

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Efficacy of an Internet-based self-help intervention to reduce co-occurring alcohol misuse and depression symptoms in adults: study protocol of a three-arm randomised controlled trial
AUTHORS	Schaub, Michael; Blankers, Matthijs; Lehr, Dirk; Boss, Leif; Riper, Heleen; Dekker, Jack; Goudriaan, Anna; Maier, Larissa; Haug, Severin; Amann, Manuel; Dey, Michelle; Wenger, Andreas; Ebert, David

VERSION 1 - REVIEW

REVIEWER	Cristina Botella Universitat Jaume I (Spain)
REVIEW RETURNED	05-Mar-2016

GENERAL COMMENTS	<p>This is a very interesting study, and the results can be very useful, both from a social a scientific point of view.</p> <p>The study is very well designed and meets the requirements that must require a study of this nature.</p> <p>The authors indicate that the approval from ethics committees have been obtained, the study has been registered and is also indicated which has been funded.</p> <p>I only would point out the following:</p> <ul style="list-style-type: none">- the authors should better explain how they will conceal the allocation sequence.- they should also recognize, as a limitation of the study, participants are going to be recruited in different countries, but they have not defined a specific number of participants in each country, so this could be a bias.- in the discussion section is said: "this will be the first randomised controlled prevention trial to compare the efficacy and cost-effectiveness...". Using the word prevention can lead to confusion regarding compliance or not the different diagnostic criteria. Moreover, given the primary outcome measure used in the study, it would be better (as in the introduction section), to say: "to reduce alcohol misuse and depressive symptoms in comparison with a...". <p>Apart from these details, the protocol is very appropriate and the study deserves to be published</p>
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REVIEWER	Sally Hunt University of New South Wales, Australia
REVIEW RETURNED	14-Mar-2016

GENERAL COMMENTS	<p>Overall this is an interesting and promising study design. A few questions and comments are detailed below:</p> <p>Abstract</p> <ul style="list-style-type: none"> - pp3 line17 Replace "would be" with "is" - pp4 line22 Kay-Lambkin et al., have published their SHADE study which was a randomised controlled trial of a combined internet-based self-help intervention for alcohol use and depression. <p>Introduction</p> <ul style="list-style-type: none"> - pp5 line 28 Dual diagnosis disorders are also known as co-morbid disorders and since you use this term later in the paragraph it would be worth including it in your list of alternative terms. - pp5 line 57 References needed regarding the trials on tobacco, alcohol, cannabis and cocaine. - pp6 line 30 I disagree with the statement that "relatively few clinical trials have examined the efficacy of CBT for substance use disorder and depression in combination or in succession" <p>Methods and analyses</p> <ul style="list-style-type: none"> - pp7 line 52 Use the more recent MI reference for Miller and Rollnick : Miller, W. R., & Rollnick, S. (2012). Motivational interviewing: Helping people change. Guilford press. - pp8 line 18 State here that the allocation is random. This is covered in a later section (see comments below) so consider merging these sections to avoid overlap. - pp12 line 25 State how long the participants have access to the forum. - pp21 line 23 By excluding people receiving psycho-social or pharmacological treatments for the reduction/cessation of alcohol use or the reduction of depressive symptoms you are selecting a very narrow portion of the co-morbid alcohol misuse and depression population. This needs to be stated as a limitation of the study and limits generalizability of results. <p>Limitations</p> <ul style="list-style-type: none"> - While there is a one line limitations section in the abstract this is not explored or discussed sufficiently in the discussion. The additional limitation regarding exclusion criteria described above should also be discussed. <p>General structure</p> <ul style="list-style-type: none"> - For clarity and flow of information, consider structuring the methods section chronologically, that is to describe recruitment, assessment and study randomization before going on to describe the study treatment arms. The current structure involves some duplication of information and led to questions earlier in the manuscript which were answered several pages later. For example, Figure 1 is referenced both on pp8 and then on pp23, only one of these sections is necessary.
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1 (Cristina Botella - Universitat Jaume I, Spain)

This is a very interesting study, and the results can be very useful, both from a social a scientific point of view. The study is very well designed and meets the requirements that must require a study of this nature. The authors indicate that the approval from ethics committees have been obtained, the study has been registered and is also indicated which has been funded. I only would point out the following:

Note 1: the authors should better explain how they will conceal the allocation sequence.

We thank the reviewer for this important note. The participants are supposed to follow the self-help program and respond to the tasks given to them. As they have no idea about the existence of two different intervention arms they will just start with the intervention without assuming a second study allocation (except for those in the control group).

Note 2: they should also recognize, as a limitation of the study, participants are going to be recruited in different countries, but they have not defined a specific number of participants in each country, so this could be a bias.

The reviewer is right when claiming that no sufficient statement on the sample size for each country has been made in the methods section. A more reflected sample size calculation has now been included in the revised study protocol. In particular, we aim at recruiting 100 study participants in the Netherlands and 328 study participants in both Switzerland and Germany. The inclusion of participants from three different countries is, however, a strength of the study as the external validity will be increased.

Note 3: in the discussion section is said: “this will be the first randomised controlled prevention trial to compare the efficacy and cost-effectiveness....”. Using the word prevention can lead to confusion regarding compliance or not the different diagnostic criteria. Moreover, given the primary outcome measure used in the study, it would be better (as in the introduction section), to say: “to reduce alcohol misuse and depressive symptoms in comparison with a...”.

We agree with the reviewer that the term “prevention” is misleading when used in this context.

Therefore, the term was excluded and changes to the text were made as suggested by the reviewer: “...this will be the first randomized controlled trial to compare the efficacy and cost-effectiveness of a web-based self-help program to reduce problematic alcohol use and depression symptoms with familiar forms of face to face treatment.

Apart from these details, the protocol is very appropriate and the study deserves to be published

Reviewer 2 (Sally Hunt - Institution and Country University of New South Wales, Australia)

Overall this is an interesting and promising study design. A few questions and comments are detailed below:

Abstract

- pp3 line17 Replace "would be" with "is"

The referring sentence has been changed to omit using the inadequate description “would be”. The new sentence is the following: “It is important to have a cost-effective intervention that is able to reach at-risk individuals in the early stages of developing alcohol use disorders and depression.” (p.3).

- pp4 line22 Kay-Lambkin et al., have published their SHADE study which was a randomised controlled trial of a combined internet-based self-help intervention for alcohol use and depression.

We thank the reviewer for this comment. In the first results of their SHADE study, Kay-Lambkin et al.

have concluded that computer-based psychological treatment for comorbid depression and problematic alcohol use is equivalent to a therapist-delivered intervention (2009) and that the reduction in alcohol use in the short-term was greater among participants in the computerized treatment condition (2011) Because our study is not the first one, we adapted the referring sentence in the strengths section (new as an alone standing section on page 5) as follows: "TCOY is a multicentre randomised controlled trial to assess the efficacy and cost-effectiveness of an Internet-based self-help intervention that aims to reduce problematic alcohol use and depression symptoms simultaneously."

Introduction

- pp5 line 28 Dual diagnosis disorders are also known as co-morbid disorders and since you use this term later in the paragraph it would be worth including it in your list of alternative terms.

This is a very valuable comment for us. People who have substance use disorders as well as mental health disorders are diagnosed as having co-occurring disorders, or dual disorders. This is also sometimes called a dual diagnosis and it obviously describes the comorbidity of two disorders. Therefore, we have extended the definition based on the recommendations of the reviewer (p.6) and introduced the concept of COD right at the beginning of the paragraph: "Co-occurring disorders (COD) are also called dual disorders, dual diagnosis or comorbid disorders and are diagnosed if at least two disorders occur simultaneously in the same person"

- pp5 line 57 References needed regarding the trials on tobacco, alcohol, cannabis and cocaine. References to recent reviews and meta-analyses on the efficacy of RCT trials evaluating Internet-based self-help to reduce tobacco (Balhara & Verma, 2014), alcohol (Riper et al., 2014) and cannabis use (Tait et al., 2013) were added. Additionally, one important study with a cannabis trial was cited because it provides new information to the existing review that has been published previously. As only one trial has focused on cocaine use so far, this was the only study that has been cited in the text (Schaub et al., 2012). Moreover, a fifth substance category was added since one trial addressed the efficacy of Internet-based self-help to reduce the use of amphetamine-type stimulants (Tait et al., 2014).

- pp6 line 30 I disagree with the statement that "relatively few clinical trials have examined the efficacy of CBT for substance use disorder and depression in combination or in succession"

We agree with the reviewer that this statement is not true. Recently, a lot of clinical trials have been conducted and a review by Riper et al. 2014 included at 12 studies. Therefore, we have deleted this statement.

Methods and analyses

- pp7 line 52 Use the more recent MI reference for Miller and Rollnick : Miller, W. R., & Rollnick, S. (2012). *Motivational interviewing: Helping people change*. Guilford press.

We thank the reviewer for this advice. The reference was changed as suggested.

- pp8 line 18 State here that the allocation is random. This is covered in a later section (see comments below) so consider merging these sections to avoid overlap.

The randomized allocation was specified as suggested and overlapping sections were deleted in the later section. A substantial change in the structure of the methods section as suggested in the last comment of the reviewer has improved the methods profoundly.

- pp12 line 25 State how long the participants have access to the forum.

The participants have unlimited access to the forum. However, such a forum is only planned for the Dutch website so far. This information has been added to the text.

- pp21 line 23 By excluding people receiving psycho-social or pharmacological treatments for the reduction/cessation of alcohol use or the reduction of depressive symptoms you are selecting a very narrow portion of the co-morbid alcohol misuse and depression population. This needs to be stated as a limitation of the study and limits generalizability of results.

We agree with the reviewer that this exclusion criterion limits the generalizability of the study results. However, the idea of TCOY is that people with problematic alcohol use and depression who do not

yet receive treatment can be reached. This limitation was added to the discussion section.

Limitations

- While there is a one line limitations section in the abstract this is not explored or discussed sufficiently in the discussion. The additional limitation regarding exclusion criteria described above should also be discussed.

A new paragraph has been added to the discussion section to discuss important limitations of the study design and in- and exclusion criteria. The causes of the limitations have been explained thoroughly.

General structure

- For clarity and flow of information, consider structuring the methods section chronologically, that is to describe recruitment, assessment and study randomization before going on to describe the study treatment arms. The current structure involves some duplication of information and led to questions earlier in the manuscript which were answered several pages later. For example, Figure 1 is referenced both on pp8 and then on pp23, only one of these sections is necessary.

We thank the reviewer for this appropriate feedback. The organisation of the study protocol was in fact confusing in some parts of the study protocol and the reviewer has very well spotted some duplication of information that is not necessary. Therefore, the whole structure of the paper has been revised carefully and repeated information has been deleted. This revision of the structure was very important to improve the study protocol.