

BMJ Open 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

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ABSTRACT

Introduction Hazardous alcohol consumption is common among people experiencing depression, often acting to exacerbate depressive symptoms. While many people with these co-occurring disorders do not seek face-to-face treatment, they do seek help online. There are effective internet interventions that target hazardous alcohol consumption or depression separately but none that combine these online interventions without the involvement of a therapist. In order to realise the potential of internet interventions, we need to develop an evidence base supporting the efficacy of internet interventions for co-occurring depression and hazardous alcohol use without any therapist involvement. This study aims to evaluate the effects on drinking, and on depressive symptoms, of combining an internet intervention targeting hazardous alcohol consumption with one for depression.

Methods and analysis A double blinded, parallel group randomised controlled trial will be used. Participants with current depression who also drink in a hazardous fashion (n=986) will be recruited for a study to 'help improve an online intervention for depression'. Participants will be randomised either to receive an established online intervention for depression (MoodGYM) or to receive MoodGYM plus a brief internet intervention for hazardous alcohol consumption (Check Your Drinking; CYD). Participants will be contacted 3 and 6 months after receiving the interventions to assess changes in drinking and depression symptoms. It is predicted that participants receiving the CYD intervention in addition to MoodGYM will report greater postintervention reductions in alcohol consumption and depressive symptoms compared with those who received MoodGYM only. Hypothesised mediation and moderation effects will also be investigated. Using an intention-to-treat basis for the analyses, the hypotheses will be tested using a generalised linear hypothesis framework, and longitudinal analyses will use either generalised linear mixed modelling or generalised estimating equation approach where appropriate.

Strengths and limitations of this study

- Targeted recruitment of participants who are seeking online support, rather than people with combined depression and hazardous alcohol consumptions concerns, will increase the generalisability of any results found.
- The recruitment method allows for a double blind design and the inclusion of a usual care control group whose members are unaware that others receive a drinking intervention.
- A limitation of this study is in not employing a two-by-two design (presence or absence of Check Your Drinking crossed with presence or absence of MoodGYM); however, we recognise that all registrants to MoodGYM have the expectation of receiving help for their depression, making it unethical to deny them access.

Ethics and dissemination This research comprises the crucial first steps in developing lower-cost and efficacious internet interventions for people suffering from depression who also drink in a hazardous fashion—promoting the widespread availability of care for those in need. This study has been approved by the standing ethics review committee of the Centre for Addiction and Mental Health, and findings will be disseminated in the form of at least one peer-reviewed article and presentations at conferences.

Trial registration number NCT03421080; Pre-results.

INTRODUCTION

Comorbidity between depression and hazardous alcohol use is common.¹ Compared with those with a single condition, such comorbid disorders are associated with

persistence of symptoms, poorer treatment outcomes and poorer social and general functioning.^{2 3} Importantly, there is emerging evidence indicating that people with co-occurring depression and hazardous alcohol use will access care for their depression up to 8 years sooner than they will for their alcohol concerns, providing a unique opportunity to provide early interventions for hazardous alcohol consumption.⁴ Efficacious treatments for comorbid depression and hazardous alcohol use have been developed in face-to-face settings and shown to be superior to single-focused treatments.⁵ However, there is a considerable gap between the need for treatment and availability of, and access to, options for care.⁶ Furthermore, the majority of people with depression and hazardous alcohol use do not access treatment services.⁷ The increasing availability of technology as a supplement to healthcare could be a potential solution to address these challenges. Internet interventions could improve both access and acceptability of treatments for these co-occurring conditions and allow for broad dissemination.^{8–10} In addition, delivery of the intervention online is cost-effective and can be offered flexibly in terms of time and location.^{10–12}

To date, only a few randomised controlled trials have examined computer-based psychological treatment for targeting both depression and hazardous alcohol use, however, with promising results. Kay-Lambkin and colleagues compared therapist-delivered and computer plus therapist-delivered treatment with a single session control condition.¹³ At a 12-month follow-up, both treatment options yielded superior outcomes, whereas computer plus therapist-based treatment showed the largest effect. A similar study compared therapist-delivered cognitive behavioural therapy and motivational interviewing, clinician-assisted computerised cognitive behavioural therapy/motivational interviewing and supportive counselling.¹⁴ After 3 months, therapist-delivered and clinician-assisted computerised cognitive behavioural therapy/motivational interviewing produced superior reductions in depression and alcohol/cannabis use compared with supportive counselling. Furthermore, change in depression levels was predicted by change in alcohol consumption. Two other trials of combined alcohol and depression internet interventions have been conducted with youth, one finding a short-term improvement in both depression and alcohol at 3 months¹⁵ and the other finding no impact of a personalised feedback intervention at a 1-month follow-up.¹⁶

Only one of these internet-based interventions targeting participants with both depression and hazardous alcohol use was conducted without the involvement of a therapist¹⁵ and had a small sample size, focused on young people, and only preliminary findings at a 3-month follow-up. Internet interventions without therapist involvement have the advantages of being scalable, available to those who cannot or will not access a therapist, and are accessible 24 hours a day. Given the potential advantages of such internet interventions, it

is crucial to conduct trials that address this significant gap in the literature. This study will be the first step in the development of such programmes by examining the impact of combining two of the most widely evaluated and empirically supported internet interventions for depression (MoodGYM) and drinking (Check Your Drinking; CYD).

Drinking to cope motives

One important rationale for addressing hazardous alcohol consumption among those with depression is that providing tools to reduce alcohol consumption may indirectly reduce depressive symptoms. In addition, this study will also explore the degree to which receiving the CYD intervention and improvements in depressive symptoms are moderated by participants' motivation to drink alcohol as a means to cope with negative affect, including depressive symptoms. People who drink in a hazardous manner are more likely to endorse the motivation of drinking to cope if they experience current depression compared with those who do not experience current depression.^{17 18} Unfortunately, drinking to 'self-medicate' depressive symptoms is counter-productive and can increase symptom severity.^{19–22} These findings support the hypothesis that reductions in drinking could lead to greater improvement in depressive symptoms among those who drink to cope (as opposed to those who do not drink to cope), provided adequate alternative coping strategies are developed. In addition, two studies^{23 24} have demonstrated that the effect of feedback comparing ones drinking with others, a central component of CYD, is moderated by coping motives. The first study²³ demonstrated stronger effects of personalised normative feedback (PNF) in reducing drinking in a sample of 252 US college students with higher drinking to cope motives. This was evident even when controlling for other motives (social, enhancement and conformity), and when examined simultaneously, coping was the only motive of the four that moderated intervention efficacy. In the second study,²⁴ results of moderated mediation analyses revealed that reductions in exaggerated perceptions of other veterans' drinking, as a function of a PNF intervention, were more strongly associated with reductions in drinking and problems among veterans scoring higher on drinking to cope with other motives controlled. While the explanations provided for the effects of coping motives on PNF efficacy in reducing drinking differed in the college sample versus the veteran sample, both offer additional support for the expectation that inclusion of the CYD intervention will be associated with less hazardous drinking, and thus less depression, among coping drinkers. Thus, examining whether and how drinking to cope may moderate the association between reductions in alcohol consumption and improvements in depressive symptoms is essential in order to identify subgroups more likely to benefit from alcohol interventions, in turn allowing us to better target interventions in this vulnerable population.

Participant sex as a moderator of impact

Participant sex is another factor that may moderate the effects of the interventions on depressive symptoms and hazardous alcohol use. Incidence of depression is higher among females than among males.²⁵ However, males who experience depression appear more likely than females to employ externalising behaviours, such as alcohol consumption, as a means of distracting themselves from their symptoms.²⁶ Previous research has demonstrated that sex and depression moderate responses to brief interventions for alcohol.²⁷ Specifically for women, those with higher levels of depression were less likely to respond to a brief intervention and reduce their alcohol consumption compared with women with lower levels of depression. The reverse was true for men—those with higher levels of depression were more likely to respond to a brief intervention for alcohol by reducing their alcohol consumption compared with men with lower levels of depression. Thus, examining the moderating effect of participant sex will be an important aspect of this study.

Aim of the study

This study will examine the impact of combining two of the most widely evaluated and empirically supported internet interventions for depression (MoodGYM) and drinking (CYD). All participants will be provided access to MoodGYM, with 50% of the sample randomised to a combined intervention group, which will also be provided feedback from the CYD intervention.

Hypothesis 1

It is predicted that participants with both hazardous drinking and depression, allocated to the combined condition (CYD+MoodGYM), will display significant reductions in drinking behaviour in 3 and 6 months compared with the control group only provided with MoodGYM.

Hypothesis 2

Participants with both hazardous drinking and depression, allocated to the combined condition (CYD+MoodGYM), will display significant improvements in depressive symptoms in 3 and 6 months compared with the control group who only receive MoodGYM.

Mediation hypothesis 3

Reductions in alcohol consumption will mediate the effect of intervention condition on reductions in depression symptoms. Specifically, we expect greater reductions in the 3-month alcohol consumption in the combined (vs individual) intervention group, with changes in the 3-month consumption accounting for a significant indirect effect between intervention condition and the 6-month depression symptoms.

Moderated mediation hypotheses 4

Coping motives will moderate the hypothesised indirect effect of intervention condition on depression symptoms via consumption. Specifically, the association between reductions in drinking and reductions in depression

symptoms will be stronger for those participants endorsing stronger coping motives for drinking.

Moderator hypotheses 5

A three-way interaction between sex, baseline depression symptoms and intervention condition is predicted, such that in males, the intervention effect on drinking will be greater for those with higher levels of depressive symptoms at baseline; for females, the intervention effect will be stronger for those with lower levels of depressive symptoms.

METHODS AND ANALYSIS

Participants

Online advertisements (eg, social media advertisements on Facebook and YouTube and website advertisements on Yahoo and Google Adwords), placed across Canada, will target people who are 'experiencing persistent low mood or depression' and who are interested in participating in a study to 'help improve an online intervention for depression'. This recruitment method allows for a double blind design and the inclusion of a usual care control group whose members are unaware that others receive a drinking intervention.²⁸ To determine eligibility, all potential participants, 18 years and older, will undergo an assessment of current depression and of whether they consume alcohol in a hazardous fashion. Participants who score 10 or more on the Patient Health Questionnaire (PHQ-9),²⁹ indicating current depression, will be eligible. Participants who indicate current suicidal ideation on the PHQ-9 will not be eligible to participate and will instead see a pop-up window encouraging them to seek help, along with relevant emergency healthcare contact information. In addition, contact information for the trial coordinator will be provided for extra assistance, and the person will continue to have access to MoodGYM for the duration of the study (but will be recommended alternate options for care). In addition, potential participants must have a score of 8 or more on the Alcohol Use Disorder Identification Test (AUDIT)^{30 31} to indicate current hazardous alcohol use. The AUDIT is ideal for this purpose because it is well validated and distinguishes social drinkers and those with hazardous alcohol consumption.³⁰ Further, a score of 8 or more on the AUDIT has clinical relevance as it is recommended that clients in clinical settings receive a brief intervention from their health professional if they score at or above this cut-off.^{30 32} All participants who are found not eligible for the study will be provided access to MoodGYM for the duration of the study. Exclusion criteria for the trial consist of not meeting the eligibility criteria.

Study design and procedures

This study is a two-arm, double blinded, parallel group randomised control trial of a combination of online interventions for problem drinking and depressive symptoms. Follow-ups will be conducted at 3 and 6 months. See

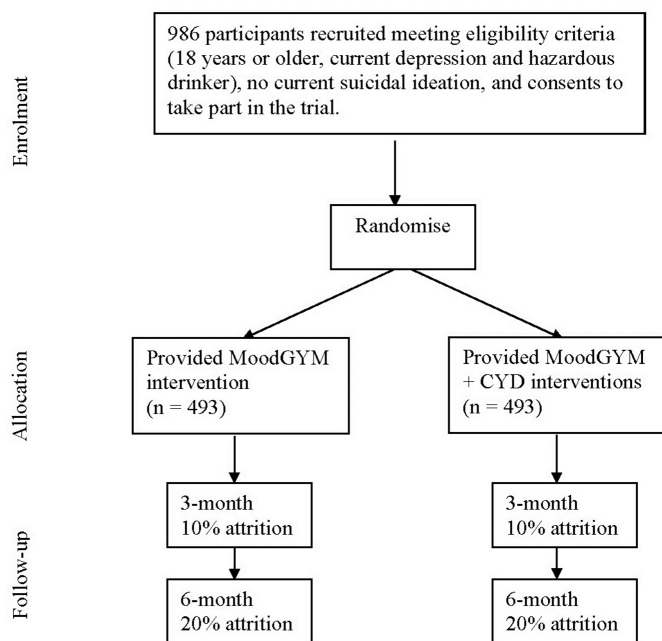


Figure 1 Overview of the proposed intervention trial.

figure 1 for a Consolidated Standards of Reporting Trials diagram of the study design.

Potential participants responding to the advertisement by clicking on a link to the study website will first be provided with a brief description of the study and complete an eligibility screener. Those found eligible will be asked for an email address to be sent a link to an online consent form (see online supplementary file for a model consent form). Participants will be asked to provide their telephone number and mailing address as additional contact information, as well as to provide permission for study staff to contact them via phone or mail for follow-up surveys if correspondence by email is unsuccessful. Those who complete the online consent form will have their postal addresses checked to ensure that it is a real address (and that there are no other participants in the trial who have the same address). Potential participants who pass this postal address check will be sent a link by email to complete the baseline survey and to be randomised into one of the two conditions. Randomisation to condition will occur via an automated replicable algorithm. Because of the large sample size and because allocation is to only two experimental conditions, stratification was judged as unnecessary for the current trial. To reduce loss of potential participants in the study, those who complete the baseline questionnaire and access the online intervention will receive a CAD\$10 Amazon.ca gift card. All participants will be followed up at 3 and 6 months postrandomisation using an online survey (notification sent as a link to the person's email address provided). In order to promote retention, participants completing the 3-month follow-up will be sent a CAD\$20 gift certificate from Amazon.ca, and those completing the 6-month follow-up will be sent an additional CAD\$30 gift certificate from Amazon.ca (ie, total honorarium of CAD\$60 total for each participant).

Participants who do not respond to their initial prompt to complete the follow-up surveys will be sent email reminders. Telephone and postal mail contact will also be attempted for those who do not respond.

Interventions

MoodGYM only

Those randomised to this condition will be provided with access to MoodGYM but will not receive the CYD final report. MoodGYM is a popular, automated, self-help cognitive behavioural therapy programme for depression comprising five modules to be completed over 5 weeks and an online workbook incorporating 29 exercises. A series of published research trials has shown MoodGYM to be effective in reducing depressive symptoms in users in a range of settings (eg, schools, universities, Life-line suicide prevention, UK NHS Choices online), for different aspects of the mental health service spectrum (eg, prevention vs treatment), and different age groups (adults, adolescents).^{33–43} The current trial will employ the latest version of MoodGYM (Mark 4) which has been updated to support mobile devices. The core design and function of the programme has not been altered.

MoodGYM plus CYD

Those assigned to this condition will be provided with access to MoodGYM. In addition, feedback from the CYD intervention will be provided as part of their MoodGYM dashboard in the form of a final report (items used to generate the CYD will be assessed as part of the baseline screening process). The CYD intervention is a brief and personalised online intervention that has been designed to assess and provide feedback on quantity and frequency of drinking and severity of hazardous drinking.⁴⁴ The user is provided with a final report that compares the person's drinking with others in the general population of the same age, sex and country of origin (in this case, Canada). The final report also includes other relevant feedback, including an assessment of severity of alcohol use, and provides recommendations for safe levels of alcohol consumption. The CYD has been subjected to seven randomised trials from two independent research groups, all of which displayed a significant impact of the CYD to reduce hazardous alcohol consumption compared with controls.^{44–50} The controlled access version of the CYD used in this study will be modified to include a brief description of the importance of addressing hazardous drinking among people experiencing depression prior to the intervention content.

Following initial login, all participants will then be sent five reminder emails in the next 2 months to log in to the website and try a different part of the programme. For participants assigned to the combined intervention condition, the email reminders will also ask them to review the content of the CYD final report (the request to review the CYD final report will be removed from the reminder email once the participant has accessed this information on the MoodGYM dashboard).

Patient and public involvement

Both MoodGYM and CYD were developed with patient and public involvement. However, the design of the study (and the conduct of the research) has been (and will be) without explicit patient and public involvement. There are no plans for dissemination of the results to study participants.

Measures

Baseline survey

All drinking outcome variables will ask participants about the past 3 months at both baseline and the corresponding follow-ups. The baseline survey will assess a series of demographic characteristics including age, participants' sex, education, employment status, marital status and family income. The survey will also include measures of Health-related Quality of Life (HRQOL) using the European Health Interview Survey—Quality of Life 8-item (EUROHIS-QoL-8). This short form version has been used in many countries, is robust psychometrically and performance is strongly correlated with scores from the original WHOQoL.⁵¹

Alcohol-related measures

The AUDIT will be used as a measure of severity of alcohol consumption.^{31 52} Drinking outcome variables will comprise: number of drinks in a typical week (identified as the primary outcome variable for drinking),^{53–55} the AUDIT-C (consumption subscale consisting of the variables, frequency of consumption, drinks per drinking day and frequency of 5+ drinking)⁵⁶ and number of consequences associated with drinking in the last 3 months (10 items adapted from Wechsler *et al*, 1994 with one item added asking about driving under the influence of alcohol).^{57–59} Any use of alcohol-related treatment access will be measured using the single item screener taken from the National Epidemiological Survey on Alcohol and Related Conditions.⁶⁰ Finally, all participants will be asked the five-item coping subscale of the Drinking Motives Questionnaire⁶¹ and several other items at baseline in order to generate the CYD final report for those in the intervention condition—usual amount paid for a drink; weight (to generate time under the influence of alcohol) and whether alcohol had a harmful effect on respondents' (1) friendships/social life, (2) physical health, (3) outlook on life (happiness), (4) home life or marriage, (5) work, studies or employment opportunities or (6) financial position.⁶²

Mental health

The 20-item Centre for Epidemiological Studies—Depression (CES-D) will be used as the outcome variable assessing depressive symptoms.⁶³ The PHQ-9 questionnaire will be employed as an eligibility criterion for the study and to identify participants with suicidal ideation.²⁹ Anxiety symptoms will be assessed using the Generalized Anxiety Disorder 7-item (GAD-7).⁶⁴ Alexithymia symptoms will be assessed using the Toronto Alexithymia

scale.⁶⁵ Use of treatment for depression will be assessed by the single item, “Have you ever received treatment for depression from a therapist or doctor?”

Follow-up surveys

All participants will be followed up at 3 and 6 months' time and asked about their current alcohol consumption and depressive symptomatology in the time since their last assessment (see [table 1](#)). Both surveys will assess:

1. drinking-related and alcohol-related harm using the same outcome variables used at baseline;
2. current depressive and anxiety symptoms using the CES-D, the PHQ-9 and the GAD-7;
3. HRQOL using the EUROHIS-QoL-8;
4. use of treatment for hazardous alcohol use or depression employing the same items as the baseline survey.

Use of interventions

The amount and type of use participants make of the MoodGYM intervention (as well as the number of times the CYD final report is viewed) will be recorded, and this information will be used in secondary analyses to test whether degree of involvement is related to reductions in drinking and depressive symptoms. Participants are free to discontinue the intervention at any time by choosing not to log onto the website and by not completing the follow-ups.

Data management

Using personal electronic devices, participants will log onto a secure server and will complete baseline and follow-up assessments. All assessment and intervention usage data will be stored on a secure server. Data on the server will be downloaded and backed up weekly. Downloaded files will be encrypted and stored on a secure network, protected by a firewall. The network has restricted access, and user accounts are password protected. Data quality monitoring including data rules, valid values, range checks and missing data rules are built into the survey software.

Power analysis

Power calculations were conducted using the G-power software application.⁶⁶ Estimates provided by G-power are based on conventions established by Jacob Cohen's work on power analysis.^{67 68} Based on previous evaluations of CYD and similar web-based brief alcohol interventions,⁶⁹ we expect effects on drinking to be in the small range (eg, Cohen, 1992; $d=0.20$). We expect small to moderate effect sizes in associations between drinking and depressive symptoms. Moreover, we estimated sample size based on ability to detect small univariate effects on drinking and depression outcomes as well as considering the need to have sufficient males and females to conduct the proposed analysis of the moderating role of sex on the impact of the CYD (approximately 70% of the sample will be female based on previous research employing similar recruitment strategies).⁷⁰ Given maximum expected attrition, a sample size of 788 will provide 80 power to detect

Table 1 Study assessment points and instruments

	Study period			
	Enrolment	Allocation	Postallocation	Close-out
Time point	$-t_1$	0	t_{3m}	t_{6m}
Enrolment				
Eligibility screen	X			
Informed consent	X			
Allocation				
		X		
Interventions				
MoodGYM only			X	
MoodGYM+CYD			X	
Assessments				
Baseline variables				
Demographics	X			
Drinking Motives Questionnaire subscale	X			
Alcohol-related treatment access	X		X	X
PHQ-9	X		X	X
GAD-7	X		X	X
Toronto Alexithymia scale	X			
Treatment for depression access	X		X	X
Primary outcomes				
No of drinks in a typical week	X		X	X
Secondary outcomes				
CES-D	X		X	X
AUDIT-C	X		X	X
Alcohol consequences	X		X	X
Other variables				
EUROHIS-QoL-8	X		X	X
Use of interventions			X	X

AUDIT, Alcohol Use Disorder Identification Test; CES-D, Centre for Epidemiological Studies—Depression; CYD, Check Your Drinking; EUROHIS-QoL-8, European Health Interview Survey—Quality of Life 8-item; GAD-7, Generalized Anxiety Disorder 7-item; PHQ-9, Patient Health Questionnaire.

effects sizes of $d=0.20$ at a significance level of $p<0.05$. Based on our previous work, we expect a retention rate of 80% across both 3-month and 6-month follow-ups.⁴⁴ Thus, we will recruit an initial sample of 986 participants.

Data analysis

Analyses will be undertaken on an intention-to-treat basis using all available data as suggested by White *et al* with the assumption that the missing data will be missing at random.⁷¹ Hypotheses will be tested using a generalised linear modelling framework.⁷² This analytic approach allows the sophisticated handling of missing data using a maximum likelihood approach. Hypotheses 1 and 2 will evaluate main effects of MoodGYM+CYD (relative to MoodGYM only) on drinking and depressive symptoms, respectively. Baseline demographic factors that are significantly different across condition at baseline will be included as covariates to address any potential

differences. A dummy-coded contrast will represent the MoodGYM+CYD versus MoodGYM only condition. Distributions of outcome variables are likely to be non-normal, and we will adjust the analysis to use an appropriate distribution (eg, negative binomial), as we have done in previous work.^{55 73} Analyses will examine specific effects on 3-month and 6-month outcomes to estimate treatment effects at these different time points. However, we will also conduct longitudinal analyses to provide a comprehensive examination of changes over the course of the trial. Longitudinal analyses will evaluate a parallel process latent growth model where both drinking and depression will be specified latent intercepts (representing baseline levels) and slopes (representing changes over time). Slope factor loadings will be specified as 0 and 1 for time 1 and time 2 for each construct with time 3 being unspecified yielding a parameter estimate that will be indicative

of the average shape of change.⁷⁴ Tests of Hypothesis 1 and Hypothesis 2 will be evaluated by testing intervention effects on the slopes of drinking and depression, respectively. Bayesian estimation with non-informative priors will be used to address missing data potential distributional issues.⁷⁵

Hypothesis 3 will evaluate changes in drinking at a 3-month follow-up as a mediator of CYD intervention effects on depressive symptoms at a 6-month follow-up. We will follow procedures described by Wang and Preacher to assess mediation with Bayesian estimation.⁷⁶ Mediation will test the indirect effect of the intervention on changes in depression at 6 months (B) through changes in 3 months of drinking (A). Both A and B paths will control for baseline outcomes. Hypothesis 4 will be an extension of this model, whereby coping motives are predicted to moderate the indirect effect and the constituent paths (A) and (B).

Hypothesis 5 will extend the main effects models and will include relevant product terms. Hypothesis 5 represents a three-way interaction between participants' sex, intervention condition and baseline depressive symptoms in predicting changes in drinking at 3 and 6 months. Predictors will include the three-way product terms, constituent two-way product terms and main effects. While the three-way interaction is our primary prediction here, we will also examine constituent two-way interactions. All significant interactions will be graphed and accompanied by tests of simple slopes using procedures described by Cohen and colleagues.⁷⁷ Moderator Hypothesis 4 will be evaluated using the same approach where depressive symptoms at 3 and 6 months will be evaluated as a function of the intervention condition, baseline coping motives and the intervention by coping motives product term.

Finally, secondary analyses not described here will investigate any impact of the interventions on health-related quality of life and test the extent to which degree of involvement with the internet interventions is related to outcome.

Data monitoring and quality assurance

Although an independent review of the trial processes and documents is not planned, all clinical research conducted by the Centre for Addiction and Mental Health is subject to review by the Research Quality Assurance programme. Monitors may review participant research records and data, confirm that the regulatory binder is complete and check research staff adherence to institutional policies, including educational requirements such as Good Clinical Practice and Tri-Council Policy Statement 2 training.

ETHICS AND DISSEMINATION

The trial has been formally registered to obtain an International Standard Randomization Controlled Trial Number. In addition to publication and presentation of the findings from this study to promote wide

dissemination, the results will directly inform the internet interventions developed within the research unit.

Confidentiality

All study-related information will be stored electronically on secure servers with access limited to authorised staff. To maintain participant confidentiality, data files will be deidentified and autonomised using an identification number. The file linking the identification number and participant identifying information will be password protected, stored separately from trial data and will be accessed by authorised staff. Identifying information will be destroyed by the principal investigator after completion of the study.

The principal investigator will have access to the data and will provide coinvestigators and trained research analysts with cleaned, deidentified data sets.

DISCUSSION

Many people with co-occurring depression and hazardous alcohol use do not access treatment services.⁷ One possible solution to address the considerable gap between need, availability and access to effective treatment is using technology as a supplement healthcare.⁶ Indeed, the growing use of the internet for health information allows online interventions to be scalable, accessible 24 hours a day and even accessible without the involvement of a therapist. Nonetheless, few studies have evaluated computer-based treatments for co-occurring mental health issues and addiction. Therefore, this study aims to address this gap in the literature by examining the impact of combining two evidence-based internet interventions for depression (MoodGYM) and for drinking (CYD). The brief nature of the CYD and the substantial research base indicating the efficacy of the CYD among people who consume alcohol in a hazardous fashion suggest that the next natural step of research on this topic is to explore the extent to which the CYD can be applied among vulnerable populations, such as those with depression. In addition, the results of this study will enhance our general understanding of internet interventions for addictions, as well as inform how treatments can be developed and matched to the needs of those with co-occurring mental health and hazardous drinking.

Trial status

Protocol version: 1

Anticipated recruitment start date: March 2018

Approximate date recruitment will be completed: December 2019

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Contributors 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, FK-L, CN and KMG conceived the design and wrote the grant application. JAC, CSH, AG, CN and CS developed the protocol and wrote the first draft of this manuscript. AB and KB developed the online tool and conceived of and developed the online RCT platform for conducting the current study. All authors have contributed to the manuscript drafting process and have read and approved the final manuscript.

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Competing interests KB and AB are owners and employees of eHub Health Pty Ltd which has a commercial license to deliver the interventions. KMG is entitled to a share of royalties generated by the commercialisation of MoodGYM. The authors declare that they have no other competing interest.

Patient consent Obtained.

Ethics approval This research was approved by the Ethics Review Board at the Centre for Addiction and Mental Health.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Study materials are available from the corresponding author.

Author note Since there are minimal risks related to receiving these online interventions, a Data Monitoring Committee will not be formed, and interim analyses will not be performed. It has been demonstrated in previous online trials evaluating internet interventions for depression that rates of symptom exacerbation and suicide risk are extremely low in this non-treatment seeking population. If participants express suicidal ideation at baseline (excluded from the trial) or at 3-month or 6-month follow-ups, they will see a pop-up window encouraging them to seek help and provide relevant contact information. In addition, contact information for trial staff will be provided at all points throughout the study. In the event that a participant contacts the trial staff because of concern about their depression or drinking and would like to access treatment, assistance will be provided.

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REFERENCES

- Bolton JM, Robinson J, Sareen J. Self-medication of mood disorders with alcohol and drugs in the National Epidemiologic Survey on Alcohol and Related Conditions. *J Affect Disord* 2009;115:367–75.
- Quello SB, Brady KT, Sonne SC. Mood disorders and substance use disorder: a complex comorbidity. *Sci Pract Perspect* 2005;3:13–21.
- Davis LL, Frazier E, Husain MM, et al. Substance use disorder comorbidity in major depressive disorder: a confirmatory analysis of the STAR*D cohort. *Am J Addict* 2006;15:278–85.
- Kay Lambkin FJ. Lifetime Affective and Alcohol Use Disorder: Impact of Comorbidity on Current Functioning and Service Use in a Rural Population. *J Addict Res Ther* 2014;s10.
- Baker AL, Kavanagh DJ, Kay-Lambkin FJ, et al. Randomized controlled trial of cognitive-behavioural therapy for coexisting depression and alcohol problems: short-term outcome. *Addiction* 2010;105:87–99.
- Kohn R, Saxena S, Levav I, et al. The treatment gap in mental health care. *Bull World Health Organ* 2004;82:858–66.
- Clarkin JF, Kendall PC. Comorbidity and treatment planning: summary and future directions. *J Consult Clin Psychol* 1992;60:904–8.
- Kaltenthaler E, Parry G, Beverley C, et al. Computerised cognitive-behavioural therapy for depression: systematic review. *Br J Psychiatry* 2008;193:181–4.
- Cuijpers P, van Straten A, Andersson G. Internet-administered cognitive behavior therapy for health problems: a systematic review. *J Behav Med* 2008;31:169–77.
- Bewick BM, Trusler K, Barkham M, et al. The effectiveness of web-based interventions designed to decrease alcohol consumption—a systematic review. *Prev Med* 2008;47:17–26.
- Cunningham JA, Humphreys K, Koski-Jännes A. Providing personalized assessment feedback for problem drinking on the Internet: a pilot project. *J Stud Alcohol* 2000;61:794–8.
- Cunningham JA, Kypri K, McCambridge J. The use of emerging technologies in alcohol treatment. *Alcohol Res Health* 2011;33:320–6.
- Kay-Lambkin FJ, Baker AL, Lewin TJ, et al. Computer-based psychological treatment for comorbid depression and problematic alcohol and/or cannabis use: a randomized controlled trial of clinical efficacy. *Addiction* 2009;104:378–88.
- Kay-Lambkin FJ, Baker AL, Kelly B, et al. Clinician-assisted computerised versus therapist-delivered treatment for depressive and addictive disorders: a randomised controlled trial. *Med J Aust* 2011;195:S44–50.
- Deady M, Mills KL, Teesson M, et al. An Online Intervention for Co-Occurring Depression and Problematic Alcohol Use in Young People: Primary Outcomes From a Randomized Controlled Trial. *J Med Internet Res* 2016;18:e71.
- Geisner IM, Varvil-Weld L, Mittmann AJ, et al. Brief web-based intervention for college students with comorbid risky alcohol use and depressed mood: does it work and for whom? *Addict Behav* 2015;42:36–43.
- Nolen-Hoeksema S, Desrosiers A, Wilsnack SC. Predictors of alcohol-related problems among depressed and non-depressed women. *J Affect Disord* 2013;150:967–73.
- Foster DW, Young CM, Steers M, et al. Tears in your beer: Gender differences in coping drinking motives, depressive symptoms and drinking. *Int J Ment Health Addict* 2014;12:730–46.
- Aneshensel CS, Huba GJ. Depression, alcohol use, and smoking over one year: a four-wave longitudinal causal model. *J Abnorm Psychol* 1983;92:134–50.
- Hartka E, Johnstone B, Leino EV, et al. A meta-analysis of depressive symptomatology and alcohol consumption over time. *Br J Addict* 1991;86:1283–98.
- Kwon TY, Kahng SK, Kim H. The Reciprocal Relationship between Depressive Symptoms and Alcohol Consumption: Group Comparison by Employment Status. *Asian Social Work and Policy Review* 2010;4:43–56.
- Holahan CJ, Moos RH, Holahan CK, et al. Drinking to cope and alcohol use and abuse in unipolar depression: a 10-year model. *J Abnorm Psychol* 2003;112:159–65.
- Young CM, Neighbors C, DiBello AM, et al. Coping Motives Moderate Efficacy of Personalized Normative Feedback Among Heavy Drinking U.S. College Students. *J Stud Alcohol Drugs* 2016;77:495–9.
- Young CM, Pedersen ER, Pearson AD, et al. Drinking to Cope Moderates the Efficacy of Changing Veteran Drinking Norms as a Strategy for Reducing Drinking among U. S. Veterans. *Psychol Addict Behav in press*.
- Kessler RC, McGonagle KA, Swartz M, et al. Sex and depression in the National Comorbidity Survey. I: Lifetime prevalence, chronicity and recurrence. *J Affect Disord* 1993;29:85–96.
- Nolen-Hoeksema S. Gender differences in depression. Hammen I, ed. *Handbook of depression*. New York: Guilford Press, 2002:492–509.
- Merrill JE, Reid AE, Carey MP, et al. Gender and depression moderate response to brief motivational intervention for alcohol misuse among college students. *J Consult Clin Psychol* 2014;82:984–92.
- Cunningham JA, Kypri K, McCambridge J. Exploratory randomized controlled trial evaluating the impact of a waiting list control design. *BMC Med Res Methodol* 2013;13:150.
- Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–13.
- Saunders JB, Aasland OG, Babor TF, et al. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on early detection of persons with Harmful Alcohol Consumption—II. *Addiction* 1993;88:791–804.

31. Babor TF, De La Fuente MF, Saunders JB, et al. *AUDIT - The alcohol use disorders identification test: Guidelines for use in primary health care*. Geneva, Switzerland: World Health Organization, 1989.
32. National Institute on Alcohol Abuse and Alcoholism. *Helping patients who drink too much: A clinician's guide*. Rockville, MD: National Institute on Alcohol Abuse and Alcoholism, 2005.
33. Bennett K, Reynolds J, Christensen H, et al. e-hub: an online self-help mental health service in the community. *Med J Aust* 2010;192:S48–52.
34. Caezar AL, Christensen H, Mackinnon A, et al. The YouthMood Project: a cluster randomized controlled trial of an online cognitive behavioral program with adolescents. *J Consult Clin Psychol* 2009;77:1021–32.
35. Christensen H, Griffiths KM, Jorm AF. Delivering interventions for depression by using the internet: randomised controlled trial. *BMJ* 2004;328:265–8.
36. Griffiths KM, Christensen H, Jorm AF, et al. Effect of web-based depression literacy and cognitive-behavioural therapy interventions on stigmatising attitudes to depression: randomised controlled trial. *Br J Psychiatry* 2004;185:342–9.
37. Hickie IB, Davenport TA, Luscombe GM, et al. Practitioner-supported delivery of internet-based cognitive behaviour therapy: evaluation of the feasibility of conducting a cluster randomised trial. *Med J Aust* 2010;192:S31–S35.
38. Høifødt RS, Lillevoll KR, Griffiths KM, et al. The clinical effectiveness of web-based cognitive behavioral therapy with face-to-face therapist support for depressed primary care patients: randomized controlled trial. *J Med Internet Res* 2013;15:e153.
39. Mackinnon A, Griffiths KM, Christensen H. Comparative randomised trial of online cognitive-behavioural therapy and an information website for depression: 12-month outcomes. *Br J Psychiatry* 2008;192:130–4.
40. O'Kearney R, Kang K, Christensen H, et al. A controlled trial of a school-based Internet program for reducing depressive symptoms in adolescent girls. *Depress Anxiety* 2009;26:65–72.
41. Phillips R, Schneider J, Molosankwe I, et al. Randomized controlled trial of computerized cognitive behavioural therapy for depressive symptoms: effectiveness and costs of a workplace intervention. *Psychol Med* 2014;44:741–52.
42. Powell J, Hamborg T, Stallard N, et al. Effectiveness of a web-based cognitive-behavioral tool to improve mental well-being in the general population: randomized controlled trial. *J Med Internet Res* 2012;15:e2.
43. Sethi S. Treating Youth Depression and Anxiety: A Randomised Controlled Trial Examining the Efficacy of Computerised versus Face-to-face Cognitive Behaviour Therapy. *Aust Psychol* 2013;48:249–57.
44. Cunningham JA, Wild TC, Cordingley J, et al. A randomized controlled trial of an internet-based intervention for alcohol abusers. *Addiction* 2009;104:2023–32.
45. Cunningham JA, Koski-Jännes A, Wild TC, et al. Treating alcohol problems with self-help materials: a population study. *J Stud Alcohol* 2002;63:649–54.
46. Doumas DM, Hannah E. Preventing high-risk drinking in youth in the workplace: a web-based normative feedback program. *J Subst Abuse Treat* 2008;34:263–71.
47. Doumas DM, Haustveit T. Reducing heavy drinking in intercollegiate athletes: evaluation of a web-based personalized feedback program. *Sport Psychol* 2008;22:212–28.
48. Doumas DM, McKinley LL, Book P. Evaluation of two Web-based alcohol interventions for mandated college students. *J Subst Abuse Treat* 2009;36:65–74.
49. Cunningham JA, Murphy M, Hendershot CS. Treatment dismantling pilot study to identify the active ingredients in personalized feedback interventions for hazardous alcohol use: randomized controlled trial. *Addict Sci Clin Pract* 2014;10:1.
50. Cunningham JA, Godinho A, Kushnir V. 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* 2017;10:12–16.
51. Schmidt S, Mühlan H, Power M. The EUROHIS-QOL 8-item index: psychometric results of a cross-cultural field study. *Eur J Public Health* 2006;16:420–8.
52. Saunders JB, Conigrave KM. Early identification of alcohol problems. *CMAJ* 1990;143:1060–9.
53. Romelsjö A, Leifman H, Nyström S. A comparative study of two methods for the measurement of alcohol consumption in the general population. *Int J Epidemiol* 1995;24:929–36.
54. Kühnhorn E, Leifman H. Alcohol surveys with high and low coverage rate: a comparative analysis of survey strategies in the alcohol field. *J Stud Alcohol* 1993;54:542–54.
55. Neighbors C, Lewis MA, Atkins DC, et al. Efficacy of web-based personalized normative feedback: a two-year randomized controlled trial. *J Consult Clin Psychol* 2010;78:898–911.
56. Dawson DA, Grant BF, Stinson FS, et al. 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. *Alcohol Clin Exp Res* 2005;29:844–54.
57. Wechsler H, Davenport A, Dowdall G, et al. Health and behavioral consequences of binge drinking in college. A national survey of students at 140 campuses. *JAMA* 1994;272:1672–7.
58. Bertholet N, Daepfen JB, McNeely J, et al. Smartphone application for unhealthy alcohol use: A pilot study. *Subst Abuse* 2017;38:285–91.
59. Bertholet N, Cunningham JA, Faouzi M, et al. Internet-based brief intervention for young men with unhealthy alcohol use: a randomized controlled trial in a general population sample. *Addiction* 2015;110:1735–43.
60. Grant BF, Moore TC, Shepard J, et al. Source and Accuracy Statement. Wave 1. *National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)*. Bethesda, MD: National Institute on Alcohol Abuse and Alcoholism, 2003.
61. Cooper ML. Motivations for alcohol use among adolescents: Development and validation of a four-factor model. *Psychol Assess* 1994;6:117–28.
62. Bondy SJ, Lange P. Measuring alcohol-related harm: test-retest reliability of a popular measure. *Subst Use Misuse* 2000;35:1263–75.
63. Radloff LS. The CES-D scale: A self report depression scale for research in the general population. *Applied Psychological Measurement* 1977;1:385–401.
64. Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006;166:1092.
65. Bagby RM, Parker JD, Taylor GJ. The twenty-item Toronto Alexithymia Scale-I. Item selection and cross-validation of the factor structure. *J Psychosom Res* 1994;38:23–32.
66. Faul F, Erdfelder E, Lang AG, et al. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 2007;39:175–91.
67. Cohen J. A power primer. *Psychol Bull* 1992;112:155–9.
68. Cohen J. *Statistical power analysis for the behavioral sciences*. Hillsdale, N.J.: Lawrence Erlbaum Associates, 1988.
69. Riper H, Blankers M, Hadiwijaya H, et al. Effectiveness of guided and unguided low-intensity internet interventions for adult alcohol misuse: a meta-analysis. *PLoS One* 2014;9:e99912.
70. Donker T, Bennett K, Bennett A, et al. Internet-delivered interpersonal psychotherapy versus internet-delivered cognitive behavioral therapy for adults with depressive symptoms: randomized controlled noninferiority trial. *J Med Internet Res* 2013;15:e82.
71. White IR, Horton NJ, Carpenter J, et al. Strategy for intention to treat analysis in randomised trials with missing outcome data. *BMJ* 2011;342:d40.
72. Fox J. *Applied regression analysis and generalized linear models*. 2nd ed. Los Angeles: Sage, 2008.
73. Atkins DC, Baldwin SA, Zheng C, et al. A Tutorial on Count Regression and Zero-Altered Count Models for Longitudinal Substance Use Data (vol 27, pg 166, 2012). *Psychol Addict Behav* 2013;27:379–79.
74. Duncan TE, Duncan SC, Strycker LA. *An introduction to latent variable growth curve modeling: Concepts, issues, and application*: Routledge Academic, 2013.
75. Muthén B, Asparouhov T. Bayesian structural equation modeling: a more flexible representation of substantive theory. *Psychol Methods* 2012;17:313–35.
76. Wang L, Preacher KJ. Moderated Mediation Analysis Using Bayesian Methods. *Structural Equation Modeling: A Multidisciplinary Journal* 2015;22:249–63.
77. Cohen J, Cohen P, West SG, et al. *Applied multiple regression/correlation analysis for the behavioral sciences*. 2nd. ed: Routledge, 2013.