted online via 'Prospero':  
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29 [www.crd.york.ac.uk/prospero/display\\_record.php?RecordID=72392](http://www.crd.york.ac.uk/prospero/display_record.php?RecordID=72392)  
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### 33 ***Eligibility criteria***

#### 34 ***Study characteristics***

35 The PICOS tool was used to guide and help specify the search criteria (Centre for Reviews and  
36 Dissemination, 2009). This defines the search under the categories of Population, Intervention,  
37 Comparison, Outcome and Study type. See Table 1.  
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#### 43 ***Information sources***

44 The databases selected for the basis of the search were, CINAHL Plus, PsycARTICLES, PsycINFO and  
45 MEDLINE via EBSCO. Web of Science, and the Cochrane library were also searched. OpenGrey,  
46 ETHOS, ProQuest, and ResearchGate (first 200 hits) were selected to conduct grey literature  
47 searches. These databases were searched between August and September 2017. An updated search  
48 was conducted March 2019.  
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#### 54 ***Search***

55 Databases were searched using the following terms: (alcohol\* OR drug OR drink\* OR addict\* OR  
56 substance) AND (anxiety OR depress\* OR "mental health" OR "dual diagnosis") AND (internet OR  
57 digital OR online OR computer\* OR web\*) AND (intervention OR treatment OR therapy OR  
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3 program\*). Searches were restricted to articles published in the English language which report on  
4 outcomes for adults (aged 16 years or older) where possible. Restrictions were also placed on the  
5 search terms: NOT sleep\*, NOT train\*, NOT sex\*, NOT gam\*, NOT smok\*. No restrictions were  
6 placed on date of publication. Terms were checked and agreed by two authors and an independent  
7 researcher. Hand searches were conducted of targeted journals, including within the reference lists  
8 of included papers, to check for additional papers that would meet the inclusion criteria.  
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### 13 ***Study selection***

14 The first author read through the titles and abstracts of the papers identified through the searching  
15 process. Papers that did not meet the inclusion criteria were excluded from further analysis. The full  
16 text of remaining papers was then screened, with 10% of these full texts checked by a second  
17 reviewer to ensure they met eligibility criteria.  
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### 23 ***Data collection***

24 Data extraction forms were developed by the lead author (SD) drawing upon guidelines from the  
25 Cochrane Review centre (2014) and the Centre for Reviews and Dissemination (2009). The form was  
26 checked by a second author, and an independent researcher, to agree the content prior to data  
27 extraction. The form facilitated extraction of study characteristics, methods used, participant  
28 information, intervention details, outcome measures and findings.  
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### 34 ***Quality assessment***

35 The 'quality assessment tool for quantitative studies' (Effective Public Health Practice Project, 1998)  
36 was used to assess the quality of included studies. This assessment tool rates the quality of a paper  
37 using the following components: selection bias, study design, confounders, blinding, data collection  
38 methods, and withdrawals and drop-outs. Components are rated as 1-strong, 2-moderate, or 3-  
39 weak. The whole paper is then also rated as such, based on the total amount of 'weak' components  
40 within the paper.  
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### 49 ***Data synthesis***

50 A narrative synthesis of papers is reported, as most papers were heterogeneous in intervention  
51 design and outcome measures used. Major changes within and between groups are reported for the  
52 papers, where information is available. Specific variations across timeframes are reported in Table 2.  
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## 57 **Results**

### 58 ***Study selection***



The study selection process is summarized in Figure 1. A total of 7,678 papers were returned from the databases after initial and later searches, of which, 2,475 duplicates were removed. An additional seven papers were found via hand searches and exploring the grey literature, bringing the total remaining papers to 5,210. After screening the titles and abstracts of papers, 5,126 were removed as they did not meet the inclusion criteria. The full texts of 84 papers were reviewed, 33 of which met the eligibility criteria. Of these, nine papers reported data from four studies (two papers reported one study, another two papers reported a second, a further two papers reported a third, and a final three papers reported a fourth). These papers were merged, leaving 28 papers for review. To assess inter-rater reliability, 10% of the full texts were corroborated by a second reviewer. Inter-rater agreement was 86%. Discrepancies were resolved between the two reviewers, however where agreement could not be reached on three papers, these were checked by a third reviewer. Table S1 highlights papers included or excluded at this final screening phase, including reasons for exclusion.

Due to the number of papers reported, reference numbers will be used within the results section as follows:

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|---|-----------------------------|
| 1. Acosta et al. (2017)                       | 16. Schaub et al. (2015)    |
| 2. Brief et al. (2013)                        | 17. Tossmann et al. (2011)  |
| 3. MERGED Cucciare et al. (2013a, 2013b)      | 18. Schaub et al. (2012)    |
| 4. Deady et al. (2016)                        | 19. Tait et al. (2015)      |
| 5. Geiser et al. (2015)                       | 20. Boß (2018)              |
| 6. Sundstrom et al. (2016)                    | 21. Wilson et al. (2015)    |
| 7. MERGED Kay-Lambkin et al. (2011, 2012)     | 22. Musiat et al. (2014)    |
| 8. Johansson et al. (2017)                    | 23. Billings et al. (2008)  |
| 9. Kay-Lambkin et al. (2009)                  | 24. Levin et al. (2017)     |
| 10. MERGED Postel et al. (2010, 2015)         | 25. Lewis et al. (2017)     |
| 11. Linke et al. (2007)                       | 26. Batterham et al. (2018) |
| 12. Rupp et al. (2012)                        | 27. Elison et al. (2014)    |
| 13. Wolitzky et al. (2018)                    | 28. Tiburcio et al. (2018)  |
| 14. Sundstrom et al. (2017)                   |                             |
| 15. MERGED Elison et al. (2015a, 2015b, 2017) |                             |

\*Note that although the Elison et al. studies all investigate the use of one program, the versions of the program differ between the 2014 paper and the 2015a, 2015b, and 2017 papers, and the research uses different samples. These papers were therefore not merged.

## ***Study characteristics***

### ***Participants***

The 28 papers included 14,279 participants targeted for different primary identifying problems. Substance misuse was defined across the included papers as hazardous (1-6), harmful (7), problematic (8-10), risky (11), or dependent (12-13) alcohol use or disorder (14), and drug use (1, 15), including specific cannabis (7, 9, 16-17), cocaine (18), or amphetamine (19) use, and was primarily targeted in 13 papers (3, 6, 8, 10-12, 14, 16-21). Mental health was specifically targeted in four studies (22-25) and was defined across the included papers as including general symptoms (22), as well as post-traumatic stress disorder (PTSD; 1, 25), and depression (4-5, 7, 9). Of the 28 papers included, participants with dual diagnosis were specifically targeted in 11 studies (1-2, 4-5, 7, 9, 13, 15, 26-28).

Specific participant groups were also targeted including veterans (1-3), employees (20, 23), youths and students (4-5, 22, 24) and deaf adults (21). The proportion of male participants ranged from 12.37% (26) to 93% (1), and the average age of participants ranged from 20 (5) to 59 (3), with a range of between 18-92. Of the papers, eight (1-3, 5, 13, 21, 23-24) were conducted in the US, five in the UK (11, 15, 22, 25, 27), five in Australia (4, 7, 9, 19, 26), three in Sweden (6, 8, 14), two in Switzerland (16, 18), two in Germany (17, 20), one in the Netherlands (10), one in Austria (12), and one in Mexico (28). Between 59.7-96.8% of participants were White, and between 0.7-12% were Black. Of those that reported further demographics, between 32.4-100% (1, 3-4, 7, 10-11, 20, 23, 25-26, 28) were employed, between 8.8-100% of participants were studying at a higher level or had graduated from university (4-5, 10, 14, 16, 18, 20, 23, 25-26, 28), and between 9.4-71% of participants (2, 8, 10, 14, 18-20, 24, 27-28) had received treatment for their specific substance use or mental health difficulties.

### ***Study design***

A total of 10,995 out of 13,970 participants were allocated to receive a CBI (note that one paper [23] did not include participant allocation numbers). In keeping with the digital theme of the interventions, online forms of recruitment were utilized including website, email and social media advertising (2, 4, 6, 8, 10, 14, 16-20, 22-23, 26). Participants were also recruited via patient clinics or services, and residential services (1, 3, 7, 9, 12-13, 15, 21, 25, 27-28). Offline advertisement articles (11, 20), random sampling (5), and presentations (24) were less frequently used to recruit participants. A total of 19 papers were randomized controlled trials (RCTS; 1-5, 7, 9-10, 12-13, 16-20, 22-23, 25-26), three were pilot RCTS (6, 24, 28), and the remaining six papers were single group studies comparing pre- and post-scores (8, 11, 14-15, 21, 27).

### Intervention and comparison

A total of 19 papers used strategies from cognitive behavioral therapy (CBT) to underpin the content of their CBI (1-2, 4, 6-11, 13-16, 18-19, 22-23, 27-28), seven of which used these strategies in combination with motivational interviewing (MI) techniques (4, 7, 9-10, 16, 18-20). Providing personalized feedback was the focus of two interventions (3, 5). The remaining papers drew upon techniques from MI (20, 26) Acceptance Commitment Therapy (24), mindfulness (26), cognitive remediation (12), psychoeducation (25), self-regulation (17), and mutual aid therapy such as Alcoholics/Narcotics Anonymous (21). These CBIs were compared against a waitlist control in nine studies (2, 10, 16-17, 19-20, 23-25), and therapist support in four studies (6-7, 9, 16). Psychoeducation or further information was given in five studies as a control (3-4, 18, 22, 26), and assessment only control was used in one study (5). In the latter study, further control conditions included alcohol only treatment and mood only treatment, compared to combined dual diagnosis intervention. Where treatment as usual was provided as a control, this included standard residential or inpatient treatment (1, 12-13, 21, 28).

The average duration of the CBIs ranged from 15 minutes – 12 weeks, and varied between simultaneous content access (8, 15, 27) where the user can access content of the program in any order, and sequential access, where the intervention has to be completed in a linear way (2, 7-11, 16, 19, 24). Although some papers specified that their CBIs could be completed via self-help (1, 6, 8, 20, 23-25), therapist involvement was discussed in six papers as a means to support users alongside their CBI (7, 9-10, 13-14, 16-17, 28).

### Analysis and effectiveness

Parametric measures were used in 27 papers, including ANOVA, ANCOVA, MANOVA, generalized estimating equations, *t*-tests, and regression. Only one paper (27) used non-parametric measures for their analysis: Wilcoxon test. Clinical outcomes measured varied between the papers. Substance use was recorded via consumption or frequency of use (1-11, 13-14, 16-20, 22-23, 27-28), hazardous and harmful use (6, 9, 14), disordered use or dependence (6-8, 10-11, 14-16, 18, 21, 25-26, 28), negative consequences associated with substance misuse (3, 5) and cravings (14, 18). Other measures were also taken; one paper reported obsessive compulsive drinking (12), one abstinence self-efficacy (14), and one drug taking confidence (17). For mental health, depression was measured in 19 studies (3-7, 9-10, 12, 14-15, 17-18, 21-23, 25-28), anxiety in 10 studies (6, 8, 10, 15, 17, 22-23, 25-27), and stress, distress, and PTSD in eight studies (1-3, 10, 13, 19, 23, 25). Overall mental health or wellness was reported in five papers (11-12, 16, 20, 24). Quality of life or life satisfaction was measured in nine papers (1, 6, 8, 10, 14-15, 17, 19, 21), and self-esteem in two papers (21-22). Work related outcomes

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3 were also reported in three papers (19, 23, 27). Other clinical outcomes reported include knowledge  
4 and management of mood disorders (23), cognitive irritation (20), social support (25), disability (25),  
5 suicidal ideation (26), help seeking (19, 23), affect (23), general health (3, 10), coping (3), panic (26),  
6 recovery progression (15), phobia (26-27), functioning (7), therapeutic alliance (7), co-morbid  
7 difficulties (24), mindfulness measures (24), eating disorder (22), and perfectionism (22). A summary  
8 of the findings of these papers may be found in Table 2.  
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#### 15 *Interventions primarily targeting dual diagnosis*

16 Regarding substance misuse and mental health difficulties, within group differences suggested  
17 significant improvements for those completing CBIs from baseline to post-intervention (2, 13, 15, 26-  
18 28) and to follow-up at 6 months (4). However, in one paper, non-significant reductions were found  
19 for CBIs at baseline to one-month follow-up (5). CBIs led to significant increases in measures of  
20 quality of life within groups (15, 27), as well as within group improvements to recovery progression  
21 (15), and work and social adjustment (27).  
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28 CBIs using CBT, CBT plus MI, and CBT plus therapist support led to significantly greater  
29 reductions in dual diagnosis measures (respectively 2, 4, 13), and substance misuse only (1) when  
30 compared against control groups at post-treatment, apart from one MI and mindfulness-based CBI  
31 which found no difference between the CBI and psychoeducation (26). When compared against  
32 inpatient treatment, two CBT-based CBIs found no differences between groups at follow-up (1, 28).  
33 When observing the combined effect of CBT-based CBIs and therapist support, this led to significant  
34 reductions in respective substance misuse and depression when compared against person-centered  
35 therapy (7), and in substance misuse only compared against brief intervention (9). In the latter case,  
36 therapist support led to a significantly greater reduction in depression compared to CBI.  
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#### 45 *Interventions primarily targeting mental health difficulties*

46 Within group outcomes found significant improvement to distress, depression, anxiety, social  
47 anxiety, PTSD, and overall mental health from pre- to post-intervention for an Acceptance  
48 Commitment Therapy CBI (24) and at one-month follow-up for a CBT-based CBI (25). Between group  
49 differences demonstrated that CBT-based CBIs led to significant reductions in distress (23),  
50 depression and anxiety (22) compared against waitlist control and psychoeducation respectively.  
51 Only one of four studies reported significant between group reductions in binge drinking for the CBI  
52 group compared against a wait-list control (23).  
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### *Interventions primarily targeting substance misuse*

Within group outcomes measured from pre- to post-intervention found a significant reduction in alcohol consumption, problems and dependency (8, 11, 20). Significant reductions in drinking frequency and overall consumption were maintained within groups at 3 months (14), 6 months (3) and 9 months (10). Significant improvements to cravings and abstinence self-efficacy were also reported from baseline to three months follow-up (14). For drug consumption, participants reported reductions in substance use over the course of the CBI (8), however no significant within group outcomes were reported (18).

Significant reductions to substance misuse and addiction between groups were reported for CBT plus MI, self-regulation, and MI CBIs against waitlist control (respectively 10, 17, 20), and psychiatric inpatient care (12). However, non-significant differences in substance misuse between groups were also found between CBIs and substance misuse inpatient support (21), a brief-intervention CBI against psychoeducation (3), and CBT plus MI CBIs against psychoeducation (18), and waitlist control (19). Additionally, significant reductions in substance misuse between groups were found for CBIs when combined with therapist support against the CBI on its own (6, 16).

Regarding secondary mental health outcomes, within group differences suggest significant reductions to mental health functioning from baseline to post-intervention (11). Improvements to depression and PTSD (3, 14) are maintained at three months, with additional reductions to anxiety and stress outcomes maintained at nine months (10). Between group differences suggest that CBIs led to significant reductions in mental health difficulties compared to waitlist control (10, 17, 20), and psychiatric inpatient care (12), however no differences were reported between CBIs and psychoeducation (18), or CBIs and substance misuse inpatient care (21).

Additional significant improvements were found for quality of life both within (8, 14) and between groups (10, 17). Significant between group differences were also found for help seeking and days out of work role (19). However, no significant differences were reported for life satisfaction or self-esteem between groups when compared to substance misuse inpatient treatment (21).

### **Quality assessment**

Quality assessment was based on the 'quality assessment tool for quantitative studies' (Effective Public Health Practice Project, 1998) and is summarized in Table 3. All but six of the studies, which were rated as of 'moderate' quality, received a global quality rating of 'weak'. The main areas which were seen to affect this score were selection bias, blinding, and withdrawals and drop-outs. Many of

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3 the studies used opportunity sampling to recruit participants, with few suggesting a systematic  
4 method to recruitment, therefore it could not be ascertained whether samples were representative  
5 of the target population. Regarding 'blinding', this data was not well reported within many studies,  
6 and again it was not clear whether participants and researchers were aware of the active  
7 intervention or not. Finally, drop-out rates and withdrawals were relatively high in many studies  
8 where this information was reported, with many studies using intention to treat analyses to present  
9 the data.  
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## 16 Discussion

17 The purpose of this systematic review was to consider the effectiveness of CBIs at reducing the  
18 symptoms of substance misuse and mental health difficulties. A total of 33 studies were found which  
19 reported on these outcomes, nine of these papers were merged into four respective studies, and  
20 thus 28 papers were reviewed.  
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26 Of the included papers, CBIs typically focused on depression and alcohol use as the primary  
27 outcome (compared to anxiety and drug use respectively). However, for most papers, regardless of  
28 primary focus of the intervention or target audience, symptoms of substance misuse and mental  
29 health difficulties improved within groups. This was observed for mental health outcomes for papers  
30 primarily targeting mental health difficulties from pre- to post-intervention (Levin et al., 2017), and  
31 in dual diagnosis symptoms for studies primarily targeting dual diagnosis from baseline to six month  
32 follow-up (Deady et al., 2016), and studies primarily targeting substance misuse from baseline to  
33 nine month follow-up (Postel et al., 2010, 2015).  
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41 Between group differences were also reported, with CBIs generally leading to an  
42 improvement of mental health and substance misuse symptoms when compared against waitlist  
43 control (Billings et al., 2008; Brief et al., 2013; Postel et al., 2010, 2015; Tossmann et al., 2011) and  
44 primary care settings (Acosta et al., 2017). Whilst there was little difference in the number of papers  
45 reporting changes to mental health outcomes, generally CBIs appeared more effective at improving  
46 alcohol use outcomes compared to drug use outcomes. Exploring program feedback on CBIs  
47 addressing drug use, participants in Tait et al. (2015) suggested that they had concerns about the  
48 privacy of the CBI. Again, knowledge of the legality of certain substances might mean that  
49 participants are less likely to engage with an intervention to address their substance use, in case  
50 sharing this information carries consequences. Similarly in Schaub et al. (2012), telephone contact to  
51 reduce attrition was removed from the methodology following the pilot, due to participants' fears  
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3 around the legal consequences of drug use. Future program developers should therefore ensure that  
4 information about privacy is clear for participants.  
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8 When investigating the combined effect of CBIs plus therapist support, it was found that these were  
9 more effective at reducing depression (Kay-Lambkin et al., 2009) and substance misuse (Schaub et  
10 al., 2015; Sundstrom et al., 2016). This may be due to the added benefit of receiving face-to-face  
11 support and developing a 'human' therapeutic relationship (Mohr et al., 2011). Although evidence  
12 has suggested that patient satisfaction levels are typically similar across CBIs and face-to-face  
13 support (Murphy et al., 2009; Zeren, 2015). Despite evidence suggesting the added benefit of  
14 therapist support, for the CBIs primarily targeting substance misuse, these were more effective at  
15 reducing comorbid mental health and substance misuse symptoms than psychiatric inpatient care  
16 (Rupp et al., 2012), but not when compared against substance misuse inpatient care (Wilson et al.,  
17 2015). This is supported in offline settings also, as further reports suggest that those with comorbid  
18 mental health and alcohol difficulties are less likely to benefit from the mental health triage system  
19 (Health and Social Care Information Centre, 2014). These findings may be accounted for by the  
20 respective focus of psychiatric and substance misuse services. In a recent combined report between  
21 Public Health and the Mental Health Foundation, although substance misuse is seen as a risk factor  
22 to mental health difficulties, there is no mention of improving both comorbid outcomes (Faculty of  
23 Public Health and Mental Health Foundation, 2016). According to the European Monitoring Centre  
24 for Drugs and Drug Addiction (2013), mental health difficulties may occur in up to 90% of those  
25 presenting to substance misuse services, and substance misuse disorder occurs in around 14-54% of  
26 those with a mental health difficulty. This highlights the disparity between these groups and how  
27 treatment may therefore differ depending on what is considered to be the difficulty of primary  
28 concern. Although there is currently no standardized approach for the treatment of dual diagnosis,  
29 guidelines recommend that treatment is integrated where possible (Morisano et al., 2014). These  
30 findings would suggest that typical substance misuse program may offer the best guidance on how  
31 these services can effectively target both conditions.  
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50 Several papers also found no differences between the CBI and control on measures of  
51 mental health (Acosta et al., 2017) and substance use (Cucciare et al., 2013a, 2013b) respectively, as  
52 well as collectively (Batterham et al., 2018; Schaub et al., 2012; Tait et al., 2015; Tiburcio et al., 2018;  
53 Wilson et al., 2015). This suggests that the CBIs may be as effective as psychoeducation and  
54 therapist support at improving co-morbid mental health and substance misuse outcomes. This could  
55 reinforce the value of online support in conjunction with therapist support. CBIs may work to  
56 provide additional care, of similar efficacy to therapist support, to clients outside of typical office  
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3 hours (Griffiths et al., 2006). This can also reduce the workload of therapists, as CBIs can be  
4 delivered to multiple clients at any one time (Griffiths et al., 2006). By incorporating CBIs into dual  
5 diagnosis treatment services, wrap-around care may be provided by offering a combination of online  
6 and offline support.  
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### 10 11 *Limitations*

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13 The papers in this study are limited by their quality, with 22 papers reported as 'weak'. Attrition was  
14 relatively high within the studies, however, this may be symptomatic of online interventions.  
15 Previous research in this area has also reported high attrition, specifically where face-to-face support  
16 is not received, and arguably therapeutic alliance has not been developed (Nguyen et al., 2004).  
17 Again, regarding substance use, privacy information of the CBI should also be made clear to  
18 participants, which may reduce attrition. Furthermore, although the age range of participants was  
19 wide, and data were reported from a range of participants from eight different countries, the  
20 demographic of White, employed, highly educated participants across the studies was high.  
21 Evidence suggests that those with a higher socio-economic status and education may be more likely  
22 to access online support (Kontos et al., 2012), therefore future CBIs need to consider how to reach  
23 those populations affected by this digital divide. Health research has already suggested several ways  
24 to close this divide. In order to overcome a lack of resources or poor internet connectivity,  
25 healthcare services or libraries may provide computer access to clients (Shaw et al., 2006), and  
26 community-based services may provide computer skills training (Kreps 2005).  
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39 This review is limited by the reporting of papers and the heterogeneity of papers included.  
40 However, heterogeneity is to be expected given the broad scope of the inclusion criteria indicating  
41 relevance for CBIs targeting substance misuse and mental health outcomes. As such, a main factor in  
42 the heterogeneity of papers was the difference in the intention of the CBI. This differed between  
43 targeting dual diagnosis and targeting either substance misuse or mental health respectively, with  
44 outcomes investigating other difficulties out of curiosity rather than an intentional purpose to treat  
45 this. Particularly within health literature which has not been previously systematically reviewed, it  
46 can be important to use broader inclusion criteria in order to generally explore what is known within  
47 the literature and from this, identify research priorities within this area (Thomson et al., 2013). This  
48 review in mind, considering the proportion of comorbid symptoms of mental health difficulties and  
49 substance misuse (Weaver et al., 2003), the proportion of CBIs for the treatment of dual diagnosis is  
50 relatively small, with about a third of papers reviewed reporting this. This is still an emerging area for  
51 researchers and designers, and further intervention development research should be conducted  
52 with consideration of dual diagnosis as a condition within itself rather than that of its respective  
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3 components. The authors also intend to conduct a further in-depth review of the dual diagnosis CBIs  
4 reported to further explore specific and shared intervention components related to efficacy, which  
5 may be of benefit for further CBI development.  
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### 10 **Conclusion**

11 Overall, CBIs for the treatment of co-morbid substance misuse and mental health difficulties were  
12 effective at improving these clinical outcomes. Against control measures, CBIs may be as effective as  
13 standard therapist support for comorbid outcomes. However, the combined effect of these two  
14 types of intervention, merging the online and offline worlds, was found to be more effective than  
15 the effects of the CBI on its own. Evidence has already suggested the utility of this approach within  
16 substance misuse (Dugdale et al., 2016), and there is scope for further research and intervention  
17 development within this area for dual diagnosis. Future research conducted in this area should  
18 consider systematically recruiting a range of participants, including those potentially affected by the  
19 digital divide, and incorporating methods to maintain engagement. Encouraging engagement is not  
20 only vital to reduce attrition and therefore develop a greater understanding of the longer-term  
21 effects of an intervention, but also in advancing research into real-world implementation and  
22 usability.  
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For Peer Review Only



Table 1.

*Inclusion Criteria using PICOS Tool*

PICOS	Criteria for inclusion
Population	Those aged 16 years or older who are experiencing symptoms of substance misuse and mental health difficulties.
Intervention	Computer-based or internet-delivered intervention. The intervention must be used as a tool to improve outcomes, and therefore does not include interventions which only record or monitor behavior change.  Interventions designed for use solely by mobile telephone devices, including applications or text messages, will not be included.
Comparison	Any control group, including pre- and post-design groups.
Outcome	Primary outcomes of relevance are clinical changes to both substance misuse and mental health outcomes. Secondary outcomes may include changes in other areas of well-being and social functioning if reported.
Study type	Quantitative experimental or intervention papers, including randomized controlled trials, single group pre- and post-measures, longitudinal, and cross-sectional studies.  Qualitative studies will be excluded, however mixed methods papers will be considered if they satisfy other eligibility criteria.

*Note.* PICOS = Population, Intervention, Comparison, Outcome and Study type, relating to the search strategy employed (Centre for Reviews and Dissemination, 2009).

Table 2.  
Summary of the Studies Included in the Systematic Review

Study	Population and sample size	Intervention	Comparison	Outcomes and measurement time	Statistical method and findings
Acosta et al., 2017	Veterans with co-morbid alcohol/drug difficulties and PTSD. 81 assigned to online intervention, 81 assigned to comparison.	Treatment as usual plus 'Thinking Forward' – Cognitive behavioral therapy (CBT)-based program to reduce drinking and manage and reduce symptoms of PTSD. 24 modules over 12 weeks.	Treatment as usual – primary care services including medical, behavioral health, pharmacy, weight management and social work services	Timeline follow-back interview (alcohol use), PTSD checklist, World Health Organization – Quality of Life (WHO-QoL). Baseline, 4 weeks, 8 weeks, 12 weeks, 1-month follow-up, 3-month follow-up.	Generalized mixed-effects piecewise regression model  In treatment (12 week) outcomes were reported. Intervention resulted in greater reductions in heavy drinking days at 12 weeks compared to treatment as usual ( $p < .05$ , effect size calculated: $r < 0.01$ ).  The paper reported no significant differences for PTSD in treatment (effect size calculated: $r = 0.01$ ) or quality of life in treatment (effect size calculated: physical $r = 0.10$ ; psychological $r = 0.05$ ; social $r = 0.06$ ; environmental $r = 0.04$ ).
Batterham et al., 2018	Adults residing in Australia. 62 assigned to static computer intervention, 66 to tailored computer intervention, and 66 to psychoeducation control. 12.37% male.	FitMindKit – An 18 module Motivational Interviewing and mindfulness-based program to target mental health difficulties, suicidal ideation and substance use.	HealthWatch - information on general areas of health not related to mental health	Patient Health Questionnaire (PHQ-9), General Anxiety Disorder (GAD-7), panic disorder screener, social phobia screener, Alcohol Use Disorder Identification Test (AUDIT), Drug Use Disorders Identification Test (DUDIT), suicidal attribution ideation attributes. Baseline, post-intervention, 3-month follow-up.	ANOVA  Within groups, participants in all conditions significantly reduced alcohol use disorders and combined mental health outcome measures (both $p = .017$ ), respectively improvements were observed for anxiety ( $p < .001$ ) and social phobia ( $p = .016$ ). No differences were observed between groups.
Billings et al., 2008	309 employees from technology company in Mid-Atlantic region. Unclear allocation.	'Stress and Mood Management' CBT-based program. Simultaneous access to modules.	Waitlist	Knowledge questionnaire (stress, anxiety and mood disorders), attitude towards help, mood management self-efficacy, symptoms of distress scale, positive and negative affect	ANCOVA  At follow-up, the CBI led to significant improvements compared to waitlist treatment for knowledge ( $p = .041$ , effect size calculated $r = 0.13$ ), attitude ( $p = .023$ , effect size calculated $r = 0.16$ ), distress ( $p = .023$ , effect size

				<p>schedule, center for epidemiological studies depression scale, Beck Anxiety Inventory, stress relief strategies questionnaire, binge drinking stages of change, work productivity-work limitations questionnaire.</p> <p>Baseline and 3-month follow-up.</p>	<p>calculated <math>r = 0.06</math>), and binge drinking (<math>p = .006</math>, effect size calculated <math>r = 0.11</math>).</p> <p>Non-significant comparisons were found for self-efficacy (<math>p = .072</math>, effect size calculated <math>r = 0.12</math>), positive mood (<math>p = .454</math>, effect size calculated <math>r = 0.02</math>), negative mood (<math>p = .738</math>, effect size calculated <math>r = 0.02</math>), depression (<math>p = .476</math>, effect size calculated <math>r &lt; 0.01</math>), anxiety (<math>p = .799</math>, effect size calculated <math>r = 0.02</math>), coping (<math>p = .083</math>, effect size calculated <math>r = 0.09</math>), and work productivity (time and scheduling: <math>p = .051</math>, effect size calculated <math>r = 0.10</math>; physical demands: <math>p = .680</math>, effect size calculated <math>r = 0.04</math>; mental demands: <math>p = .118</math>, effect size calculated <math>r = 0.07</math>; output demands: <math>p = .076</math>, effect size calculated <math>r = 0.08</math>).</p>
<p>Boss et al., 2018</p>	<p>Alcohol intervention for employees. 146 allocated to unguided intervention, 144 to guided intervention supported by therapists online, and 144 to a waiting list control. 41% male, average age 47 years.</p>	<p>Motivational Interviewing-based program, including normative feedback, goal setting and emotional regulation.</p>	<p>Waitlist</p>	<p>Timeline follow-back (average drinks/week), weekly alcohol consumption (units), depression, anxiety and stress scale, irritation scale, effort reward imbalance. Baseline, post-intervention, 6-month follow-up.</p>	<p>Multiple regression</p> <p>Within group reduction of weekly alcohol consumption from baseline to follow-up for unguided (<math>r = 0.22</math>) and guided support (<math>r = 0.19</math>), combined intervention (<math>r = 0.21</math>) and control (<math>r = 0.19</math>). Also for stress (unguided <math>r = 0.13</math>, guided <math>r = 0.22</math>, combined <math>r = 0.19</math>), depression (unguided <math>r = 0.07</math>, guided <math>r = 0.15</math>, combined <math>r = 0.11</math>), and anxiety (unguided <math>r = 0.09</math>, guided <math>r = 0.21</math>, combined <math>r = 0.15</math>).</p> <p>Combined intervention groups led to significant improvements between baseline and follow-up on alcohol consumption, depression, stress, anxiety, emotional irritation, and cognitive irritation, compared against control (all <math>p &lt; .001</math>).</p>
<p>Brief et al., 2013</p>	<p>Veterans drinking above safer drinking guidelines. 404 allocated to intervention, 196 allocated to comparison.</p>	<p>'VetChange' CBT-based program, including motivational enhancement, self-</p>	<p>Delayed intervention</p>	<p>Timeline follow-back (drinks/day, average drinks/week, percentage of heavy drinking days), PTSD checklist. Baseline and post-intervention</p>	<p>Linear regression</p> <p>Intervention led to significant improvements within groups for drinks per day (<math>p &lt; .001</math>), average drinks per week (<math>p &lt; .001</math>), percentage of heavy drinking days (<math>p &lt; .001</math>), and PTSD (<math>p &lt; .001</math>).</p>

	86.3% male, average age 32 years.	control training, and support network.		(repeated baseline for comparison).	The intervention also led to significant improvements compared to the delayed intervention on drinks per day ( $p < .001$ ), average drinks per week ( $p < .001$ ), percentage of heavy drinking days ( $p < .001$ ), and PTSD ( $p = .009$ ).
Cucciare et al., 2013, 2013 [MERGED]	Veterans presenting to primary care with alcohol as presenting problem. 89 allocated to intervention (82 completed at three months, 75 completed at six months), and 78 allocated to comparison (68 completed at three months, 67 completed at six months). 88% male, average age 59 years.	Web-delivered brief alcohol intervention – assessment and normative feedback.	Treatment as usual – recommended drinking limits and information on health risks	Short form 12 health survey, PTSD checklist (military version), PHQ-9, coping response inventory, timeline follow-back (drinks/day, average drinks/week, % heavy drinking days), short inventory of problems. Baseline, 3-month follow-up, 6-month follow-up.	Between samples <i>t</i> -test and between person parameter estimates  Comparisons within groups demonstrated significant improvements in the intervention group from baseline to 3-months follow-up for quality of life ( $p < .05$ , effect size calculated $r = 0.14$ ), and depression ( $p < .05$ , effect size calculated $r = 0.11$ ), and from baseline to follow-up at six months for PTSD ( $p < .05$ , effect size calculated $r = 0.06$ ), percentage of heavy drinking days ( $p < .05$ , effect size calculated $r = 0.18$ ), mean drinking days ( $p < .05$ , effect size calculated $r = 0.11$ ), total number of drinking days ( $p < .05$ , effect size calculated $r = 0.22$ ), and severity of problems ( $p < .05$ , effect size calculated $r = 0.13$ ).
Deady et al., 2016	Australian residents aged 18-25. 60 assigned to intervention, 44 assigned to control. 60% female, average age 21.74 years.	'DEAL Project' – CBT and motivational interviewing (MI) based online program.	'Healthwatch' – online attention control program on health concerns	PHQ-9, total alcohol consumption (TOT-AL). Baseline, post-treatment, 3-month follow-up, 6-month follow-up.	Generalized estimating equations  Within groups comparisons demonstrate significant improvements in the intervention group from baseline to 6-months follow-up for depression ( $p < .001$ , $r = 0.59$ ), drinks per week ( $p = .020$ , $r = 0.19$ ), and drinking days per week ( $p = .030$ , $r = 0.21$ ).  The intervention led to significant improvements in outcomes compared to 'Healthwatch' at post-intervention only for depression ( $p = .020$ , $r = 0.33$ ), drinks per week ( $p = .05$ ), and drinking days per week ( $p = .02$ , $r = 0.35$ ). No significant differences were found between the groups at 3- or 6-month follow-up for any of the measures.

Elison et al., 2015, 2015, 2017 [MERGED]	Individuals treated for SUD in the UK. Total 2311. 55% male, average age 42.2 years.	Breaking Free Online – CBT-based online program.	-	Recovery progression measure (RPM), WHO-QoL (five items), PHQ-4, GAD-7, Severity of Dependence Scale (SDS). Baseline and post-treatment.	ANOVA  The program demonstrated significant improvements to recovery progression ( $p < .001$ , $r = 0.35$ ), quality of life ( $p < .001$ , $r = 0.33$ ), depression ( $p < .001$ , $r = 0.45$ ), anxiety for alcohol ( $p < .001$ , $r = 0.64$ ), non-opiate/crack ( $p < .001$ , $r = 0.71$ ), and opiate/crack users ( $p = .014$ , $r = 0.65$ ), and severity of dependence for both drugs ( $p < .001$ , $r = 0.60$ ), and alcohol ( $p < .001$ , $r = 0.51$ ).
Elison et al., 2014	Service users seeking treatment for dual diagnosis at a service in Manchester, UK. 74 allocated, data reported on only those with complete data ( $N = 47$ ). 62% male, age not reported.	Breaking Free Online – CBT-based online program.	-	Work and Social Adjustment Scale (WSAS), PHQ-9, GAD-7, AUDIT, DUDIT, Improving Access to Psychological Therapies phobia scale. Baseline and post-treatment.	Wilcoxon signed-ranks test  The program demonstrated significant improvements to work and social adjustment ( $p < .001$ , $r = 0.68$ ), depression ( $p < .001$ , $r = 0.59$ ), anxiety ( $p < .001$ , $r = 0.63$ ), alcohol use disorders ( $p = .002$ , $r = 0.45$ ), drug use disorders ( $p = .028$ , $r = 0.32$ ), and social anxiety ( $p = .027$ , $r = 0.32$ ).
Geisner et al., 2015	339 students from one university in US. 85 each to intervention, control, and mood condition, 84 allocated to alcohol only. 62.4% female, average age 20.14 years.	Integrated alcohol and mood intervention – psychoeducation, social norms, coping strategies and feedback.	Assessment only control, alcohol only intervention, mood only intervention	Beck depression Inventory (BDI), daily drinking questionnaire, Rutgers alcohol problem index. Baseline, 1-month follow-up	ANOVA  Non-significant effects were found for the main effects of the integrated CBI intervention against assessment only control at follow-up for depression ( $p = .780$ , effect size calculated $r = 0.05$ ), daily drinking ( $p = .540$ , effect size calculated $r < 0.01$ ), and alcohol problems ( $p = .280$ , effect size calculated $r = 0.09$ ).
Johansson et al., 2017	Those accessing a Swedish alcohol self-help site. 3898 received intervention, 48% male sample, average age of 41.88 years.	CBT based alcohol reduction intervention.	-	Timeline follow-back, AUDIT, DUDIT, Hospital Anxiety and Depression Scale (HADS), WHO-QoL, European Quality of Life (EuroQol), readiness to change questionnaire. Baseline, 10-week follow-up	Logistic regression  Compared to baseline, at follow-up participants had improved on measures of alcohol use disorders ( $p < .001$ , $r = 0.44$ ), anxiety ( $p < .001$ , $r = 0.33$ ), depression ( $p < .001$ , $r = 0.30$ ), quality of life ( $p < .001$ , $r = 0.17$ ), and readiness to change ( $p < .001$ , $r = 0.11$ ).

Kay-Lambkin et al., 2009	Those with concurrent depressive symptoms and alcohol/other drug use. 32 allocated to intervention, 35 to therapist control, and 30 to brief advice. 54% female, average age 35.37 years.	'SHADE'- CBT based online program.	Therapist delivered CBT (face-to-face), brief advice	BDI, OTI, Structured Clinical Interview for DSM – substance misuse (SCID). Baseline, post treatment (3 months following baseline), 6-month follow-up, 12-month follow-up.	ANOVA  For the CBI, significant improvements were found within groups for depression only ( $p < .001$ , effect size calculated $r = 0.61$ ).  At 12-month follow-up, between group analyses demonstrated that the therapist group lead to greater improvements to depression than the online intervention ( $p < .001$ , effect size calculated $r = 0.18$ ).  Therapist+online intervention groups compared against brief advice at 12-month follow-up led to greater improvements to cannabis use ( $p < .010$ , effect size calculated $r = 0.24$ ), and substance abuse and dependence ( $p < .010$ , effect size calculated $r = 0.34$ ).
Kay-Lambkin et al., 2011, 2012	Those with concurrent depressive symptoms and alcohol/cannabis use. 97 allocated to online intervention, 89 allocated to person centered therapy control and 88 allocated to therapist only control. 57% men, average age 40 years.	'SHADE' – CBT and MI based online intervention.	Person centered therapy and supportive counselling, therapist only support (CBT and MI face-to-face)	BDI, Opiate Treatment Index (OTI), Agnew Relationship Measure (therapeutic alliance). Baseline, post treatment (3-month following baseline).	ANOVA using planned orthogonal contrasts  At 3-month follow-up, therapist+online intervention significantly reduced depression and alcohol use compared to person centered therapy, respectively ( $p = .024$ , effect size calculated $r = 0.14$ ) and ( $p = .004$ , effect size calculated $r = 0.26$ ).  Online intervention significantly reduced alcohol use compared to therapist at 3-months follow-up ( $p = .006$ , effect size calculated $r = 0.27$ ). Although there were no significant differences between groups for cannabis use ( $p = .347$ , $r = 0.02$ ).
Levin et al., 2017	Students from one US university. 40 assigned to program 39 to waiting list. 66% female, average age 20.51.	Acceptance and commitment therapy-based online program.	Waiting list	Counseling Center Assessment of Psychological Symptoms (CCAPS), mental health continuum, acceptance and action questionnaire, Philadelphia mindfulness scale, cognitive	Mixed model repeated measures  For the intervention, significant improvements were found within groups for distress ( $p = .005$ , $r = 0.25$ ), depression ( $p = .024$ , $r = 0.20$ ), general anxiety ( $p = .031$ , $r = 0.19$ ), social anxiety ( $p < .001$ , $r = 0.33$ ), academic

				fusion questionnaire, valuing questionnaire. Pre and post-intervention.	<p>concerns (<math>p = .014</math>, <math>r = 0.22</math>), mental health (<math>p = .001</math>, <math>r = 0.29</math>), acceptance (<math>p = .001</math>, <math>r = 0.30</math>), and obstruction (<math>p &lt; .001</math>, <math>r = 0.38</math>).</p> <p>Between group analyses demonstrated greater improvements for the intervention against the waitlist control for distress (<math>p = .013</math>, <math>r = 0.31</math>), social anxiety (<math>p = .004</math>, <math>r = 0.36</math>), academic concerns (<math>p = .020</math>, <math>r = 0.30</math>), mental health (<math>p = .027</math>, <math>r = 0.28</math>), acceptance (<math>p = .038</math>, <math>r = 0.26</math>), and obstruction (<math>p = .012</math>, <math>r = 0.31</math>).</p> <p>The paper reported no significant interactions for acceptance and action, awareness, cognitive fusion, and progress (<math>p &gt; .100</math>).</p>
Lewis et al., 2017	Sufferers of PTSD presenting to traumatic stress and mental health services in UK. 21 allocated to treatment, 21 allocated to waitlist control. Group 59.5% female, average age 39 years.	CBT-based online intervention incorporating psychoeducation, relaxation, cognitive techniques, behavioral activation and relapse prevention.	Waitlist	Clinician administered PTSD assessment, PTSD checklist, BDI, Beck Anxiety Inventory (BAI), AUDIT, social support questionnaire, disability scale. Baseline, post-intervention, 1-month follow-up, 3-month follow-up.	<p>Regression</p> <p>Significant differences between intervention and control group were reported for PTSD at post-intervention (MD = 18.60 [CI: -24.65, -13.41]), and 1-month follow-up (MD = 17.16 [CI: -23.78, -10.68]), but this a not maintained at 3-month follow-up after the waitlist group had finished their intervention (MD = 0.97 [CI: -7.84, 8.44]).</p> <p>Significant differences between intervention and control group were reported at post-intervention for depression (MD = 10.83 [CI: -16.66, -5.14]), anxiety (MD = 13.40 [CI: -19.91, -6.35]) and functional impairment (MD = 9.36 [CI: -13.56, -3.93]).</p>
Linke et al., 2007	General population (mostly UK based) identified as risky drinkers. 1654 completed intervention. 51.1% female, average age 37.44 years.	'Down your drink' – CBT and motivational enhancement based online intervention.	-	Substance Abuse and Dependency Questionnaire (SADQ), Alcohol Problems Questionnaire (APQ), CORE-Outcome Measure (CORE-OM). Weeks 1, 2, 3, 4, 5, 6.	<p>Paired <i>t</i>-tests</p> <p>The intervention demonstrated improvements from baseline-week 6 on alcohol dependency (men: <math>p &lt; .001</math>, <math>r = 0.37</math>; women: <math>p &lt; .001</math>, <math>r = 0.36</math>), alcohol problems (men: <math>p &lt; .001</math>, <math>r = 0.40</math>; women: <math>p &lt; .001</math>, <math>r = 0.41</math>), functioning (men: <math>p &lt; .001</math>, <math>r = 0.30</math>; women: <math>p &lt; .001</math>, <math>r = 0.33</math>), problems (men: <math>p &lt; .001</math>, <math>r = 0.34</math>; women: <math>p &lt; .001</math>,</p>



					$r = 0.39$ ), well-being (men: $p < .001$ , $r = 0.29$ ; women: $p < .001$ , $r = 0.36$ ), and risk (men: $p < .001$ , $r = 0.21$ ; women: $p < .001$ , $r = 0.20$ ).
Musiat et al., 2014	Students from 2 London Universities. 519 allocated to intervention, 528 allocated to control. Separated into students at high or low risk of developing a mental health problem. 70.5% female, median age of 21 years (range 19-57).	'PLUS' - CBT and trait-based transdiagnostic online intervention.	Three online modules addressing relevant topics of student life, namely how to find accommodation, how to live on a tight budget, and study skills	PHQ, GAD, AUDIT, Eating disorders diagnostics scale, frost multidimensional perfectionism scale, Rosenberg self-esteem scale. Baseline, 12 weeks.	Logistic regression  Within group analyses for the intervention demonstrate that students who were at high risk of developing a mental health difficulty significantly improved on depression (MD = 3.58 [CI: 1.98, 5.19], $p < .001$ ), anxiety (MD = 2.87 [CI: 1.31, 4.43], $p < .001$ ), concern over mistakes (MD = 2.42 [CI: 0.60, 4.25], $p = .005$ ), and self-esteem (MD = -1.44 [CI: -2.74, -0.14], $p = .024$ ). Students who were at low risk of developing a mental health difficulty were more likely to reduce their alcohol use (MD = 0.88 [CI: 0.47, 1.30], $p < .001$ ).  Between group analyses demonstrated greater improvements for the intervention against psychoeducation modules for depression ( $p = .002$ ), anxiety ( $p = .001$ ), concern over mistakes ( $p = .029$ ), and personal standards ( $p = .046$ ).  No significant between group differences were found for alcohol use ( $p = .277$ ), eating disorders ( $p = .761$ ), doubts over actions ( $p = .068$ ) or self-esteem ( $p = .082$ ).  Effect sizes could not be calculated from standard error reported.
Postel et al., 2010, 2015	Problem drinkers from general population of Dutch-speakers. 78 allocated to intervention, 78 allocated to waiting list control. 12 control participants did not start	'Alcohol de baas' – CBT and MI-based website intervention.	Waiting list and psychoeducation (2010 study), and pre-post intervention (2015 study)	Weekly alcohol consumption, depression anxiety stress scale-21, general health questionnaire, Maudsley Addiction Profile health symptom scale, Euro-QoL-5, Visual Analogue Scale. Baseline, 3-, 6-, and 9-month follow-up.	<i>T</i> -tests  For the CBI, significant improvements were found within groups from baseline to 9 months for alcohol consumption ( $p < .001$ , $r = 0.53$ ), depression, anxiety, and stress ( $p < .001$ , $r = 0.46$ ), general health ( $p < .001$ , $r = 0.46$ ), addiction ( $p < .001$ , $r = 0.38$ ), and quality of life ( $p < .001$ , $r = 0.30$ ).



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	intervention after waiting period, so merged data at follow-up from 144 participants. 58% female, average age 45.8 years old.				Between group analyses demonstrated greater improvements for the intervention compared to waiting list control at 3-month follow-up for alcohol consumption ( $p < .001$ , effect size calculated $r = 0.52$ ), depression, anxiety, and stress ( $p < .001$ , effect size calculated $r = 0.37$ ), general health ( $p < .005$ , effect size calculated $r = 0.35$ ), addiction ( $p < .001$ , effect size calculated $r = 0.43$ ), and quality of life ( $p = .080$ , effect size calculated $r = 0.14$ ).
Rupp et al., 2012	Participants from inpatient alcohol dependence unit in Austria. 20 allocated to intervention, 21 allocated to control (4 dropped out at follow-up). 36.6% female, average age 45 years.	Cognitive remediation exercises.	Treatment as usual at inpatient unit, including psychiatric management (cognitive behavioral therapy, group therapy, relapse prevention, self-control, relaxation) and occupational therapy	BDI, symptom checklist-90, obsessive-compulsive drinking scale. Pre and post-treatment	MANOVA  For the intervention, significant improvements were found within groups for depression ( $p < .05$ , effect size calculated $r = 0.42$ ), distress ( $p < .05$ , effect size calculated $r = 0.61$ ), intensity of symptoms ( $p < .05$ , effect size calculated $r = 0.30$ ), number of symptoms ( $p < .05$ , effect size calculated $r = 0.61$ ), and obsessive drinking ( $p < .05$ , effect size calculated $r = 0.45$ ).  Between group analyses demonstrated greater improvements for the intervention compared against treatment as usual for distress ( $p = .017$ , effect size calculated $r = 0.14$ ), number of symptoms ( $p = .040$ , effect size calculated $r = 0.12$ ), and compulsive drinking ( $p = .050$ , effect size calculated $r = 0.19$ ).  The paper reported no significant changes for depression, intensity of symptoms and obsessive drinking.
Schaub et al., 2012	Cocaine users who wanted to stop. 96 allocated to intervention, 100 allocated to control. 21.9% female, average age 34.2 years.	'Snow Control'-CBT and MI based online program.	Psychoeducation	SDS, cocaine craving questionnaire, BDI, Addiction Severity Index (ASI). Baseline, 4 weeks, 6 weeks and 6-month follow-up	Generalized estimating equation  Non-significant differences were found between groups at 6-month follow-up for severity of substance dependence ( $p = .750$ , effect size calculated $r = 0.05$ ), cocaine craving ( $p = .900$ , effect size calculated $r = 0.05$ ), depression ( $p = .570$ , effect size calculated $r = 0.03$ ), and addiction

					severity (cannabis: $p = .860$ ; cocaine: $p = .720$ ; alcohol: $p = .950$ ; binge drinking: $p = .730$ ).
Schaub et al., 2015	Problematic cannabis users in Switzerland. 114 allocated to program + counseling, 101 allocated to program, 93 allocated to waiting list. 75.3% male, average age of 29.8 years old.	'Can reduce' – CBT and MI online program in addition to face-to-face counseling.	Online intervention only or waiting list control	Cannabis use/week, cannabis use disorders identification test, SDS, Mental Health Inventory (MHI-5). Baseline, 3-month follow-up.	ANOVA  CBI+counseling led to greater improvements compared to waiting list control on frequency of cannabis use ( $p = .030$ , $r = 0.07$ ), and quantity of cannabis use ( $p = .060$ , $r = 0.03$ ).  CBI+counseling led to greater improvements compared to CBI alone on frequency of cannabis use ( $p = .020$ , $r = 0.12$ ).  No significant differences were found for outcomes of cannabis use disorders (CBI+counseling compared to CBI alone: $p = .410$ , $r = 0.04$ ; compared to waiting list: $p = .850$ , $r = 0.03$ ), severity of dependence (CBI+counseling compared to CBI alone: $p = .900$ , $r = 0.01$ ; compared to waiting list: $p = .960$ , $r = 0.03$ ), or mental health (CBI+counseling compared to CBI alone: $p = .480$ , $r = 0.04$ ; compared to waiting list: $p = .780$ , $r < 0.01$ ).
Sundstrom et al., 2016	Those accessing a Swedish alcohol self-help site. 40 allocated to online intervention only, 20 to intervention+text support, 20 to intervention+choice of counselor text-based support. 60% were women and the mean age was 42.3 years, ranging from 18 to 74.	Online self-help intervention to reduce alcohol consumption (self-help only).	Self-help intervention with counselor support via secure text message. OR Online self-help program with choice of counselor support delivered via either i) asynchronous secure text messaging, or ii) synchronous chat messaging (guidance: choice)	Timeline follow-back, AUDIT, AUDIT-C, HADS, Euro-QoL-5, WHO-QoL. Baseline and one week post-treatment.	ANOVA and <i>t</i> -tests  Significant decreases in alcohol consumption were reported in the combined guidance groups vs online self-help ( $p = .001$ , $r = 0.36$ ). Similarly, significant decreases in hazardous alcohol consumption were reported in the combined guidance groups vs online self-help ( $p = .003$ , $r = 0.32$ ).  No significant differences were found for anxiety ( $p = .887$ , $r = 0.01$ ), depression ( $p = .364$ , $r = 0.10$ ), or quality of life ( $p = .947$ , $r = 0.00$ ).

Sundstrom et al., 2017	High-intensity therapist guided ICBT program for people with a diagnosed alcohol use disorder. 13 participants received intervention. 69% female. Average age 49.5 years, range 24-71.	Internet CBT program with therapist support.	None	Timeline follow-back, AUDIT, alcohol self-efficacy scale, Penn alcohol craving scale, Montgomery-Asberg depression rating scale, WHO-QoL-BREF. Baseline, post-intervention, 3-month follow-up.	Generalized estimating equations  Significant improvements were reported for the intervention group from baseline to three month follow-up for alcohol use ( $p < .001$ , $r = 0.51$ ), hazardous alcohol consumption ( $p < .001$ , $r = 0.67$ ), alcohol self-efficacy ( $p < .001$ , $r = 0.62$ ), alcohol craving ( $p < .001$ , $r = 0.55$ ), depression ( $p < .01$ , $r = 0.35$ ), physical quality of life ( $p < .01$ , $r = 0.38$ ), psychological quality of life ( $p < .01$ , $r = 0.36$ ), social quality of life ( $p < .05$ , $r = 0.31$ ), and environmental quality of life ( $p < .05$ , $r = 0.32$ ).
Tait et al., 2015	Australian resident with reported use of amphetamine-type stimulant. 81 allocated to intervention, 79 allocated to waitlist control. 75.6% male, average age 22.4 years old.	'Breakingtheice' – CBT and MI-based online program.	Waitlist control	Alcohol, smoking and substance involvement screening test-amphetamine use (ASSIST), help-seeking intentions, actual help-seeking, Kessler psychological distress scale, ASSIST - poly-drug use, Euro-QoL, days out of role. Baseline, 3-month and 6-month follow-up.	Logistic regression.  Significant improvements were found for the intervention when compared against waitlist control for help seeking intentions ( $p < .001$ , $r = 0.15$ ), actual help seeking ( $p = .020$ , $r = 0.00$ ), and days out of work role ( $p < .001$ , $r = 0.01$ ) at 6-month follow-up.  No significant differences were found for amphetamine use ( $p = .650$ , $r = 0.05$ ), distress ( $p = .640$ , $r = 0.05$ ), poly-drug use ( $p = .680$ , $r = 0.02$ ), or quality of life ( $p = .690$ , $r = 0.09$ ).
Tiburcio et al., 2018	Individuals attending treatment for substance use difficulties. 27 were allocated to receive the online program with help from a counselor, 27 received a self-help guide and treatment as usual, and 29 received treatment as usual. 87.8% of participants were male.	8-week long intervention based on the Transtheoretical Model of change, and drawing upon strategies from CBT.	Self-help+ treatment as usual Treatment as usual – care as would be given in the treatment center, typically face-to-face CBT sessions	Timeline follow-back, drug abuse screening test (severity of substance use difficulty), PHQ-9, readiness to change. Baseline, post-intervention, 1-month follow-up.	MANOVA/ANOVA  Significant within group differences were found for substance use frequency, severity of use and depression (all $p < .001$ ).  This paper reported no significant differences between the treatment conditions across the measures reported above.

1 2 3 4 5 6 7 8 9 10 11 12	Tossmann et al., 2011	Anyone wanting to reduce/stop cannabis use. 863 allocated to intervention, 360 received intervention, 100 analyzed. 429 allocated to waitlist, 106 analyzed. 70.5% male, average age of 24.7 years.	Self-regulation and self-control online program.	Waitlist control	Frequency of use/month, quantity of use/month, drug taking confidence questionnaire, state trait anxiety inventory, general depression scale, satisfaction with life scale. Baseline, 3-month follow-up.	ANCOVA  Significant improvements were found for the intervention when compared against waitlist control for frequency of substance use ( $p < .001$ , $r = 0.44$ ), quantity of substance use ( $p < .001$ , $r = 0.35$ ), drug taking confidence ( $p < .001$ , $r = 0.29$ ), trait anxiety ( $p < .001$ , $r = 0.22$ ), depression ( $p = .021$ , $r = 0.13$ ), and satisfaction with life ( $p = .007$ , $r = 0.14$ ).
13 14 15 16 17 18 19 20 21 22	Wilson et al., 2015	Deaf persons seeking treatment for substance misuse at residential services. 95 participants, 8 attending service in Ohio where intervention delivers, 87 from other locations receiving control. 60% men.	Online substance use dependence program – techniques unclear.	Treatment as usual at residential service with trained counselors	Substance abuse screener, ASI, satisfaction with life scale, Rosenberg self-esteem scale, BDI. Baseline, 6-month follow-up.	The paper reported no significant differences between intervention sites for substance abuse, addiction severity, satisfaction with life, self-esteem, or depression.
23 24 25 26 27 28 29 30 31 32 33 34 35 36	Wolitzky-Taylor et al., 2018	Service users seeking support at a substance use clinic in the US. 56 allocated to receive the program and usual care, 41 allocated to receive just usual care. 57.3% male with an average age of 35.89 years.	CBT-based intervention over six session, with support from therapist.	Treatment as usual at clinic – face-to-face support with therapist	Brief symptom inventory (anxiety), Timeline follow back Baseline, post-treatment, 6-month follow-up.	Anxiety significantly decreased from baseline to post-treatment for the CBI group ( $p < .001$ ), and anxiety significantly reduced within this time for those completing the intervention compared against control ( $p < .05$ ). No effects were reported between post-treatment and follow-up.  Drinking days significantly decreased from baseline to post-treatment for the intervention group ( $p < .05$ ), and drinking significantly reduced within this time for those completing the intervention compared against control ( $p < .01$ ). There was no significant within group effect for drug use ( $p = .99$ ), and drug use significantly increased between baseline and post-treatment ( $p < .05$ ).

Note. CBI = computer-based intervention; CBT = cognitive behavioral therapy; MD = mean difference; MI = motivational interviewing; PTSD = post-traumatic Stress disorder; SUD = substance use dependence. APQ = Alcohol Problems Questionnaire; ASI = Addiction Severity Index; ASSIST = Alcohol, Smoking and Substance Involvement Screening Test; AUDIT = Alcohol Use Disorder Identification Test; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; CCAPS = Counseling Center Assessment of

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Psychological Symptoms; CORE-OM = Clinical Outcomes in Routine Evaluation – Outcome Measure; DUDIT = Drug Use Disorder Identification Test; EuroQol = European Quality of Life; GAD = Genal Anxiety Disorder; HADS = Hospital Anxiety and Depression Scale; OTI = Opiate Treatment Index; PHQ = Patient Health Questionnaire; RPM = Recovery Progression Measure; SADQ = Substance Abuse and Dependency Questionnaire; SCID = Structured Clinical Interview for DSM; SDS = Severity of Dependence Scale; TOT-AL = Total Alcohol Consumption; WHO-QoL = World Health Organization Quality of Life; WHO-QoL-BREF = World Health Organization Quality of Life – brief version; WSAS = Work and Social Adjustment Scale.

For Peer Review Only

Table 3.  
Quality Assessment

	Quality Assessment Ratings						
	Selection bias	Study design	Confounders	Blinding	Data collection method	Withdrawals and drop-out	Global rating
Acosta et al., 2017	2	1	1	3	1	2	Moderate
Batterham et al., 2018	3	1	3	3	1	3	Weak
Billings et al., 2008	3	1	1	3	1	3	Weak
Boss et al., 2018	3	1	1	3	1	3	Weak
Brief et al., 2013	3	1	1	3	1	3	Weak
Cucciare et al., 2013, 2013 MERGED	2	1	1	3	1	1	Moderate
Deady et al., 2016	3	1	1	2	1	3	Weak
Elison et al., 2014	3	2	1	3	1	2	Weak
Elison et al., 2015, 2015, 2017 MERGED	3	2	1	3	1	3	Weak
Geisner et al., 2013	3	1	1	3	1	1	Weak
Johansson et al., 2017	3	2	1	3	1	3	Weak
Kay-Lambkin et al., 2009	3	1	1	2	1	2	Moderate

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Kay-Lambkin et al., 2011, 2012 MERGED	3	1	3	1	1	3	Weak
Levin et al., 2017	3	1	1	3	1	2	Weak
Lewis et al., 2017	2	1	3	2	1	2	Moderate
Linke et al., 2007	3	2	3	3	1	3	Weak
Musiat et al., 2014	3	1	1	2	1	3	Weak
Postel et al 2010, 2015 MERGED	3	1	3	3	1	2	Weak
Rupp et al., 2012	3	1	1	3	1	1	Weak
Schaub et al., 2012	3	1	1	3	1	3	Weak
Schaub et al., 2015	3	1	3	3	1	3	Weak
Sundstrom et al., 2016	3	1	1	3	1	3	Weak
Sundstrom et al., 2017	3	2	1	3	1	1	Weak
Tait et al., 2015	3	1	1	3	1	3	Weak
Tiburcio et al., 2018	2	1	1	3	1	2	Moderate
Tossman et al., 2011	3	1	1	3	1	3	Weak
Wilson et al., 2015	3	2	3	3	1	3	Weak
Wolitzky-Taylor et al., 2018	2	1	1	2	1	3	Moderate

Note. 1 = strong; 2 = moderate; 3 = weak.

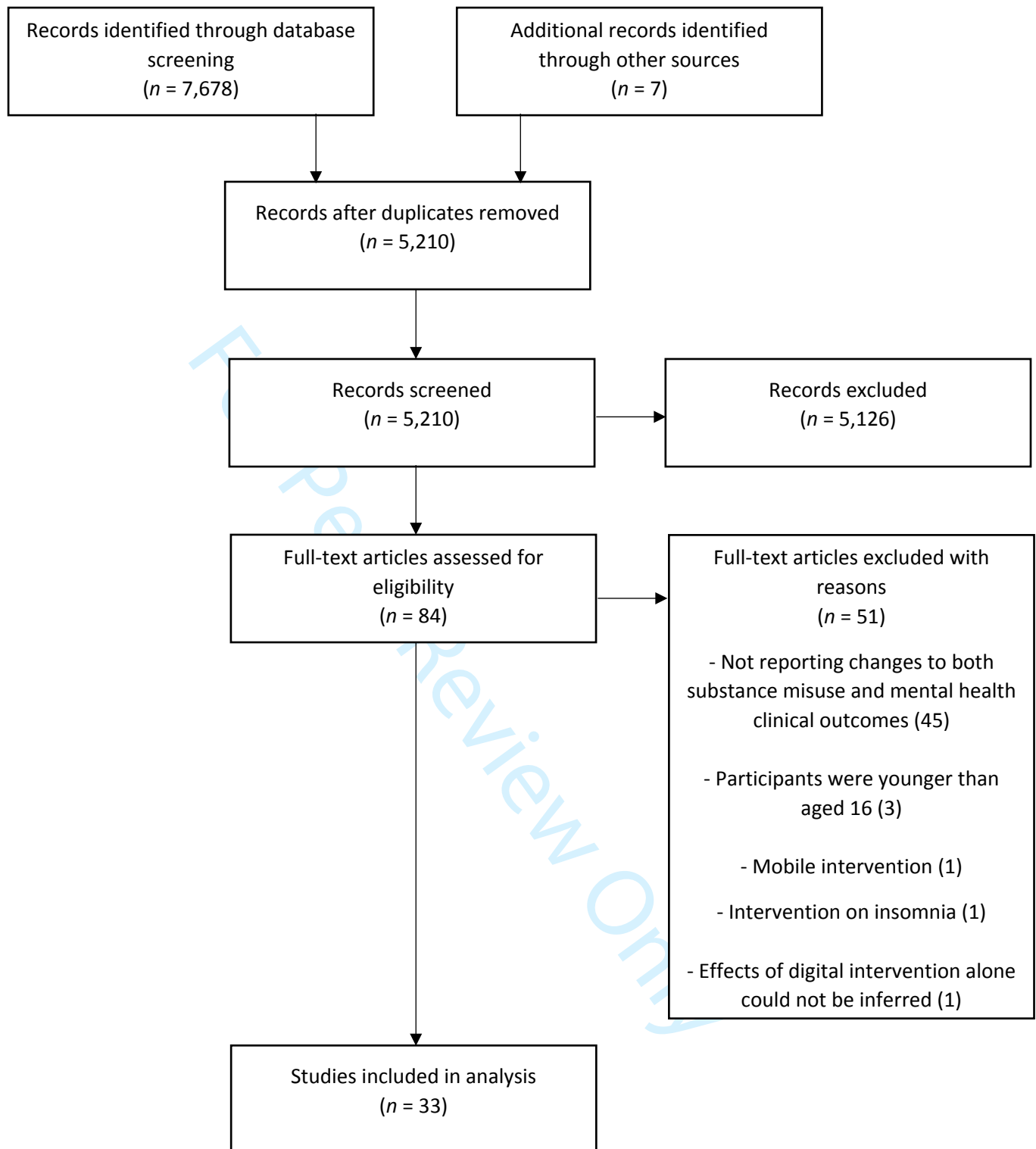


Figure 1.

Results of search



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Table S1  
*Papers Where Full Text was Screened and Decision*

First author	Date of publication	Title	Decision (with reasons for exclusion)
Postel, M.	2015	A 9-month follow-up of a 3-month web-based alcohol treatment program using intensive asynchronous therapeutic support	MERGE 1 Shares data with Postel et al., 2010
Tossmann, H.	2011	A controlled trial of an internet-based intervention program for cannabis users	INCLUDE
Pedersen, E.	2017	A randomized controlled trial of a web-based, personalized normative feedback alcohol intervention for young-adult veterans	EXCLUDE Only reports changes to alcohol outcomes
Cucciare, M.	2013	A randomized controlled trial of a web-delivered brief alcohol intervention in Veterans Affairs primary care	MERGE 2 Shares data with Cucciare et al., 2013
Tzilos, G.	2011	A randomized phase I trial of a brief computer-delivered intervention for alcohol use during pregnancy	EXCLUDE Only reports changes to alcohol outcomes
Donovan, E.	2012	A randomized, controlled trial to test the efficacy of an online, parent-based intervention for reducing the risks associated with college-student alcohol use	EXCLUDE Only reports changes to alcohol outcomes
Billings, D.	2008	A web-based approach to managing stress and mood disorders in the workforce	INCLUDE
Schaub, M.	2015	A web-based self-help intervention with and without chat counselling to reduce cannabis use in problematic cannabis users: Three-arm randomized controlled trial	INCLUDE
Deady, M.	2016	An online intervention for co-occurring depression and problematic alcohol use in young people: Primary outcomes from a randomized controlled trial	INCLUDE
Elison, S.	2015	An outcomes evaluation of computerized treatment for problem drinking using Breaking Free Online	MERGE 3 Shares data with Elison et al., 2017

Elison, S.	2014	An outcomes study of eTherapy for dual diagnosis using Breaking Free Online	INCLUDE	
Rooke, S.	2014	Applying technology to the treatment of cannabis use disorder: Comparing telephone versus internet delivery using data from two completed trials	EXCLUDE	Only reports changes to substance use outcomes
Fazzino, T.	2015	Assessment reactivity within the context of a web-based brief intervention for alcohol use	EXCLUDE	Only reports changes to alcohol outcomes
Cucciare, M.	2013	Brief alcohol counselling improves mental health functioning in veterans with alcohol misuse: Results from a randomized trial	MERGE 2	Shares data with Cucciare et al., 2013
Pedersen, E.	2013	Brief online interventions targeting risk and protective factors for increased and problematic alcohol use among American college students studying abroad	EXCLUDE	Only reports changes to alcohol outcomes
Geisner, I.	2015	Brief web-based intervention for college students with comorbid risky alcohol use and depressed mood: Does it work and for whom?	INCLUDE	
Berman, A.	2015	Changes in mental and physical well-being among problematic alcohol and drug users in 12-month internet-based intervention trials	EXCLUDE	Effects of digital intervention alone could not be inferred
Kay-Lambkin, F.	2011	Clinician-assisted computerized versus therapist-delivered treatment for depressive and addictive disorders: A randomized controlled trial	MERGE 4	Shares data with Kay-Lambkin et al, 2012
Rupp, C.	2012	Cognitive remediation therapy during treatment for alcohol dependence	INCLUDE	
Wilson, J.	2015	Comparing outcomes from an online substance abuse treatment program and residential treatment programs for consumers who are deaf: A pilot study	INCLUDE	
Copeland, J.	2017	Comparison of brief versus extended personalized feedback in an online intervention for cannabis users: Short-term findings of a randomized trial	EXCLUDE	Only reports changes to cannabis use
Cunningham, J.	2012	Comparison of two internet-based interventions for problem drinkers: Randomized controlled trial	EXCLUDE	Only reports changes to alcohol outcomes

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Carroll, K.	2008	Computer-assisted delivery of cognitive-behavioral therapy for addiction: A randomized trial of CBT4CBT	EXCLUDE	Only reports changes to substance use outcomes
Kay-Lambkin, F.	2009	Computer-based psychological treatment for comorbid depression and problematic alcohol and/or cannabis use: A randomized controlled trial of clinical efficacy	INCLUDE	
Vinson, D.	2000	Computer-generated written behavioral contracts with problem drinkers in primary medical care.	EXCLUDE	Only reports changes to alcohol outcomes
Ondersma, S.	2015	Computer-delivered screening and brief intervention for alcohol use n pregnancy: A pilot randomized trial	EXCLUDE	Only reports changes to alcohol outcomes
Boon, B.	2011	Curbing alcohol use in male adults through computer generated personalized advice: Randomized controlled trial	EXCLUDE	Only reports changes to alcohol outcomes
Postel, M.	2010	Effectiveness of a web-based intervention for problem drinkers and reasons for dropout: Randomized controlled trial	MERGE 1	Shares data with Postel et al., 2015
Elison, S.	2015	Effectiveness of computer-assisted therapy for substance dependence using Breaking Free Online: Subgroup analyses of a heterogeneous sample of service users	MERGE 3	Shares data with Elison et al., 2017
Schulz, D.	2013	Effects of a web-based tailored intervention to reduce alcohol consumption in adults: Randomized controlled trial	EXCLUDE	Only reports changes to alcohol outcomes
Gajecki, M.	2014	Effects of baseline problematic alcohol and drug use on internet-based cognitive behavioral therapy outcomes for depression, panic disorder and social anxiety disorder	EXCLUDE	Only reports changes to mental health outcomes
Boß, L.	2018	Efficacy of a web-based intervention with and without guidance for employees with risky drinking: Results of a three-arm randomized controlled trial	INCLUDE	
Farrell, S.	2009	Electronic screening for mental health in rural primary care feasibility and user testing	EXCLUDE	Only reports screening measures at baseline
Carroll, K.	2009	Enduring effects of a computer-assisted training program for cognitive behavioral therapy: A 6-month follow-up of CBT4CBT	EXCLUDE	Only reports changes to substance use outcomes

Elison, S.	2017	Examining effectiveness of tailorable computer-assisted therapy programs for substance misuse: Program usage and clinical outcomes data from Breaking Free Online	MERGE 3	Combines data from both Elison et al., 2015 studies
Johnson, E.	2009	Feasibility and validity of computerized ambulatory monitoring in drug-dependent women	EXCLUDE	Mobile intervention
Batterham, P. J.	2018	FitMindKit: Randomized controlled trial of an automatically tailored online program for mood, anxiety, substance use and suicidality.	INCLUDE	
Sundstrom, C.	2016	Guided and unguided internet-based treatment for problematic alcohol use – A randomized controlled pilot trial	INCLUDE	
Mathiasen, K.	2018	Guided internet-based cognitive behavioral therapy for adult depression and anxiety in routine secondary care: Observational study	EXCLUDE	Only reports changes to mental health outcomes
Wodarski, J.	2015	Health information technology: An expanded care coordination in rural Tennessee	EXCLUDE	Does not report changes to substance misuse and mental health clinical outcomes
Sundstrom, C.	2017	High-intensity therapist-guided internet-based cognitive behavior therapy for alcohol use disorder: A pilot study	INCLUDE	
Hermes, E.	2016	Implementing computer-based psychotherapy among veterans in outpatient treatment for substance use disorders	EXCLUDE	Intervention on insomnia
Cunningham, J.	2005	Internet and paper self-help materials for problem drinking: Is there an additive effect?	EXCLUDE	Only reports changes to alcohol outcomes
Lewis, C. E.	2017	Internet-based guided self-help for post-traumatic stress disorder (PTSD): Randomized controlled trial.	INCLUDE	
Linke, S.	2007	Internet-based interactive health intervention for the promotion of sensible drinking: Patterns of use and potential impact on members of the general public	INCLUDE	
Ruggiero, K.	2006	Internet-based intervention for mental health and substance use problems in disaster-affected populations: A pilot feasibility study	EXCLUDE	Does not report changes to substance misuse and mental health clinical outcomes
Kay-Lambkin, F.	2012	It's worth a try: The treatment experiences of rural and	MERGE 4	Shares data with Kay-Lambkin et al., 2011

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		urban participants in a randomized controlled trial of computerized psychological treatment for comorbid depression and alcohol/other drug use	
Fang, L.	2014	Mediation effects of a culturally generic substance use prevention program for Asian American adolescents	EXCLUDE Participants were younger than aged 16
Buckner, J.	2019	Online personalized normative feedback intervention to reduce event-specific drinking during Mardi-Gras	EXCLUDE Only reports changes to alcohol outcomes
Cunningham, J.	2012	Pragmatic randomized controlled trial of providing access to a brief personalized alcohol feedback intervention in university students	EXCLUDE Only reports changes to alcohol outcomes
Kim, S.	2015	Predictors of outcome from computer-based treatment for substance use disorders: Results from a randomized clinical trial	EXCLUDE Only reports changes to substance use outcomes
Montag, A.	2015	Preventing alcohol-exposed pregnancy among an American Indian/Alaska Native population: effect of a screening, brief intervention, and referral to treatment intervention	EXCLUDE Only reports changes to alcohol outcomes
Schinke, S.	2011	Preventing substance use among Black and Hispanic adolescent girls: Results from a computer-delivered, mother-daughter intervention approach	EXCLUDE Participants were younger than aged 16
Byrnes, H.	2019	Prevention of alcohol use in older teens: A randomized trial of an online family prevention program	EXCLUDE Only reports changes to alcohol outcomes
Wolitzky-Taylor, K.	2018	Randomized clinical trial evaluating the preliminary effectiveness of an integrated anxiety disorder treatment in substance use disorder specialty clinics	INCLUDE
Wagener, T.	2012	Randomized trial comparing computer-delivered and face-to-face personalized feedback interventions for high-risk drinking among college students	EXCLUDE Only reports changes to alcohol outcomes
Tait, R.	2015	Six-month outcomes of a web-based intervention for users of amphetamine-type stimulants: Randomized controlled trial	INCLUDE
Musiat, P.	2014	Targeted prevention of common mental health disorders	INCLUDE

		in university students: Randomized controlled trial of a transdiagnostic trait-focused web-based intervention	
Monahan, C.	2013	The impact of elevated post-traumatic stress on the efficacy of brief alcohol interventions for heavy drinking college students	EXCLUDE Only reports changes to alcohol outcomes
Schuckit, M.	2016	The low level of response to alcohol-based heavy drinking prevention program: One-year follow-up	EXCLUDE Only reports changes to alcohol outcomes
Wodarski, J.	2012	The use of computer technology to reduce and prevent college drinking	EXCLUDE Only reports changes to alcohol outcomes
Riper, H.	2009	Translating effective web-based self-help for problem drinking into the real world	EXCLUDE Only reports changes to alcohol outcomes
Cunningham, J.	2014	Treatment dismantling pilot study to identify the active ingredients in personalized feedback interventions for hazardous alcohol use: Randomized controlled trial	EXCLUDE Only reports changes to alcohol outcomes
Cunningham, J.	2010	Twelve-month follow-up results from a randomized controlled trial of a brief personalized feedback intervention for problem drinkers	EXCLUDE Only reports changes to alcohol outcomes
Fang, L.	2013	Two-year outcomes of a randomized, family-based substance use prevention trial for Asian American adolescent girls	EXCLUDE Participants were younger than aged 16
Ospina-Pinillos, L.	2018	Using new and innovative technologies to assess clinical stage in early intervention youth mental health services: Evaluation study	EXCLUDE Does not report changes to mental health and substance misuse clinical outcomes
Brief, D.	2013	Web intervention for OEF/OIF veterans with problem drinking and PTSD symptoms: A randomized clinical trial	INCLUDE
Levin, M.	2017	Web-based acceptance and commitment therapy for mental health problems in college students: A randomized controlled trial	INCLUDE
Sugarman, D.	2009	Web-based alcohol feedback intervention for heavy drinking college students: Does drinking control strategy use mediate intervention effects?	EXCLUDE Only reports changes to alcohol outcomes
Kypri, K.	2013	Web-based alcohol intervention for Maori university	EXCLUDE Only reports changes to alcohol outcomes

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		students: Double-blind, multi-site randomized controlled trial	
Hustad, J.	2010	Web-based alcohol prevention for incoming college students: A randomized controlled trial	EXCLUDE Only reports changes to alcohol outcomes
Kypri, K.	2014	Web-based alcohol screening and brief intervention for university students: A randomized trial	EXCLUDE Only reports changes to alcohol outcomes
Marsch, L.	2014	Web-based behavioral treatment for replacement of standard methadone substance use disorders as a partial maintenance treatment	EXCLUDE Only reports changes to substance use outcomes
Farrer, L.	2012	Web-based cognitive behavior therapy for depression with and without telephone tracking in a national helpline: secondary outcomes from a randomized controlled trial	EXCLUDE Only reports changes to alcohol outcomes
Schaub, M.	2012	Web-based cognitive behavioral self-help intervention to reduce cocaine consumption in problematic cocaine users: randomized controlled trials	INCLUDE
Tiburcio, M.	2018	Web-based intervention to reduce substance abuse and depression: A three arm randomized trial in Mexico.	INCLUDE
Fingfeld-Connett, D.	2008	Web-based treatment of alcohol problems among rural women: Results of a randomized pilot investigation	EXCLUDE Only reports changes to alcohol outcomes
Johansson, M.	2017	Web-based self-help for problematic alcohol use: a large naturalistic study	INCLUDE
Acosta, M.	2017	Web-delivered CBT reduces heavy drinking in OEF-OIF veterans in primary care with symptomatic substance use and PTSD	INCLUDE

Note. CBT = cognitive behavioral therapy; OEF/OIF = Operation Enduring Freedom/Operation Iraqi Freedom; PTSD = post-traumatic stress disorder.