Author's response to reviews

Title: Evaluation and treatment of low and anxious mood in Chinese speaking international students studying in Scotland: Study protocol of a pilot randomised controlled trial.

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Author's response to reviews: see over
Editors comments

1) It is not clear whether all outcome measures will be taken at baseline. The way the manuscript reads now, it seems possible that the WSAS will only be administered at the end of the study.

Thank you for highlighting this. A table outlining the data collections and time points has now been added on p. 19.

2) The description of the randomization process is insufficient for a reader to understand how it will work. Precisely how will a given subject be randomized?

As participants entered the study, they are assigned a participant ID. Participants ID numbers will be passed to a separate researcher who will use the randomisation function in Excel to remotely assign participants to the IA or DAC group. Additional information regarding the randomisation has been added to p. 11.

3) There seems to be a mismatch between the eligibility criteria and the study design. To be eligible, a student must be residing in the UK for at least two months, yet the final assessment takes place at three months. Please clarify or correct this mismatch.

Thank you, I have added a sentence clarifying this on p. 9. We state that participants must be residing in the UK for at least 2 months in order to ensure that they are in the UK when using the intervention. This is a safety measure that we intend to employ in order to ensure that we can respond effectively if a participant reports that their conditions has deteriorated.

Follow-up measures will be collected online; therefore, participants do not need to be residing in the UK at the follow-up points.

4) It seems likely that many of the study participants will know each other and that there could be some contamination between the active and control arms. The pilot offers a good opportunity to explore whether or not there is any contamination. It is suggested that you incorporate this into your design or else discuss and justify why you choose not to do so.

At the 3 month follow-up we will collect data on any support participants have received since entering the study, including access to the online intervention. We will ask participants whether they have received support for their low mood/anxiety/depression since entering the study at the 3 month follow-up. As an extra check the website is protected by a registration code, and also all registrants provide their name and an email at registration. We will review registrations in the database as a double check of contamination.

5) The fact that you tested the intervention with focus groups and identified changes to content and delivery is interesting but is only mentioned in passing. This could potentially help other researchers who might be designing similar interventions. Some elaboration on the changes that were made would be useful.

Thank you for this suggestion, a brief section has been added on p. 15 outlining the changes made to the intervention. The focus group paper is in preparation and will be published separately.
6) The statement of why you chose not to make any diagnoses as part of the study isn’t convincing. You should either remove that statement or else elaborate.

We agree with this, the statement regarding our reason for not carrying out a diagnostic interview has been removed from p. 7.

7) You state that you are targeting mild-to-moderate depression or anxiety but there is no upper cut-off in the eligibility criteria. Will you exclude subjects with severe symptoms?

Thank you for raising this important issue. A recent review of the literature on guided self-help found that LI CBT is effective even for those with severe levels of depression. Our previous work (Williams et al, 2013) also opted not to have an upper cut-off for depression and found benefits across the range of depressive severity. Therefore, we chose not to exclude those scoring highly on the PHQ-9. We appreciate that the wording in the manuscript is confusing so we have omitted references to ‘mild to moderate symptoms’ and replaced with ‘symptoms of low mood’ (scoring at least 5 on PHQ-9) throughout.

8) The statement in the discussion that "We know that depression is significant in this group" and that "access to help in the appropriate language is limited" should be either justified or else downgraded to a belief rather than knowledge.

Thank you for your suggestion. We have re-written this statement as suggested p 20.

9) The references for the statement that cCBT is effective are all to your own manuscripts, all of which are under preparation and not published. Please refer to something like a meta-analysis that has actually been published.

Thank you – we have modified this to the NICE (2009) depression guidance which recommends cCBT as a treatment option for depression.

10) There has been some suggestion in the literature that internet interventions have the potential to actually cause harm: Rozental A. et al (2014) Consensus statement on defining and measuring negative effects of internet interventions. Internet Interventions, 1(1). The pilot offers an opportunity to explore this possibility and thereby to get more information out of your work.

Thank you for highlighting this paper, we have added a short discussion of this on p. 21. We have also now added an extra evaluation question at 8 weeks addressing whether any adverse effects are experienced (page 21-22)

11) The study results paper often does not provide enough space for a truly detailed discussion of the intervention. You might consider using this manuscript as an opportunity to provide such a discussion, as the current manuscript is rather light on the actual content and delivery of the internet program.
Additional information regarding the content of the intervention has been added at pages 12-14. Specifically, a short description of each module has been added in addition to details of the changes made following the focus group study.

Reviewer 1 comments

1. The need for this study on the basis what is already known should be elaborated in the introduction.
   Thank you for your suggestion, the previously supported points, like the efficacy of online CBT resources for use in Chinese speaking populations, the effectiveness of the original living life to the full course for western populations, have been added.

2. The authors might also want to consider including prevalence rates of anxiety and depression in students in general and in foreign students in particular.

   The reference of prevalence rates of anxiety and depression in international students has been added in introduction part on page 3.

3. Gellatly (2007) could be replaced by something more up to date (e.g. Richardson 2012 Clin Psych Rev; Baumeister, Internet Interventions 2014)

   Thank you, this reference has been added in addition to the Gellatly reference as we believe it is a high quality study with a greater number of studies than in the Richardson (2012) paper.

4. I also miss a basic review of the literature what has been already done in the field a) with regard to the effectiveness of cCBT for anxiety and depression in general.

   Thank you, the literature relating to the effectiveness of cCBT for anxiety and depression in has been added in the introduction part. P. 4-5

5. The authors state that the intervention has been evaluated extensively, but do not review the results, I think this would be helpful to get an impression about the evidence base of the intervention. Has the intervention in English been evaluated as internet-version, if so what were the results?

   The online intervention has not been evaluated extensively. The content has been evaluated in face to face delivery using key components such as modules and books present in the online course (McClay et al, 2015). We have also added the Pittaway et al (2009) study.

6. The rational the authors give in the introduction for why they do not want to assess a diagnosis of participants (i.e. non-clinical sample, symptom and not diagnose inclusion criteria) is not convincing. One can still assess a diagnose in order to get an impression what sample one has included. Thus I would suggest that the authors remove this explanation. If the authors leave it in, I would suggest to remove it from the introduction to the method section.

   Please see response number 6 response to editor above.

7. Reference for the PHQ-9 version is missing in the inclusion criteria section.
8. The authors indicate that they use measurements both in English and Chinese, but do not give references to validated Chinese versions.

This has been added.

9. The measurement section could benefit from more information about the reliability of the scales e.g. alphas.

Thank you, the information about the reliability of measures has been added.

10. Inclusion criteria: the authors state that the trial is aimed at mild-to moderate depression/anxious individuals, but do not indicate that they plan to use an uppercut-off for exclusion.

Please see previous response to the editor’s query on this at number 7 above.

11. In general the authors make quite a few statements in the manuscript without referring to adequate literature to support their statements. E.g. Discussion: "we know that depression is significant in this group" and that "access to help in the appropriate language is limited".

Thank you, literature to support these statements has been added on page 20.

12. The authors refer for statements that cCBT is effective only to their own manuscripts instead of available meta-analysis. Moreover the manuscripts they refer to are all under preparation and not published. I would suggest to refer to published meta-analysis.

We have now quoted the NICE (2009) depression guidance as justification for this.

13. Is the trial registered? if yes, please include the information about it. If not, I would suggest to register it, otherwise the authors might have problems to publish the results (as most, also open access journals nowadays require a prioritrial registration).

The trial is registered, the details are at the end of the abstract.

14. The information about the ethical approval could be removed from the discussion section to the method section.

The methods section is lengthy and the authors think that the ethical issues and ethical approval associated with this study are discussion points so we would prefer to keep them in the discussion. If necessary however, we will move them to the methodology section.

15. The authors state that it is unlikely that participants will experience worsening of symptoms. On what basis do the authors come to this conclusion? There are so far almost no studies on deterioration rates in internet-based treatments for depression/anxiety.

We have now added a check of whether adverse symptoms arise. We agree this is an area that hasn’t been examined in detail. We have moderated the statement that it is unlikely that participants will experience a worsening of symptoms (pages 19 and 22)
16. Having said this, the authors might want to consider also to assess potential negative effects of the treatment, as it has been recently suggested for internet-intervention trials (e.g. Rozental, A., Andersson, G., Boettcher, J., Ebert, D. D., Cuijpers, P., Knaevelsrud, C., & Carlbring, P. (2014). Consensus statement on defining and measuring negative effects of Internet interventions. Internet Interventions, 1(1), 12-19. doi:10.1016/j.invent.2014.02.001)

Please see response above.

17. The authors might want to consider elaborating in the discussion how this study add significant knowledge to the literature.

Thank you for your suggestion, the significant knowledge to the literature has been added to the discussion on pages 21.

18. Most of the information about ethical consideration could be removed from the discussion section into the method section.

We have been advised to add more information about the intervention in the methodology section and we feel that moving the ethical considerations to this section would make it too lengthy.

19. I think it would be very interesting to have more information about the specific intervention used in the study described in the manuscript. The study protocol is a great possibility to provide detailed information, that usually do not fit into the study results paper.

Please see response above to the same issue raised in the Editors comments point number 11.

Reviewer 2 comments

1. The manuscript does not meet the acceptable English standards and should be proofread thoroughly. It was too hard to read, understand and review.

We hope we have addressed this issue.

2. Many information in the abstract are not clear. The authors mentioned that levels of depression, anxiety, social functioning and satisfaction will be assessed in the methods section. However when these information will be assessed - baseline, 3 months after randomization, or at both time points?

This has been clarified and a table added summarising when these are completed.

3. In the background section, the authors mentioned low mood. What is the definition of “low mood”?

We refer to “low mood” in the manuscript because we are not including a diagnostic interview for depression. Low mood is defined as a score of 5 or more on the PHQ-9, a widely used and validated depression measure. A score of 5 or more indicated at least mild depression.

4. What is the relationship between low mood and the level of depression, social functioning and satisfaction?
We have opted to assess and describe these separately. Low mood often reduces social function. Satisfaction as measured by the CSQ8 refers specifically to satisfaction with the intervention rather than with life.

5. In the discussion section, the author mentioned “test the trial design”. What does this mean? How would you “test” the trial design? The word “test” was abused in this manuscript and sometimes should be changed to “assess”, “investigate” or “study” etc.

Thank you for your suggestion, we have reviewed and rephrased throughout as needed.

6. In the introduction section the author should provide a clear rationale about why this pilot study is important and necessary. For example, if the lost to follow-up rate can be estimated from published literature, conducting a pilot study just for obtaining some knowledge about the lost to follow-up rate will be completely unnecessary and waste of money.

Thank you. The details of rationale have been added in the introduction part. There are many areas of uncertainty about the intervention- recruitment, ability to gather data, deliver and support the course- all of which need testing in order to increase the credibility of any future substantive study being funded (page 7).

7. One of your research questions is “how many participants will be needed for a sufficiently powered future RCT” (page 7). This research question is too general and should be very specific. For example you should explain what information are needed but not available in the current literature for calculating the sample size of the future RCT.

We have stated now that we are gathering information about take-up, retention, ability to gather data, as well as obtain an estimate of treatment effect, in order to provide a sample size for the future substantive study.

8. In the Participants section (page 7), you mentioned one of the aim is to identify any problems with recruitment and delivery of the intervention and completion of evaluation measures. What kind of problems with recruitment and delivery of the intervention and completion of evaluation measures do you expect to have?

Thank you. Such problems like no replies from potential participants during the recruitment, drop-out during the intervention, and incompletion of the whole online course have been added in the participants section. We have also identified this in (7) above.

9. Researcher should have an idea about the problems they will have when conducting a large CRT, propose strategies to solve these problems, and assess the performance of these strategies in a pilot study. And a pilot study should be designed very carefully to provide as much useful information as possible for the design of the future RCT.

Thank you- we agree that is the purpose of our pilot study.

10. On the top of page 8, eligible participants of the pilot study must be students living in the UK for the next two months is. Why do you choose “next two months” as the inclusion criteria given the primary end points will be measured at 3 months after randomization?

We hope we have addressed this. Please see response above (Editors similar point 3).
11. The participants of this pilot study are all from the University of Glasgow. They are all Chinese international students and are very likely to know each other or have some connections with each other. How do you handle the “contamination” between the intervention and control? Will the future RCT have the same target population, i.e. the students from the University of Glasgow? Or you are going to include the international students from other universities? Have you considered a cluster randomized design?

*Please see response above to the same point made by the Editor (point number 4). We have not considered a cluster design, as the design utilised also has to suit the needs and lack of funding of a PhD student research dissertation.*

12. The randomization will take place using the randomization algorithm contained within SPSS or Excel as mentioned in the randomization section on page. You can’t make final decision on which software to use?

*Excel will be used. This has been amended on p. 11.*

14. Four questionnaires - patient health questionnaire-9, generalized anxiety disorder 7, and work and social adjustment scale, and the client satisfaction questionnaire – are adopted in this pilot study. Why do you use these questionnaires? What is the rationale? Are they proved to be valid measurement tools for this population?

*These questionnaires are widely used in this type of research and are valid measures.*

15. In the statistical analysis section (on page 14), you wrote: Evaluable data and intention to treat analysis will occur”. I wonder what “evaluable data” are? I am curious about how the “intention to treat analysis” will be applied in this pilot study? How the PHQ9 data are used for power calculation for the future RCT?

*In the pilot study we recognise that the study cannot answer the substantive question of whether the intervention is effective. Our primary outcome is ability to recruit, gather data etc. However it will provide useful estimates of clinical effect to see the impact on mood and social function. In the evaluable data analysis we will explore all before-after data collected. In the intention to treat analysis we will adopt a more conservative approach taking forward baseline data for missing data.*