Internet Interventions 26 (2021) 100477

Contents lists available at ScienceDirect

Internet Interventions

journal homepage: www.elsevier.com/locate/invent

Randomized controlled trial of online interventions for co-occurring depression and hazardous alcohol consumption: Primary outcome results

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ARTICLE INFO

Keywords:
Clinical trial
Randomized controlled trial
Brief intervention
Internet intervention
Depression
Hazardous alcohol use
Problem drinking
Comorbidity

ABSTRACT

Background and aims: The current trial tested the benefits of offering a brief online intervention for hazardous alcohol consumption along with one for depression among people experiencing both conditions.
Methods: Online advertisements were used to recruit people with persistent low mood. Those who also had current hazardous alcohol consumption were identified and invited to take part in the trial (those not eligible were offered access to the online depression intervention). Participants were randomized to an established intervention for depression (MoodGYM; M-only) or to receive MoodGYM plus a brief personalized feedback intervention for hazardous drinking (Check Your Drinking; M + CYD). Participants were followed-up at three and six months.
Results: While levels of depression symptoms ($p < .001$) and hazardous alcohol consumption ($p < .001$) reduced in both the M-only and the M + CYD groups, there was no difference between groups on drinking ($p = .374$) or depression outcomes ($p = .752$). Further, participants who were provided both interventions logged into the intervention website less often ($M = 4.1$, $SD = 3.9$) compared to participants only offered the depression intervention ($M = 4.9$, $SD = 5.2$), $t(986) = 2.47$, $p = .014$. However, there was no significant difference ($p > .05$) in the number of MoodGYM modules completed between the two groups.
Discussion and conclusion: The current trial found no benefit to providing a brief online intervention for hazardous alcohol consumption alongside one for depression among people experiencing these co-occurring disorders. Further, the finding that adding an online intervention for drinking to one for depression led to a small reduction in the number of times the interventions were accessed implies the need for caution when deciding how best to provide online help to those with co-occurring depression and hazardous alcohol consumption.
Trial Registration: ClinicalTrials.gov NCT03421080.

1. Introduction

Depression and hazardous alcohol consumption are both significant contributors to the preventable burden of disease (Rehm and Shield, 2019). When they co-occur, there is increased risk of negative health consequences (Davis et al., 2006; Quello et al., 2005). In addition, because depression and hazardous alcohol use can be functionally interrelated, there may be benefit in addressing both concerns simultaneously to optimize the chances of improvements in each health condition (Quello et al., 2005).

How do you help people with depression who also drink alcohol in a hazardous fashion? Successful treatment models have been developed (Baker et al., 2010). Still, people with co-occurring disorders can often 'fall between the gaps' of treatment facilities that focus either on the

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https://doi.org/10.1016/j.invent.2021.100477
Received 22 September 2021; Received in revised form 30 October 2021; Accepted 1 November 2021
Available online 2 November 2021

treatment of mental health concerns or on addictions (Kohn et al., 2004). One additional challenge is that the large majority of people with depression or with hazardous alcohol consumption, or those who experience both conditions, will never seek treatment for their concerns (Clarkin and Kendall, 1992).

In order to provide additional options to access help, there have been extensive efforts to develop self-directed tools to help those with depression or hazardous alcohol consumption, including an expanding range of services available over the Internet (Cuijpers et al., 2017; Kaner et al., 2017). A smaller but active area of Internet intervention research involves the design and evaluation of interventions that address both depression and hazardous alcohol use simultaneously. A recent systematic review and meta-analysis of randomized controlled trials (RCT) of combined digital interventions for co-occurring hazardous alcohol use and depression found evidence for the positive impact of these interventions on improvements in symptoms of depression at three-month follow-up and on reductions in alcohol consumption at six-month follow-up (Schouten et al., 2021). However, the research base is limited, with only six trials included in the review and with insufficient studies to separate the research that targeted people in treatment from those which recruited people with co-occurring disorders outside of clinical settings.

The current study was underpinned by some pragmatic assumptions of how people with both depression and hazardous alcohol consumption might seek help online. We thought that the majority would seek help for whichever health concerns they regarded as the most troubling rather than actively searching for a combined Internet intervention. Further, there was existing evidence that indicated that people with co-occurring depression and hazardous alcohol consumption might seek help for their depression earlier than for their alcohol consumption (Kay-Lambkin, 2014). As such, the focus of the study was to recruit people who were concerned about their depression and then to identify those who also had hazardous alcohol consumption. The latter would then be offered either a well-established and evidence-based online intervention for depression (MoodGYM) (Twomey and O'Reilly, 2017) or would be offered MoodGYM plus a brief online intervention targeting hazardous alcohol consumption (Check Your Drinking; CYD) (Cunningham et al., 2006).

The primary hypotheses for the study were:

Hypothesis 1. Among participants with both depression and hazardous alcohol consumption, those provided both MoodGYM and the CYD intervention would display significant reductions in drinking behaviour at three- and six-month follow-ups compared to those provided with MoodGYM alone.

Hypothesis 2. Among participants with both depression and hazardous alcohol consumption, those provided both MoodGYM and the CYD would display significant reductions in depressive symptoms at three-

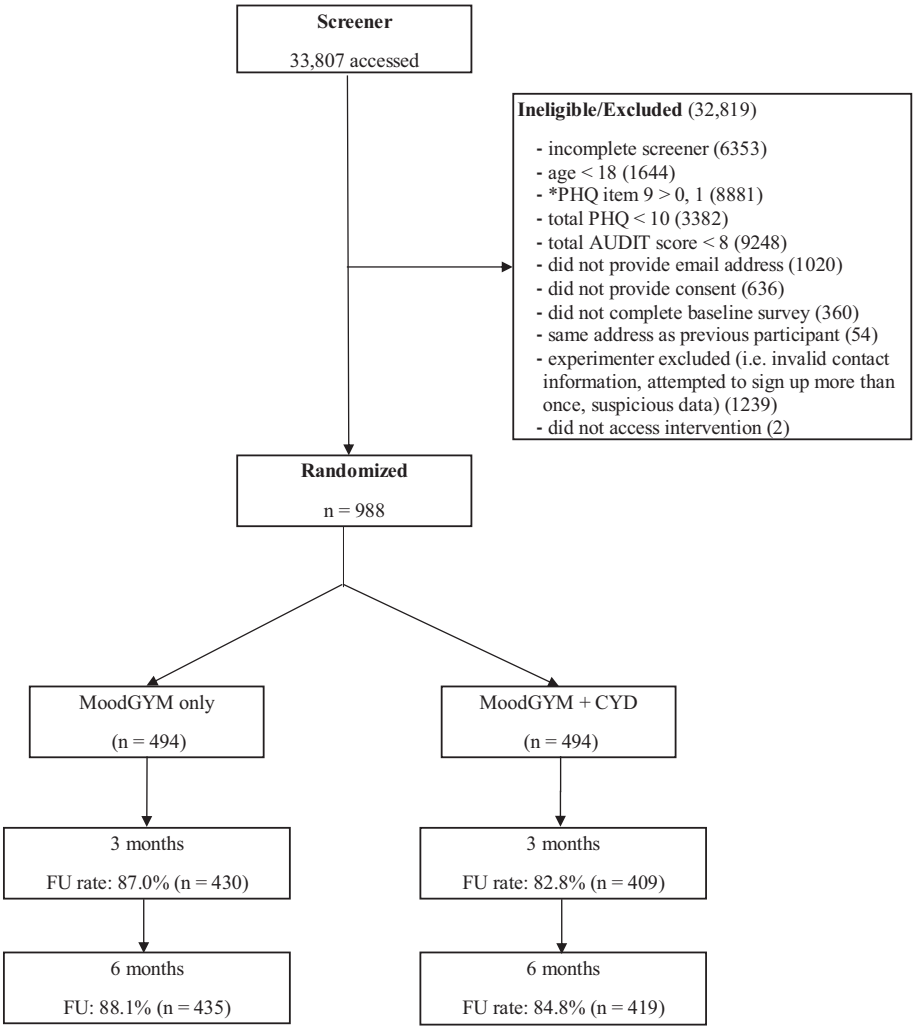

Fig. 1. Consort diagram.
*Eligibility criteria changed from PHQ item # 9 < 1 to PHQ item # 9 < 2 on July 29 2018. In total 557 participants were recruited as a result of this change and scored 1 on item 9 of the PHQ.

and six-month follow-ups compared to those provided with MoodGYM alone.

Mediation Hypothesis 3. Among participants with both depression and hazardous alcohol consumption, reductions in alcohol consumption would mediate the effect of intervention group on reductions in depression symptoms. Specifically, it was predicted that greater reductions in alcohol consumption at three-month follow-up would be observed in the MoodGYM plus CYD group versus the MoodGYM only group. Further, these changes in three-month alcohol consumption would account for a significant indirect effect between intervention group and depression symptoms at six-month follow-up.

2. Methods

This study was a two-arm, double-blinded, parallel-group randomized control trial with three- and six-month follow-ups. See the study protocol for full details of the trial (Cunningham et al., 2018). See Fig. 1 for a CONSORT diagram of the trial.

2.1. Recruitment

2.1.1. Inclusion and exclusion criteria

Inclusion criteria were being 18 years or older, having a Patient Health Questionnaire (PHQ-9) (Kroenke et al., 2001) score of 10 or more indicating current depression, and an Alcohol Use Disorder Identification Test (AUDIT) (Babor et al., 1989; Saunders et al., 1993) score of eight or more indicating current hazardous alcohol use. Exclusion criteria consisted of the experience of current suicidal ideation. For the first four months of recruiting, this was indicated by a score greater than zero on item nine of the PHQ. However, due to recruitment issues, this was changed to a score greater than one for the remainder of the recruitment period (Godinho et al., 2021). In addition, only one participant per household was recruited for the trial to reduce the chances of contamination between experimental groups.

2.1.2. Procedure

Participants were recruited from across Canada using Google Adwords (including YouTube) and Facebook advertisements between April 2018 and July 2020. The advertisements targeted people who were 'experiencing persistent low mood or depression' and who were interested in participating in a study to 'help improve an online intervention for depression.' Those interested completed an eligibility screener asking the participant's age, and incorporating the PHQ and the AUDIT. Participants who were not eligible for the study were offered access to the MoodGYM online intervention for the duration of the study. Participants who were eligible for the study were provided an online consent form. The consent form advised participants that they would be accessing a website that provided self-help tools for depression and that not everyone would be provided access to the same website. However, no mention was made that some participants would be provided an intervention for alcohol in addition to one for depression. Those agreeing to participate were asked to provide their contact details including their name, email address, telephone number and postal address. The contact details were manually checked (i.e., was the postal address real and had it been used before) to identify people attempting to register multiple times in the trial. Those passing the contact detail check were sent an email with a link to the baseline survey.

2.2. Randomization, experimental groups

Prospective participants who completed the survey were asked to set up their login and password on the intervention website and were randomized in a 1:1 ratio to experimental group using an automated replicable algorithm with no stratification. Participants were then immediately routed to the homepage of their assigned online intervention (i.e., M-only or M + CYD). Participants who completed the baseline survey and accessed the intervention were provided a $10 gift certificate to Amazon.ca to promote retention at this point in the trial. Participants were sent emails with a link to complete online follow-up surveys at three and six months. Those who did not complete the surveys were sent up to two reminder emails. Participants who completed the follow-up surveys were provided an honorarium (Amazon.ca gift certificates for CAD$20 and CAD$30 respectively).

2.2.1. Experimental groups

2.2.1.1. MoodGYM only (M-only). Participants in the M-only group were provided access to MoodGYM, a popular automated online intervention for depression with multiple trials demonstrating its efficacy (Bennett et al., 2010; Calear et al., 2009; Christensen et al., 2004; Griffiths et al., 2004; Hickie et al., 2010; Hoifodt et al., 2013; Mackinnon et al., 2008; O'Kearney et al., 2009; Phillips et al., 2014; Powell et al., 2013; Sethi, 2013). MoodGYM consists of five modules containing cognitive behavioural techniques targeting depression and an online workbook incorporating 29 exercises.

2.2.1.2. MoodGYM plus Check Your Drinking (M + CYD). The homepage for participants assigned to this group contained separated icons to click to access MoodGYM or to open the CYD Final Report. The CYD is a brief online personalized normative feedback intervention with multiple trials demonstrating its efficacy in reducing alcohol consumption (Cunningham et al., 2017a; Cunningham et al., 2002; Cunningham et al., 2014; Cunningham et al., 2009; Doumas and Hannah, 2008; Doumas and Haustveit, 2008; Doumas et al., 2009). The Final Report provides a summary of the participant's drinking and compares it to others of the same age, sex, and country (in this case, Canada). For the current study, the Final Report was generated using items assessed on the baseline survey.

2.3. Content of surveys

All outcome variables were assessed at baseline, three- and six-months. For alcohol consumption, the primary outcome variable was number of drinks in a typical week in the past three-months (asked as the number of drinks typically consumed on each day of the week) (Kühlhorn and Leifman, 1993; Neighbors et al., 2010; Romelsjö et al., 1995). Secondary outcome variables consisted of the AUDIT-C (consumption subscale of the AUDIT consisting of the variables, frequency of consumption, drinks per drinking day, and frequency of 5+ drinks – asked about the previous three months) (Dawson et al., 2005), and number of consequences associated with drinking in the last three months (10 items adapted from Wechsler et al., 1994 with one item added asking about driving under the influence of alcohol) (Bertholet et al., 2015; Bertholet et al., 2017; Wechsler et al., 1994). For depression, the primary outcome variable was the total score on the 20-item Centre for Epidemiological Studies Depression scale (CES—D) (Radloff, 1977). Use of the online interventions was measured as the number of times the participant logged into the study intervention website (excluding the time that participants were automatically taken to the study website after completing the baseline survey). In addition, the number of MoodGYM modules completed, and the number of times the CYD Final Report was viewed were recorded. Treatment for alcohol was assessed (ever and past three-months) using the single item screener taken from the National Epidemiological Survey on Alcohol and Related Conditions (Grant et al., 2003). Treatment for depression was assessed (ever and past three months) by the single item, "Have you ever received treatment for depression from a therapist or doctor?"

2.4. Sample size estimate

Based on findings from previous trials examining the efficacy of the CYD and of similar web-based interventions (Riper et al., 2014), the power calculations assumed that the impact on drinking outcomes of the addition of the CYD to the MoodGYM intervention would be in the small range (i.e., $d = 0.20$). Power analysis indicated that a sample of 788 would provide 0.80 power to detect effects sizes of $d = 0.20$ at a significance level of $p < .05$ (two-sided tests, normal distributions assumed). Further, based on our previous work, we expected a retention rate of 80% across both three- and six-month follow-ups (Cunningham et al., 2009) resulting in the need to recruit an initial sample of 986 participants at baseline.

2.5. Data analysis

Prior to conducting the main analyses, the two groups (i.e., M-only, M + CYD) were compared across demographic and clinical characteristics. The first two hypotheses of this trial (i.e., impact of intervention on drinking and depression outcomes) were examined using a series of linear mixed effects models with random intercepts. More specifically, four independent models were conducted to examine the main effects of time, group assignment, and the time by group assignment interaction on drinking (i.e., weekly drinks, AUDIT-C and alcohol-related consequences) and depression (i.e., CES-D scores). Missing data were addressed using maximum likelihood to estimate variances, covariances, and means. Outcomes which were counted variables (i.e. weekly drinks, and alcohol related consequences) were also analysed using a negative binomial generalized estimating equation (GEE). For ease of interpretation, mixed-effect models results were reported when results matched corresponding GEE results, and model residuals were normally distributed. In addition, to test if changes in alcohol use mediated the effect of group assignment on depression symptoms, a mediation analysis was performed through the Hayes Process Macro v3.5 (Hayes, 2018). This assessed whether reductions in weekly drinking from baseline to three months (difference score; mediator variable) was positively associated with reductions in participant's depression outcomes at six months (measured by a difference score between total CES-D at baseline vs. six-month follow-up; outcome variable). Intervention condition was specified as the independent variable to examine whether reductions in weekly drinking mediated the effect of the intervention on reductions in depression outcomes. Bootstrapping was used (with 5000 replications) to calculate a bias-corrected confidence interval for the indirect effect. Lastly, group differences in intervention usage were examined using a series of bivariate analyses. Intervention usage was defined by the most accurate metrics available to our intervention: total logins, and active engagement in the intervention as measured by the number of modules completed (rather than passive measures such as time spent reading, page views, etc.) All analyses were performed using SPSS, version 25.0.

2.6. Ethics approval

The research was approved by the standing research ethics board of the Centre for Addiction and Mental Health.

3. Results

There were 988 participants recruited for the trial (494 in each group). Table 1 presents the demographic characteristics of each group, along with the baseline values for the outcome variables measuring drinking and depression. There were no significant differences ($p > .05$) between groups on demographic characteristics, levels of drinking or depression status, or rates of follow-up at three (84.9%) and six months (86.4%), and thus subsequent modelling analyses did not control for any demographic or clinical data.

Table 1
Differences between MoodGYM only and MoodGYM + CYD on baseline demographic and clinical characteristics.

Variable	Intervention		p
	MoodGYM (n = 494)	MoodGYM + CYD (n = 494)	
Age, mean years (SD)	35.6 (13.5)	36.8 (13.5)	0.165
Males, % (n)	26.3 (130)	26.7 (132)	0.885
Some post-secondary or greater[a], % (n)	71.4 (352)	67.2 (332)	0.153
Married/Common law, % (n)	30.6 (151)	34.6 (171)	0.175
Full/Part-time employed, % (n)	52.0 (257)	56.7 (280)	0.142
Household income[b] ≤$30,000	40.4 (184)	36.3 (167)	0.198
AUDIT at baseline	14.1 (5.7)	14.3 (6.1)	0.490
Typical weekly drinks, mean (SD)	15.7 (14.8)	15.9 (14.6)	0.840
AUDIT-C, mean (SD)	6.3 (2.6)	6.5 (2.5)	0.250
# alcohol-related consequences, mean (SD)	4.6 (3.4)	4.6 (3.6)	0.661
Past 3 month use of formal treatment for alcohol use, % (n)	7.3 (36)	8.7 (43)	0.412
Ever attended formal treatment for alcohol use, % (n)	20.2 (100)	24.3 (120)	0.126
CES-D, mean (SD)	35.4 (8.3)	35.2 (8.3)	0.744
Past 3 month use of formal treatment for depression, % (n)	33.6 (166)	36.0 (178)	0.423
Ever attended formal treatment for depression, % (n)	70.6 (349)	65.6 (324)	0.088
3-month follow up complete,% (n)	87.0 (430)	82.8 (409)	0.062
6-month follow up complete,% (n)	88.1 (435)	84.8 (419)	0.137

AUDIT, Alcohol Use Disorders Identification Test.
AUDIT-C, Alcohol Use Disorders Identification Test – Consumption subscale.
CES-D, Center for Epidemiologic Studies Depression Scale.
[a] Missing data $n = 1$.
[b] $n = 73$ reported "Don't know".

A mixed effects model was conducted to compare changes to the primary outcome variable, number of drinks in a typical week, between participants in the M-only versus the M + CYD groups from baseline to three- and six-month follow-ups. There were significant reductions in the typical number of drinks reported over time ($p < .001$). However, group by time interaction was not significant ($p = .374$). See Table 2 for details of this mixed model analysis. A similar pattern of results was observed for the mixed effect model analyses of the secondary outcome drinking variables – AUDIT-C scores and number of alcohol-related consequences (see Table 2). Finally, for the depression outcome variable, CES-D score (Hypothesis 2), the same pattern of results was observed (i.e., a reduction in depression scores over time, $p < .001$, but no significant intervention by time interaction, $p = .703$; see Table 2).

A serial mediation analysis was performed (i.e., Model 4 of the SPSS PROCESS macro) to test whether reductions in drinking at three-month follow-up mediated the association of experimental condition with observed reductions in depressive symptoms at six-month follow-up (Hypothesis 3). The results of the analysis did not support the hypothesis (see Table 3, indirect effect estimate = −0.12, 95% CI [−0.33, 0.08]). However, independent of intervention group, a reduction in drinks consumed per week at three months demonstrated a significant effect on depression outcomes at six months, such that those who reduced their drinking were more likely to experience reductions in their depression scores ($p < .001$).

3.1. Use of the interventions

Participants logged into the intervention homepage an average of 4.4 ($SD = 4.6$) times throughout the study. Participants assigned to the M-only group ($M = 4.9$, $SD = 5.2$) logged into the intervention homepage significantly more often than those who were assigned to the M + CYD group ($M = 4.1$, $SD = 3.9$), $t(986) = 2.47$, $p = .014$. However, the groups

Table 2
Mixed-effect model results of time, intervention, and time by intervention on the primary and secondary outcome variables.

Number of drinks in a typical week	Estimate	*t*	*p*
Intercept	15.7	25.3	**<0.001**
Time (Reference: Baseline)			
3-months	−3.97	−7.78	**<0.001**
6-months	−4.29	−8.44	**<0.001**
Intervention (Reference: MoodGYM only)			
MoodGYM + CYD	0.19	0.22	0.830

Interactions	*F*	*p*
Time by Intervention	0.98	0.374

AUDIT-C score	Estimate	*t*	*p*
Intercept	6.32	51.34	**<0.001**
Time (Reference: Baseline)			
3-months	−0.94	−8.66	**<0.001**
6-months	−1.07	−9.91	**<0.001**
Intervention (Reference: MoodGYM only)			
MoodGYM + CYD	0.18	1.06	0.290

Interactions	*F*	*p*
Time by Intervention	0.92	0.400

Number of alcohol-related consequences	Estimate	*t*	*p*
Intercept	4.55	32.31	**<0.001**
Time (Reference: Baseline)			
3-months	−1.98	−15.00	**<0.001**
6-months	−2.14	−16.22	**<0.001**
Intervention (Reference: MoodGYM only)			
MoodGYM + CYD	0.10	0.49	0.626

Interactions	*F*	*p*
Time by Intervention	0.554	0.575

CES-D score	Estimate	*t*	*p*
Intercept	35.4	78.4	**<0.001**
Time (Reference: Baseline)			
3-months	−7.10	−14.3	**<0.001**
6-months	−7.50	−15.2	**<0.001**
Intervention (Reference: MoodGYM only)			
MoodGYM + CYD	−0.17	−0.27	0.787

Interactions	*F*	*p*
Time by Intervention	0.29	0.752

Note: AUDIT-C: Alcohol Use Identification Test consumption subscale; CES—D: Center for Epidemiologic Studies Depression Scale.

Table 3
Mediation model of indirect effect of condition on change in depression from baseline to 6 months (CES—D) via reduced alcohol consumption (# of drinks per week) at 3-months.

Antecedent	Consequent					
	Change in # drinks per week			Depression		
	Coeff.	SE	*p*	Coeff.	SE	*p*
Constant	3.77	0.51	**<0.001**	7.01	0.57	**<0.001**
Condition	−0.91	0.74	0.218	0.86	0.79	0.272
Change in # drinks per week	–	–	–	0.14	0.04	**<0.001**
Model Summary	$R^2 = 0.002$, MSE = 107.52			$R^2 = 0.017$, MSE = 122.55		
	$F(1, 793) = 1.52$, $p = .218$			$F(2, 792) = 6.86$, $\boldsymbol{p = .001}$		

Note: CES—D: Center for Epidemiologic Studies Depression Scale.

did not differ significantly in the number of MoodGYM modules completed, t (986) = 1.08, $p = .278$, with participants completing an average of 2 modules of the MoodGYM intervention ($SD = 1.6$). Of those assigned to receive both MoodGYM and the CYD, 86.8% viewed their CYD Final report, with some viewing the report more than once ($M = 1.5$ times, $SD = 1.0$).

4. Discussion

The current study recruited participants by advertising for people with persistent low mood and then selecting those who also reported hazardous alcohol consumption. Among these participants, providing the CYD Final Report in addition to MoodGYM did not appear to impact levels of alcohol consumption. Further, provision of the CYD did not result in changes in the experience of depression symptoms. Finally, consistent with the lack of effect of experimental group on alcohol consumption, mediation tests did not support the hypothesized indirect effect of group on six-month depression symptoms via changes in

alcohol consumption.

These results are in contrast with the limited existing evidence base indicating that digital interventions for combined depression and drinking can reduce alcohol consumption and improve symptoms of depression among people with these co-occurring conditions (Schouten et al., 2021). Why might the results from this trial differ? Of note, while the MoodGYM intervention does not contain specific content addressing alcohol consumption, analyses of secondary measures in an RCT found that participants receiving MoodGYM reduced their alcohol consumption more than those assigned to a waiting-list control (Farrer et al., 2012). Thus, it is possible that the addition of the CYD intervention to MoodGYM did not result in greater reductions in alcohol consumption compared to MoodGYM alone because use of MoodGYM already motivates people to reduce their drinking (or felt less need to drinking when they experienced fewer depression symptoms).

Another potential explanation for the lack of observed impact of the CYD in the current study relates to the method of recruitment employed. While the advertising method was designed to mimic how we thought participants might search for help online (i.e., search for an intervention targeting one concern rather than an intervention targeting both), it may have had unanticipated consequences. That is, when participants seek help online for one concern, they may not appreciate also receiving an intervention for a separate health concern (in this case, drinking), even when that health concern may be functionally related. Moreover, individuals interested in receiving help to address low mood or depression may have little or no interest in reducing their alcohol use. Of relevance, this is the second trial where the CYD has not demonstrated a significant impact on alcohol consumption ($p > .05$) when those receiving the intervention have been recruited for another health concern (problem gambling in the earlier trial) (Cunningham et al., 2019). Further, in the current trial, the finding that those who received the CYD Final Report logged into the intervention website less often than those who did not receive the CYD intervention ($p < .05$) may also be an indication that the inclusion of the CYD was off-putting. Thus, these findings indicate that caution should be applied as to what additional health information to provide to those specifically seeking help for persistent low mood beyond an intervention clearly targeting depression. This is because the additional health information could actually result in less use of the depression intervention provided.

One other difference between the current trial and other research investigating digital interventions for co-occurring depression and hazardous drinking was in the way the intervention(s) for these health concerns were structured. In the current trial, the MoodGYM and CYD interventions were not integrated in any way. In other trials examining online interventions targeting these co-occurring disorders, the interventions for depression and for hazardous alcohol consumption have been integrated into one intervention package (Kay-Lambkin, 2014). Our reason for structuring the interventions in this way was that we sought preliminary information on how a 'one-stop shop' for multiple health concerns might be received – one where interventions for multiple health concerns might be presented on a single online dashboard. However, the current trial, while not ruling out the benefits of a 'one-stop shop,' certainly does not provide positive support that providing multiple interventions is helpful when their presence is a surprise to the recipient.

The characteristics of the participants recruited for the current trial were also systematically different from our previous online trials targeting hazardous drinking, which could have implications for the observed lack of findings in this trial. First, about three-quarters of participants indicated that they were female. While online trials targeting hazardous alcohol consumption often recruit more females than are commonly seen in research conducted in treatment settings, our experience is that the proportion of males to females in online trials is usually evenly distributed (Cunningham et al., 2017b). The observed higher rate of females in this trial may be because the recruitment advertisement targeted those with persistent low mood rather than asking for those who were concerned about their drinking. In addition, the levels of hazardous drinking reported in the current trial were lower than those generally observed in a trial recruiting for people concerned about their alcohol consumption. As an example, in our previous RCT which also used an AUDIT score of 8 or more as an inclusion criterion, the average AUDIT score of participants at baseline was 19 (compared to 14 here) and participants reported typically consuming 23–24 drinks in a typical week (compared to 15–16 here) (Cunningham et al., 2017a). The relatively low level of alcohol consumption, which might also be expected in a predominantly female sample (in which less alcohol consumption is observed in population samples compared to males) could conceivably result in some form of 'floor' effect regarding possible reductions in drinking. Finally, the mean CES-D score at baseline was 35, indicating significant levels of depression, and the majority of participants had received some form of formal treatment for depression in the past. This implies a population that is struggling and, while access to online interventions might be helpful, participants may have required more assistance than could be adequately provided in an online setting.

There were a number of limitations associated with the trial, including reliance on self-report for drinking and depression outcomes. Of note, the number of potential participants excluded from the trial was large (almost 33,000 people; see Fig. 1). The most common reasons for exclusion were incomplete screener questionnaires ($n = 6353$), endorsing the experience of suicidal ideation (item nine of the PHQ; $n = 8881$), having a PHQ score of less than 10 (3382) or an AUDIT score of less than eight (9248). While all participants excluded from the trial were offered access to MoodGYM, the large numbers speak to the trial only targeting a small proportion of those experiencing persistent low mood. In addition, roughly 19% of participants were recruited after the start of the COVID-19 pandemic and 45% percent completed at least one of their follow-up surveys during the pandemic. The impact of this major event on the use and efficacy of the interventions is unknown. Additionally, as this trial compared groups assigned to different condition on multiple outcomes (i.e. depression and alcohol use), it is likely that this multiplicity inflated the potential for type I errors. While there was a previously defined primary outcome variable (number of drinks in a typical week) and none of our findings were statistically significant, it is important to note that the significance level of the trial was not controlled for. Finally, the trial focussed on participants with depression who also consumed alcohol in a hazardous fashion. It is unknown what the impact would be of adding a drinking intervention to one for depression among people with depression who do not drink in a hazardous fashion. Such information would be important as the use of online interventions increases and service providers make decisions regarding the best way to structure Internet interventions for people with and without co-occurring disorders.

CRediT authorship contribution statement

All authors have made an intellectual contribution to this research trial. JAC is the principal investigator of the trial, with overall responsibility for the project. JAC, CSH, FKL, CN, and KMG conceived the design and wrote the grant application. AG and CS conducted the trial. All authors have contributed to the manuscript drafting process and have read and approved the final manuscript.

Declaration of competing interest

KMG is entitled to a share of royalties generated by the commercialization of MoodGYM. The authors declare that they have no other competing interest.

Acknowledgements

John Cunningham is currently supported by the Nat & Loretta Rothschild Chair in Addictions Treatment & Recovery Studies. This

research was undertaken in part thanks to funding from the Canada Research Chairs program for support of Dr. Cunningham, who was the Canada Research Chair in Addictions and Dr. Hendershot, who was the Canada Research Chair in Etiology and Treatment of Alcohol Use Disorders at the time of the conduct of this study.

Funding

This research is funded by the Canadian Institutes of Health Research grant number PJT 153 324 however, the findings and conclusions of this paper are solely of the authors and do not necessarily represent the views of the Canadian Institutes of Health Research. The funding body had no role or influence on the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

References

Babor, T.F., De La Fuente, M.F., Saunders, J.B., Grant, M., 1989. AUDIT - The Alcohol Use Disorders Identification Test: Guidelines for Use in Primary Health Care. World Health Organization.

Baker, A.L., Kavanagh, D.J., Kay-Lambkin, F.J., Hunt, S.A., Lewin, T.J., Carr, V.J., Connolly, J., 2010. Randomized controlled trial of cognitive–behavioural therapy for coexisting depression and alcohol problems: short-term outcome. Addiction 105 (1), 87–99. https://doi.org/10.1111/j.1360-0443.2009.02757.x.

Bennett, K., Reynolds, J., Christensen, H., Griffiths, K.M., 2010. e-hub: an online self-help mental health service in the community. Jun 7 Med. J. Aust. 192 (11), S48–S52. <Go to ISI>://WOS:000278950600011.

Bertholet, N., Cunningham, J.A., Faouzi, M., Gaume, J., Gmel, G., Burnand, B., Daeppen, J.B., 2015. Internet-based brief intervention for young men with unhealthy alcohol use: a randomized controlled trial in a general population sample. Aug Addiction 110 (11), 1735–1743. https://doi.org/10.1111/add.13051. doi:UNSP e153.

Bertholet, N., Daeppen, J.B., McNeely, J., Kushnir, V., Cunningham, J.A., 2017. Smartphone application for unhealthy alcohol use: a pilot study. Feb 7 Subst. Abus. 38, 285–291. https://doi.org/10.1080/08897077.2017.1281860.

Calear, A.L., Christensen, H., Mackinnon, A., Griffiths, K.M., O'Kearney, R., 2009. The youthmood project: a cluster randomized controlled trial of an online cognitive behavioral program with adolescents. Dec J. Consult. Clin. Psychol. 77 (6), 1021–1032. https://doi.org/10.1037/A0017391.

Christensen, H., Griffiths, K.M., Jorm, A.F., 2004. Delivering interventions for depression by using the internet: randomised controlled trial. Jan 31 Br. Med. J. 328 (7434), 265–268A. https://doi.org/10.1136/Bmj.37945.566632.Ee.

Clarkin, J.F., Kendall, P.C., 1992. Comorbidity and treatment planning: summary and future directions. Dec J. Consult. Clin. Psychol. 60 (6), 904–908.

Cuijpers, P., Kleiboer, A., Karyotaki, E., Riper, H., 2017. Internet and mobile interventions for depression: opportunities and challenges. Jul Depress. Anxiety 34 (7), 596–602. https://doi.org/10.1002/da.22641.

Cunningham, J.A., Koski-Jannes, A., Wild, T.C., Cordingley, J., 2002. Treating alcohol problems with self-help materials: a population study. J. Stud. Alcohol 63 (6), 649–654.

Cunningham, J.A., Humpheys, K., Kypri, K., van Mierlo, T., 2006. Formative evaluation and three-month follow-up of an online personalized assessment feedback intervention for problem drinkers. J. Med. Internet Res. 8 (2), e5. http://www.jmir.org/2006/2/e5.

Cunningham, J.A., Wild, T.C., Cordingley, J., van Mierlo, T., Humphreys, K., 2009. A randomized controlled trial of an internet-based intervention for alcohol abusers. Addiction 104 (12), 2023–2032. https://doi.org/10.1111/j.1360-0443.2009.02726.x.

Cunningham, J.A., Murphy, M., Hendershot, C.S., 2014. Treatment dismantling pilot study to identify the active ingredients in personalized feedback interventions for hazardous alcohol use: randomized controlled trial. Addict. Sci. Clin. Pract. e9, 22.

Cunningham, J.A., Godinho, A., Kushnir, V., 2017. Can Amazon's mechanical turk be used to recruit participants for internet intervention trials? A pilot study involving a randomized controlled trial of a brief online intervention for hazardous alcohol use. Internet Interv. 10, 12–16.

Cunningham, J.A., Shorter, G.W., Murphy, M., Kushnir, V., Rehm, J., Hendershot, C.S., 2017. Randomized controlled trial of a brief versus extended internet intervention for problem drinkers. Oct 21 Int. J. Behav. Med. (5), 760–767. https://doi.org/10.1007/s12529-016-9604-5.

Cunningham, J.A., Hendershot, C.S., Kay-Lambkin, F., Neighbors, C., Griffiths, K.M., Bennett, K., Bennett, A., Godinho, A., Schell, C., 2018. Does providing a brief internet intervention for hazardous alcohol use to people seeking online help for depression reduce both alcohol use and depression symptoms among participants with these co-occurring disorders? Study protocol for a randomised controlled trial. Jul 19 BMJ Open 8 (7), e022412. https://doi.org/10.1136/bmjopen-2018-022412.

Cunningham, J.A., Hodgins, D.C., Mackenzie, C.S., Godinho, A., Schell, C., Kushnir, V., Hendershot, C.S., 2019. Randomized controlled trial of an Internet intervention for problem gambling provided with or without access to an Internet intervention for co-occurring mental health distress. Sep Internet Interv. 17, 100239. https://doi.org/10.1016/j.invent.2019.100239.

Davis, L.L., Frazier, E., Husain, M.M., Warden, D., Trivedi, M., Fava, M., Cassano, P., McGrath, P.J., Balasubramani, G.K., Wisniewski, S.R., Rush, A.J., 2006. Substance use disorder comorbidity in major depressive disorder: a confirmatory analysis of the STAR*D cohort. Am. J. Addict. 15 (4), 278–285. https://doi.org/10.1080/10550490600754317.

Dawson, D.A., Grant, B.F., Stinson, F.S., Zhou, Y., 2005. Effectiveness of the derived Alcohol Use Disorders Identification Test (AUDIT-C) in screening for alcohol use disorders and risk drinking in the US general population. May Alcohol. Clin. Exp. Res. 29 (5), 844–854. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15897730.

Doumas, D.M., Hannah, E., 2008. Preventing high-risk drinking in youth in the workplace: a web-based normative feedback program. Apr J. Subst. Abus. Treat. 34 (3), 263–271. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17600650.

Doumas, D.M., Haustveit, T., 2008. Reducing heavy drinking in intercollegiate athletes: evaluation of a web-based personalized feedback program. Sport Psychol. 22, 213–229.

Doumas, D.M., McKinley, L.L., Book, P., 2009. Evaluation of two Web-based alcohol interventions for mandated college students. Jan J. Subst. Abus. Treat. 36 (1), 65–74. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18657941.

Farrer, L., Christensen, H., Griffiths, K.M., Mackinnon, A., 2012. Web-based cognitive behavior therapy for depression with and without telephone tracking in a national helpline: secondary outcomes from a randomized controlled trial. J. Med. Internet Res. 14 (3), e68 https://doi.org/10.2196/jmir.1859.

Godinho, A., Schell, C., Cunningham, J.A., 2021. Falling between the cracks: the effect of using different levels of suicide risk exclusion criteria on sample characteristics when recruiting for an online intervention for depression. May 7 Suicide Life Threat. Behav. 51, 736–740. https://doi.org/10.1111/sltb.12761.

Grant, B.F., Moore, T.C., Shepard, J., Kaplan, K., 2003. Source and Accuracy Statement. Wave 1. National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).

Griffiths, K.M., Christensen, H., Jorm, A.F., Evans, K., Groves, C., 2004. Effect of web-based depression literacy and cognitive-behavioural therapy interventions on stigmatising attitudes to depression - randomised controlled trial. Br. J. Psychiatry 185, 342–349. https://doi.org/10.1192/Bjp.185.4.342.

Hayes, A.F., 2018. Introduction to Mediation, Moderation, and Conditional Process Analysis : A Regression-based Approach, Second edition. Guilford Press.

Hickie, I.B., Davenport, T.A., Luscombe, G.M., Moore, M., Griffiths, K.M., Christensen, H., 2010. Practitioner-supported delivery of internet-based cognitive behaviour therapy: evaluation of the feasibility of conducting a cluster randomised trial. Jun 7 Med. J. Aust. 192 (11), S31–S35. <Go to ISI>://WOS:000278950600007.

Hoifodt, R.S., Lillevoll, K.R., Griffiths, K.M., Wilsgaard, T., Eisemann, M., Waterloo, K., Kolstrup, N., 2013. The clinical effectiveness of web-based cognitive behavioral therapy with face-to-face therapist support for depressed primary care patients: randomized controlled trial. Aug J. Med. Internet Res. 15 (8). doi:UNSP e153.

Kaner, E.F., Beyer, F.R., Garnett, C., Crane, D., Brown, J., Muirhead, C., Redmore, J., O'Donnell, A., Newham, J.J., de Vocht, F., Hickman, M., Brown, H., Maniatopoulos, G., Michie, S., 2017. Personalised digital interventions for reducing hazardous and harmful alcohol consumption in community-dwelling populations. Sep 25 Cochrane Database Syst. Rev. 9, CD011479. https://doi.org/10.1002/14651858.CD011479.pub2.

Kay-Lambkin, F.J., 2014. Lifetime affective and alcohol use disorders: impact of comorbidity on current functioning and service use in a rural population. J. Addict. Res. Ther. S10, 009.

Kohn, R., Saxena, S., Levav, I., Saraceno, B., 2004. The treatment gap in mental health care. Nov Bull. World Health Organ. 82 (11), 858–866. doi:/S0042-96862004001100011.

Kroenke, K., Spitzer, R.L., Williams, J.B.W., 2001. The PHQ-9 - validity of a brief depression severity measure. Sep J. Gen. Intern. Med. 16 (9), 606–613. https://doi.org/10.1046/J.1525-1497.2001.016009606.X.

Kühlhorn, E., Leifman, H., 1993. Alcohol surveys with high and low coverage rate: a comparative analysis of survey strategies in the alcohol field. J. Stud. Alcohol 54, 542–544.

Mackinnon, A., Griffiths, K.M., Christensen, H., 2008. Comparative randomised trial of online cognitive-behavioural therapy and an information website for depression: 12-month outcomes. Feb Br. J. Psychiatry 192 (2), 130–134. https://doi.org/10.1192/Bjp.Bp.106.032078.

Neighbors, C., Lewis, M.A., Atkins, D.C., Jensen, M.M., Walter, T., Fossos, N., Lee, C.M., Larimer, M.E., 2010. Efficacy of web-based personalized normative feedback: a two-year randomized controlled trial. Dec J. Consult. Clin. Psychol. 78 (6), 898–911. https://doi.org/10.1037/A0020766.

O'Kearney, R., Kang, K., Christensen, H., Griffiths, K., 2009. A controlled trial of a school-based internet program for reducing depressive symptoms in adolescent girls. Jan Depress. Anxiety 26 (1), 65–72. https://doi.org/10.1002/Da.20507.

Phillips, R., Schneider, J., Molosankwe, I., Leese, M., Foroushani, P.S., Grime, P., McCrone, P., Morriss, R., Thornicroft, G., 2014. Randomized controlled trial of computerized cognitive behavioural therapy for depressive symptoms: effectiveness and costs of a workplace intervention. Apr Psychol. Med. 44 (4), 741–752. https://doi.org/10.1017/S0033291713001323.

Powell, J., Hamborg, T., Stallard, N., Burls, A., McSorley, J., Bennett, K., Griffiths, K.M., Christensen, H., 2013. Effectiveness of a web-based cognitive-behavioral tool to improve mental well-being in the general population: randomized controlled trial. Jan J. Med. Internet Res. 15 (1), 2–18. https://doi.org/10.2196/Jmir.2240.

Quello, S.B., Brady, K.T., Sonne, S.C., 2005. Mood disorders and substance use disorder: a complex comorbidity. Sci. Pract. Perspect. 3 (1), 13–21.

Radloff, L.S., 1977. The CES-D scale: a self report depression scale for research in the general population. Appl. Psychol. Meas. 1, 385–401.

Rehm, J., Shield, K.D., 2019. Global burden of disease and the impact of mental and addictive disorders. Feb 7 Curr. Psychiatry Rep. 21 (2), 10. https://doi.org/10.1007/s11920-019-0997-0.

Riper, H., Blankers, M., Hadiwijaya, H., Cunningham, J., Clarke, S., Wiers, R., Ebert, D., Cuijpers, P., 2014. Effectiveness of guided and unguided low-intensity internet interventions for adult alcohol misuse: a meta-analysis. PLoS One 9 (6), e99912. https://doi.org/10.1371/journal.pone.0099912.

Romelsjö, A., Leifman, H., Nyström, S., 1995. A comparative study of two methods for the measurement of alcohol consumption in the general population. Int. J. Epidemiol. 24, 929–936.

Saunders, J.B., Aasland, O.G., Babor, T.F., De La Fuente, J.R., Grant, M., 1993. Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption— II. Addiction 88, 791–804.

Schouten, M.J.E., Christ, C., Dekker, J.J.M., Riper, H., Goudriaan, A.E., Blankers, M., 2021. Digital interventions for people with co-occurring depression and problematic alcohol use: a systematic review and meta-analysis. Feb 15 Alcohol Alcohol.. https://doi.org/10.1093/alcalc/agaa147.

Sethi, S., 2013. Treating youth depression and anxiety: a randomised controlled trial examining the efficacy of computerised versus face-to-face cognitive behaviour therapy. Aug Aust. Psychol. 48 (4), 249–257. https://doi.org/10.1111/Ap.12006.

Twomey, C., O'Reilly, G., 2017. Effectiveness of a freely available computerised cognitive behavioural therapy programme (MoodGYM) for depression: meta-analysis. Mar Aust. N. Z. J. Psychiatry 51 (3), 260–269. https://doi.org/10.1177/0004867416656258.

Wechsler, H., Davenport, A., Dowdall, G., Moeykens, B., Castillo, S., 1994. Health and behavioral consequences of binge drinking in college: a national survey of students at 140 campuses. J. Am. Med. Assoc. 272, 1672–1677.