ADDICTION
SSA SOCIETY FOR THE STUDY OF ADDICTION
TRIAL PROTOCOL
doi:10.1111/add.14034

Alcohol e-Help: study protocol for a web-based self-help program to reduce alcohol use in adults with drinking patterns considered harmful, hazardous or suggestive of dependence in middle-income countries

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ABSTRACT

Background and aims Given the scarcity of alcohol prevention and alcohol use disorder treatments in many low and middle-income countries, the World Health Organization launched an e-health portal on alcohol and health that includes a Web-based self-help program. This paper presents the protocol for a multicentre randomized controlled trial (RCT) to test the efficacy of the internet-based self-help intervention to reduce alcohol use. **Design** Two-arm randomized controlled trial (RCT) with follow-up 6 months after randomization. **Setting** Community samples in middle-income countries. **Participants** People aged 18+, with Alcohol Use Disorders Identification Test (AUDIT) scores of 8+ indicating hazardous alcohol consumption. **Intervention and comparator** Offer of an internet-based self-help intervention, 'Alcohol e-Health', compared with a 'waiting list' control group. The intervention, adapted from a previous program with evidence of effectiveness in a high-income country, consists of modules to reduce or entirely stop drinking. **Measurements** The primary outcome measure is change in the Alcohol Use Disorders Identification Test (AUDIT) score assessed at 6-month follow-up. Secondary outcomes include self-reported the numbers of standard drinks and alcohol-free days in a typical week during the past 6 months, and cessation of harmful or hazardous drinking (AUDIT < 8). **Analysis** Data analysis will be by intention-to-treat, using analysis of covariance to test if program participants will experience a greater reduction in their AUDIT score than controls at follow-up. Secondary outcomes will be analysed by (generalized) linear mixed models. Complier average causal effect and baseline observations carried forward will be used in sensitivity analyses. **Comments** If the Alcohol e-Health program is found to be effective, the potential public health impact of its expansion into countries with underdeveloped alcohol prevention and alcohol use disorder treatment systems world-wide is considerable.

Keywords Alcohol, internet, middle-income countries, public health, self-help, World Health Organization.

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Submitted 16 March 2017; initial review completed 9 June 2017; final version accepted 13 September 2017

INTRODUCTION

The burden of mental, neurological and substance use disorders (SUD) continues to grow, impacting individual and public health significantly, and having major social and economic consequences. Taken together, SUD and other mental disorders have been estimated to account for 7.4% of the total global burden of disease [1], with alcohol misuse

alone accounting for 5.1 and 5.9% of all deaths world-wide [2]. Its economic consequences are equally large [1].

In recent years, internet-based preventative and treatment self-help programs targeting alcohol misuse and alcohol use disorders have been developed [3], with the largest effect sizes reported for low-intensity, cognitive–behavioural therapy and self control-based internet programs that target alcohol misuse in high-income countries [4–6]. Such web-based programs can reach higher-risk individuals earlier, when more pronounced alcohol use disorders are not yet established fully [6]. Moreover, these programs have the capacity to reach 'hidden' drinkers in the general population who fail to contact any health professional, which is also of great importance from a public health perspective [7].

Web-based programs to reduce alcohol use are characterized generally by their low treatment threshold and non-restrictive setting for intervention [8], and for remarkably positive cost–benefit ratios [8]. The latter is of interest for low- and middle-income countries, as such programs may increase access to cost-effective addiction treatments.

On 6 December 2012, the World Health Organization (WHO) launched its e-health portal for alcohol and alcohol-related consequences on health. This portal provides information for policymakers, professionals and the lay public on alcohol and alcohol-related health. Developing a generic portal such as this, which can be translated easily into other languages and adapted to different cultures, is part of the WHO's Global Strategy to reduce the harmful use of alcohol [9]. The portal includes the WHO web-based self-help program called 'Alcohol e-Health', an evidence-based intervention developed initially in the Netherlands [10] as a means to reduce harmful or hazardous alcohol use, and use suggestive of dependence. This program has been implemented by the WHO Department of Mental Health and Substance Abuse, in collaboration with the Netherlands' Trimbos Institute, and with institutes and organizations in Belarus, Brazil, India and Mexico. As this self-help program was revised completely from its original version [10] and translated into different languages, the currently intended WHO study will test the revised interventions' effectiveness in a cluster-randomized controlled trial (RCT) across four countries. The study's primary hypothesis is that Alcohol e-Health program participants will exhibit greater reductions in their Alcohol Use Disorders Identification score (AUDIT, primary outcome) [11] at 6-month follow-up than subjects allocated to a waiting-list. We also expect that those in the active program will reduce the number of standard drinks they consume weekly and increase their weekly number of alcohol-free days more than controls; and that a smaller proportion of participants in versus not in the program will be classified as harmful or hazardous drinkers at 6-month follow-up.

METHODS

Design

The study will be conducted and reported in accordance with the CONSORT-EHEALTH Checklist [12] that extends the Consolidated Standards of Reporting Trials (CONSORT) statement for clinical trials reporting for internet-based intervention requirements, and is registered currently at Current Controlled Trials (registration number: ISRCTN14037475).

Study population

Recruitment will be conducted via information flyers (e.g. in waiting rooms of hospitals and private offices) and by newspapers, magazines, radio, social media, websites and informational events related to alcohol and health to promote the WHO portal between January and September 2017. This broad recruitment strategy allows for different recruitment conditions in the participating countries. Study inclusion and exclusion criteria are: patient age from 18–75 years; residency in one of the participating countries; at least weekly internet access; and a screening AUDIT score ≥ 8. Exclusion criteria are either illicit drug use or cannabis/synthetic cannabinoids > 4 days during the past month. Further details and the rationale behind these criteria are provided in Table 2.

Study interventions

Subjects in the active study arm will participate in the Alcohol e-Health program, while those in the control arm will be assigned to a waiting-list where they will be offered general information on alcohol and its effects on health, with program access granted 6 months later. The Alcohol e-Health program is an accessible self-help tool for people seeking to reduce or discontinue their use of alcohol. Participants can register and use the program in their own time, at their own pace and free of charge. They are encouraged to complete all parts of the program, to repeat any parts they feel they perceive as helpful and to use the program for at least 6 weeks. Alcohol e-Health provides support to encourage individuals to think about their drinking habits, decide whether or not to change their drinking behaviours, set goals regarding their drinking, take action towards reducing or stopping their drinking, measure their progress and deal with relapses to their previous drinking pattern.

When participants enlist for the Alcohol e-Health program they are directed to complete the AUDIT and subsequently receive personalized feedback, according to their individual drinking level. Personalized feedback is provided according to defined AUDIT risk levels for non-risky (< 8 drinks/week), potentially harmful or hazardous drinking

(8–19 drinks/week) and drinking that is suggestive of dependence (≥ 20 drinks/week). Participants are asked to consider the advantages and disadvantages of drinking and have access to a comprehensive diary, where they can record how much alcohol they have consumed, what and when they drank, where and with whom they drank, how they feel about it and other comments. The concept of a standard drink is explained in detail and a separate drink calculator is available to assist participants. Drinks are visualized by pictures of common—sometimes country-specific—drinks and can be dragged and dropped into the consumption diary. Diary data are used to generate tailored feedback on how well participants are meeting the drinking goals they set during the first stage of the program, and to create longitudinal, graphic records of their progress. Participants are advised to complete the diary daily. Based on diary entries, risky situations are identified and motivational strategies provided to help participants to maintain higher levels of resistance under such circumstances. Tools also are made available to help them develop their own personal ways to cope if they relapse, and to explore how they can resist social pressures to drink excessively. Throughout the program participants are permitted to contact, by e-mail in their native language, a practitioner qualified to deliver brief alcohol interventions and provide any other assistance they need. At the end of the 6-week program, participants are encouraged to complete a questionnaire describing their progress and are offered tailored feedback. They also are free to continue the Alcohol e-Health program, even after the recommended program duration of 6 weeks, if they feel the need.

Conversely, those within in the waiting-list control group will be told that they will have access to the program in 6 months, and referred to a web page containing information about the various types of alcoholic beverage, standard drink definitions, the effects of alcohol on the mind and body, the social effects of drinking alcohol, risk factors for alcohol dependence, women and alcohol and adolescent alcohol use. If the study fails to document the program's effectiveness, corresponding waiting-list controls will be informed about this result and offered program access as an option.

Measurement instruments

The main outcome will be change in the AUDIT [11] score. Corresponding AUDIT versions are available in Russian, Spanish and Portuguese. A score ≥ 8 indicates a strong likelihood of hazardous or harmful alcohol consumption. As follow-up will be limited to 6 months, the AUDIT will be assessed for the last 6 months instead of the last 12 for items 9 and 10, both at baseline and follow-up. However, additional questions employing the 12-month period will be included for comparison, and given the study inclusion criteria (AUDIT ≥ 8).

Secondary outcomes will be (Table 1): (1) falling below the cut-off of hazardous or harmful alcohol use (AUDIT score < 8); (2) weekly number of standard drinks; (3) weekly alcohol-free days (recalling the previous week); and (4) program satisfaction, rated using the eight-item Client Satisfaction Questionnaire [13]. Moreover, all study participants will be asked about any other alcohol use disorder treatment services they used between baseline and the 6-month follow-up. They also will be asked to grade any negative effects they have experienced, as per Rozental *et al.* [14].

Estimating expected effect sizes and required sample size

In a recent meta-analysis [4], the average effect size of a single, web-based self-help intervention to reduce alcohol misuse, measured as Cohen's *d*, was 0.20. However, in internet-based studies involving waiting-list controls, Cohen's *d* doubles to approximately 0.40 as they tend to overestimate intervention effects, largely because the disappointment of highly motivated participants allocated to the waiting list can affect their outcomes negatively [15]. Using G*Power software to achieve the 95% confidence (alpha = 0.05) and 95% power (1-beta = 0.95) required to satisfy the requirements of practical/clinical relevance, for analysis of covariance with one covariate (country) the required sample size, per study arm, is 195, which means 2 × 195 = 390 subjects combining program participants and controls. Assuming an intraclass correlation coefficient of 0.02, this number must be multiplied by 1.651 ($D = 1 + (30.5 \times 1.1–1) \times 0.05 = 1.651$), yielding an

Table 1 Overview of measurements, instruments and assessment points planned for the trial.

Assessments/instruments	*Baseline*	*6-month follow-up*
Socio-demographics	x	
Alcohol Use Disorders Identification Test (AUDIT) score	x	x
Weekly number of standard drinks[a]	x	x
Weekly number of alcohol-free days[a]	x	x
8-item Client Satisfaction Questionnaire	x	x
Negative effects[b]		x

[a]Based on a single question with seven answering fields asking about alcohol use, in standard drinks, on each day of a typical week during the preceding 6 months. [b]Negative effects experienced will be graded by asking participants if they have experienced any unwanted side effects they believe are either attributable to or potentially related otherwise to the intervention. For each listed effect, they are then asked to provide the time of onset, frequency and duration and to rate how much they were affected by the effect, both when it occurred and at the time of assessment (Rozental *et al.* [14]). Note that where 'x' is indicated both at baseline and 6-month follow-up, the outcome of interest is 'change between baseline and 6-month follow-up'.

overall sample size of $1.651 \times 390 = 643$. However, as the data collected will be clustered by country (four countries), and cluster size may vary, some statistical power will be lost. To compensate, we will add 10% to the overall sample, as recommended by van Breukelen & Candel [16], resulting in a final target sample size of $643 \times 1.10 \sim 708$ participants across all four countries, which averages to 177 ($708 \div 4$) per country.

Screening and obtaining consent

Once potential participants arrive on the Alcohol e-Health program home page, they will be asked to complete the AUDIT. Those with an AUDIT score < 8 will receive individual feedback on their low-risk drinking, and are assured that they do not need to complete the program. Other than being provided with alcohol education material, they will not take further part in the study. Those with an AUDIT score ≥ 8 will be given further details about the study, including: (1) study aims and duration; (2) inclusion and exclusion criteria (Table 2); (3) the two different study conditions and the 50 : 50 likelihood that they will be allocated to one or the other; (4) the potential risks of participation and all safety agreements that apply for the 6-month period between their baseline assessment and follow-up; (5) that Alcohol e-Health cannot replace face-to-face therapy for problematic alcohol use/abuse; (6) how their participation is entirely voluntary and they have the right to withdraw from the study at any time without consequences; (7) that the study has already been approved by the WHO Research Ethics Committee and the four country-specific ethics committees; and (8) that they will be informed about country-specific contacts if they have further questions. They will also be assured that the telephone number they submit for a contact person, in case problems arise, will be used for this purpose only and not shared with any third party. Informed consent will be assumed when they select all the necessary fields on the on-line informed consent form and click the submission icon. Those who provide informed consent will then be asked to create an anonymous login name and password, with which they can access their user account at any time.

Randomization and group allocation

Once participants are confirmed eligible for the study and have completed their baseline assessment they will be time–space randomized, by computer, to either the Alcohol e-Health program in their respective language or the waiting list, in a 1 : 1 ratio in each country. This non-blinded assignment will be registered automatically in the background database. An IP address check will be performed to minimize the risk of individuals participating multiple times, and the risk that those allocated to the waiting-list will re-enlist in an attempt to join the active treatment group.

Trial flow

Once participants complete the baseline assessment successfully (t_0) they will be introduced, step by step, to their allocated study arm, and informed either that they can start with the first part of the program (active treatment) or that they will be eligible to access the Alcohol e-Health program after 6 months (the waiting-list).

The 6-month follow-up assessment will be performed in two steps. First, an electronic follow-up version will be sent to all participants. Where necessary, an electronic reminder will be sent, up to twice. Should participants fail to complete the follow-up assessment despite two electronically delivered reminders, they will be contacted by telephone and interviewed by study collaborators in their

Table 2 Overview of study inclusion and exclusion criteria, and the rationale behind them.

Criteria	*Rationale*
Inclusion criteria	
Age between 18 and 75 years	To ensure a minimal age of participation
A resident of one of the participating pilot countries	To be covered by local ethics board approval
At least weekly internet access	To ensure at least minimal program access
A screening AUDIT score ≥ 8	To include adults with potentially hazardous or harmful alcohol consumption, and those whose drinking habits are suggestive of dependence
Exclusion criteria	
Current substance abuse treatment	To avoid confounding treatment effects
Use of opioids, inhalants, cocaine/crack or amphetamine/amphetamine-like stimulants, sedatives during the past month or cannabis/synthetic cannabinoids for more than 4 days during the past month	To prevent confounding effects with other frequently used, mind-altering drugs

AUDIT = Alcohol Use Disorders Identification Test.

own language. These calls will be made from numbers that cannot be traced to any institution or agency linked to alcohol prevention or treatment, and nothing will be revealed regarding the nature of the call until the person has been identified clearly as the study participant of interest. Participants who decline to be interviewed will be asked, respectfully, to provide a reason for refusing, which will be documented.

Study compensation

Once all 6-month follow-up assessments have been completed, a raffle will be held in every country, with each participant—whether in active treatment or on the waiting-list—eligible to win a tablet. This was selected as the prize because we deemed it likely to be attractive to all participants and of comparable, non-monetary value in every country. Any subject who wins a tablet will be given the choice to either keep it or donate its value to charity.

Program dropouts

During each of the 6 program weeks, participants in the Alcohol e-Health program condition will be sent an automated e-mail containing a reminder for them to log in and continue with the program, a direct link to the country-specific Alcohol e-Health login site and a motivational hint linked to their progress in the program and program contents. Any participant who fails to log in will receive a reminder e-mail every 3 days for the following 2 weeks. If they do not resume their participation despite these reminders, they will still have program access should they decide to continue their participation later (e.g. after their holidays). Thus, except for those who withdraw their informed consent, there will be no program dropouts and all participants allocated to either study condition will be included in intention-to-treat (ITT) analyses.

Data analysis

Data will be analysed according to ITT principles, and expected to be missing at random (MAR). For ITT analyses, we will thus apply the multiple imputations procedure (AMELIA II) of the statistical software package R (R Foundation for Statistical Computing, Vienna, Austria), which imputes missing data using all available baseline variables (socio-demographic and health- and alcohol-related).

Analysis of the primary outcome

We will test the primary hypothesis—that program participants will experience a greater reduction in their AUDIT score than controls at 6-month follow-up—using analysis of covariance (ANCOVA), entering country as the covariable in the imputed ITT data set. A difference in mean AUDIT scores between the program and waiting-list groups at a two-sided P-value ≤ 0.05 will be interpreted as significant.

Analysis of secondary outcomes

Differences in primary and secondary outcome variables between baseline and follow-up will be tested using linear mixed models. Linear mixed models will be specified appropriately to model the clusters and repeated measures by defining random effects for clusters and time (repeated measures). Appropriate covariance matrices for the random effects will be used; e.g. AR(1) for repeated measures and unstructured covariance matrix for centre effects. For binary or non-normal outcomes, generalized linear mixed models will be employed to define appropriate link functions. Robust variance estimators will be used. For generalized linear mixed-model fixed effects, coefficients will be interpreted in the context of subject-specific (non-marginal) model fit.

Results from the imputed data set will be compared and reported together with the non-imputed data set (complete case analysis). To incorporate the effect of compliance on the primary analysis, we will perform baseline observation carried forward (BOCF) analysis [17] and complier average causal effect (CACE) analysis (cf. [18,19]) to analyse the sensitivity of the intended ITT analysis. Compliance in the CACE is defined as ≥ three logins during the 6-week program. Assumptions of the CACE analysis—(1) well-balanced study arms and (2) that benefit is comparable among noncompliers in both study arms—will be assessed beforehand. The significance of the CACE analysis will be evaluated by calculating a 95% confidence interval for the mean effect difference between the two study arms. A shifted 95% confidence interval—e.g. excluding zero—indicates a P-value < 0.05.

Safety

Throughout the 6-week program, participants will be encouraged to see a health professional if they experience acute alcohol withdrawal or other severe physical or mental symptoms, and afforded access to a country-specific medical advisory and emergency list. At all times, this list will remain accessible to participants in both study arms before, during and up to 6 months after their study participation, even if they withdraw.

Ethics review

This RCT will be executed in compliance with the Helsinki Declaration, and was approved by the WHO Ethics Review Committee in October 2015 (RPC756) and four country-specific ethic committees.

DISCUSSION

To our knowledge, this will be the first RCT to compare the effectiveness of an international web-based self-help program for harmful or hazardous drinkers in middle-income countries. We start with three typical middle-income countries (Belarus, Brazil and Mexico) and one lower middle-income country (India), anticipating that the public health effect will be stronger in middle- than low-income countries. However, because internet access has been increasing steadily in low-income countries, we anticipate that web-based alcohol interventions will also soon be of public health relevance there. Consequently, if the Alcohol e-Health program is proved to be effective in the four countries we are evaluating, it opens up its potential use in other diverse countries world-wide, and renders it much more attractive to authorities in countries where it has not yet been introduced. Moreover, individuals who fear stigmatization for their alcohol use and, thus, purposefully avoid seeking face-to-face services, might benefit from this easy-to-access and anonymous program, as might individuals with impaired physical function and/or mobility. Conversely, the program should be ineffective among individuals who are unable to read and write in any of the available project languages, and among those lacking internet access. However, internet access is increasing rapidly in middle-income countries [20], probably at a much greater pace than access to adequate face-to-face services for alcohol use disorders.

We have chosen to use waiting-list controls for ethical reasons as we feel that, if the program is proved to be effective, these individuals also deserve access, especially in countries in which alcohol use disorder services are either very poorly developed or virtually non-existent, such as the ones studied here. We recognize that potential problems might arise in adopting a waiting-list as the alternative 'treatment'. One problem relates to the risk that participants may interpret their waiting-list allocation as a reason for them to delay change, which would potentially widen the outcome gap between active and inactive treatment, thereby resulting in an overestimation of treatment effects and the potential for type I error [15]. However, an opposing possibility is that controls will become cross-contaminated, motivated to change through the screening procedure itself and finding other means to manage problem drinking (such as Alcoholics Anonymous), which would result in type II error. This said, all the information provided to our controls is freely accessible via the internet, and we have intentionally selected countries in which other such alternative methods are currently sparse.

Our power calculation fails to account directly for a certain percentage of participants dropping out of the program, instead adopting the effect sizes reported for similar studies in which dropout rates should be comparable. We have learned from these earlier studies that a substantial number of subjects will take breaks for 2 or more weeks during the recommended 6-week intervention (e.g. for vacations), but then resume their participation later [7]. This reflects one disadvantage of self-help internet interventions that are available 24/7, in that those who partake of such interventions might feel less invested and be more likely to either interrupt or discontinue their involvement [7].

Such anticipated high attrition rates, both during the program and at follow-up, will be addressed by: (1) sending participants weekly, motivational reminders by e-mail and further motivational messages displayed prominently every time they log onto the program website; (2) performing ITT analyses and imputing all missing values in the final data set; (3) attempting to conduct telephone interviews of participants who fail to complete the online follow-up questionnaire after receiving two e-mail reminders; and (4) in each of the four participating countries, raffling a computer tablet among all individuals completing the 6-month assessment, irrespective of treatment arm.

If the program is proved to be effective, the public health impact of its expansion into many low- and middle-income countries world-wide, with underdeveloped alcohol prevention and alcohol use disorder treatment systems, could be enormous.

Clinical trial registration

This trial is registered at Current Controlled Trials and traceable as ISRCTN14037475.

Declaration of interests

None.

Acknowledgements

The authors want to thank the following additional members of the WHO e-health project on Alcohol and Health Investigators Group: Ekaterina Lapushinskaya, Pavel Rynkov and Dmitry Statkevich from Belarus; Roseli Boerngen Lacerda, Telmo Ronzani and Laisa Sartes from Brazil; Asunción Lara and Morise Fernández from Mexico; and Anubha Dhall, Monica Mongia and Urvashi Raj from India.

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