PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A clinical audit of changes in suicide ideas with internet treatment for depression.
AUTHORS	Mewton, Louise ; Watts, Sarah; Newby, Jill; Andrews, Gavin

VERSION 1 - REVIEW

REVIEWER	Andersson, Gerhard Linkoping University
REVIEW RETURNED	06-Jul-2012

GENERAL COMMENTS	Dear authors Since I have worked with this issue for many years, I read the ms with great interest. I do have some detailed suggestions for the authors to consider. 1. Intro. The authors write that "patients reporting suicidal ideas are often arbitrarily excluded from internet treatment trials", but I suggest rewording that since in my experience it is not arbitrary but based on a low threshold (defensive medicine). This is not the same thing as being arbitrary. Moreover, the citation of my group (erectile dysfunction) is perhaps not perfect since there are other more relevant papers on depression and anxiety from my and other groups (2/3 are self citations also). 2. I am well aware of the work done by the group, but perhaps references to their depression program should be added in the "Intervention" section? 3. Nothing is said about online administration of PHQ9. Please add psychometric info or at least reference that it has been used in icbt studies. 4. Results. Add confidence intervals and mean standardized differences (Cohen's d). I would suggest categorical presentation of the suicide item as well since the figure is not easy to grasp. 5. There are more limitations. For examle, suicidial ideation was only based on self-report and we have managed to reduce the exclusion rate by adding an interview section (telephone). This could be mentioned as it improves the situation: Johansson R, Ekbladh S, Hebert A, Lindström M, Möller S, Petitt E, et al. Psychodynamic guided self-help for adult depression through the Internet: a randomised controlled trial. PLoS ONE. 2012;7 (5):e38021.

	In addition numerous researchers sit on the data here that might show the same thing (eg reductions on PHQ9 suicide item). 6. There is no mentioning of risk of including suicidal persons. If assessment is based on only self-report this is not unlikely. A pros and cons analysis would be helpful are alternatively crisis management procedures. Overall, however I welcome this open trial as there is a need for effectiveness data in the field of ICBT. Gerhard Andersson

REVIEWER	Helen Christensen The Black Dog Institute, The University of NSW.
REVIEW RETURNED	14-Jul-2012

THE STUDY	This is an interesting paper which addresses the question of whether CBT internet interventions are associated with changes in suicide ideation, and whether there is any reason NOT to include suicide ideation in people undertaking online CBT. There are a few key features that need comment. The PHQ-9 is a one item measure of suicide ideation, and hence limited.
RESULTS & CONCLUSIONS	The study is not a RCT, and, although the authors are clear that the paper is not an effectiveness trial, they need to clearly articulate the limitations of the their design. The drop in suicide ideation may have little to do with the online intervention, but be due to spontaneous change or the passage of time. The literature from telephone and helplines research suggests that any form of intervention is associated with drops in suicide ideation- The authors may wish to comment on whether depression change mediates the change in ideation? The reduction in suicide ideation is directly attributed to "an internet CBT course for depression" in the discussion. The research team are also unable to report on any other interventions experienced by their participants. Further review necessary of other interventions associated with ideation reduction. Figure: the data have been truncated into categories. Is there data for "not at all" pre and post? A number of participants seem to get worse? Needs comment? Figure data are descriptive, interesting, but these drops are not individually significant?
REPORTING & ETHICS	The study is reported as a quality assurance activity.
GENERAL COMMENTS	I think the content of this paper is important. However, I think the issues raised above need to be addressed before publication. In short, the study does establish that suicide ideation drops. However, the effects cannot be attributed to the online intervention. The central conclusion that inclusion of patients with suicide ideation into these services is not contra-indicated is reasonable, however, there is no comparision with pre post rates established in other services.

REVIEWER	Jo Robinson Research Fellow Orygen Youth Health Research Centre University of Melbourne Australia

REVIEW RETURNED	17-Jul-2012

THE STUDY	1. Is this study nested in a bigger RCT? If so this should be clearly stated 2. The authors state that "They were advised to exclude people who were 'actively suicidal", however 54% of patients were reported to being suicidal. Can the authors please explain this more clearly? It also appears that they have only included data here for those people who completed the program - could the authors please explain this fully, included rates of adherence / attrition for the overall study? A participant flow diagram and clear inclusion / exclusion criteria may be helpful here. 3. It would also be helpful to know what other treatment patients were receiving at the time. 4. "Clinicians are advised to contact patients at least twice during the course" - more information is needed here - e.g. what was the nature of this contact? Was it the same for all participants? How was it recorded? 5. Leading on from my point above - what safety measures were in place for participants? Were there any withdrawal criteria for the study? 6. Were participants only followed up post-intervention or was a longer follow-up period included? Were assessments conducted face-to-face or on-line and by whom? 7. Were possible adverse effects assessed in any way?
RESULTS & CONCLUSIONS	1. It would be of interest to know what happened to the depression scores of this sample over the treatment period. The authors state in the conclusion that these reduced over time but this is not reported in the results. 2. What were the overall rates of adherence / attrition for the study? 3. The authors state that neither age nor gender were predictors of SI at follow-up. Did they test for any other potential predictors (e.g. depression scores / level of SI at baseline)?
REPORTING & ETHICS	1. A participant flow diagram would be helpful - this may also go some way to addressing my first comment above. 2. Did the study receive ethical approval? This seems to be more than QA to me - especially as they are seeking to publish their findings in the peer-reviewed literature and if it is part of a bigger RCT.
GENERAL COMMENTS	I think this paper addresses an important topic. Hopefully the comments made above will help strengthen the findings.

VERSION 1 – AUTHOR RESPONSE

Reviewer: Gerhard Andersson
Linkoping University

Dear authors

Since I have worked with this issue for many years, I read the ms with great interest. I do have some detailed suggestions for the authors to consider.

1. Intro. The authors write that "patients reporting suicidal ideas are often arbitrarily excluded from internet treatment trials", but I suggest rewording that since in my experience it is not arbitrary but based on a low threshold (defensive medicine). This is not the same thing as being arbitrary. Moreover, the citation of my group (erectile dysfunction) is perhaps not perfect since there are other

more relevant papers on depression and anxiety from my and other groups (2/3 are self citations also).

We no longer include the term “arbitrary”. We no longer refer to the article on erectile dysfunction and instead refer to a more recent publication by the same group (Johansson et al., 2012). 5/21 are now citations to our own work.

2. I am well aware of the work done by the group, but perhaps references to their depression program should be added in the "Intervention" section?

References by Perini et al. (2009) and Titov et al. (2010) have now been included in the Intervention section.

3. Nothing is said about online administration of PHQ9. Please add psychometric info or at least reference that it has been used in icbt studies.

We have now included at Titov et al. (2011) reference demonstrating that the PHQ-9 is reliable valid and sensitive to change in previous iCBT studies. We also now report Cronbach’s alpha for the PHQ-9 in the current sample.

4. Results. Add confidence intervals and mean standardized differences (Cohen's d). I would suggest categorical presentation of the suicide item as well since the figure is not easy to grasp.

The results section has been expanded to include relevant statistics. We also now include the additional table in the results.

5. There are more limitations. For examle, suicidial ideation was only based on self-report and we have managed to reduce the exclusion rate by adding an interview section (telephone). This could be mentioned as it improves the situation:
Johansson R, Ekbladh S, Hebert A, Lindström M, Möller S, Petitt E, et al. Psychodynamic guided self-help for adult depression through the Internet: a randomised controlled trial. PLoS ONE. 2012;7 (5):e38021.

We have now expanded the limitations section (please see response to Reviewer 2).

In addition numerous researchers sit on the data here that might show the same thing (eg reductions on PHQ9 suicide item).

And we would encourage such reports as there is a paucity of information about the frequency of suicidal ideation in depression

6. There is no mentioning of risk of including suicidal persons. If assessment is based on only self-report this is not unlikely. A pros and cons analysis would be helpful are alternatively crisis management procedures.

The data are too sparse to support such a detailed analysis

Overall, however I welcome this open trial as there is a need for effectiveness data in the field of ICBT.

Reviewer: Helen Christensen
The Black Dog Institute, The University of NSW.

This is an interesting paper which addresses the question of whether CBT internet interventions are associated with changes in suicide ideation, and whether there is any reason NOT to include suicide ideation in people undertaking online CBT.
There are a few key features that need comment.
The PHQ-9 is a one item measure of suicide ideation, and hence limited.

The study is not a RCT, and, although the authors are clear that the paper is not an effectiveness trial, they need to clearly articulate the limitations of the their design. The drop in suicide ideation may have little to do with the online intervention, but be due to spontaneous change or the passage of time. The literature from telephone and helplines research suggests that any form of intervention is associated with drops in suicide ideation- The authors may wish to comment on whether depression change mediates the change in ideation? The reduction in suicide ideation is directly attributed to "an internet CBT course for depression" in the discussion. The research team are also unable to report on any other interventions experienced by their participants. Further review necessary of other interventions associated with ideation reduction.

We have now expanded the limitations section. Whilst a more detailed analysis of the relationship between depression and suicidality would be interesting, we did not have a measure of suicidality that was independent of our measure of depression, precluding further exploration of this relationship.

Figure: the data have been truncated into categories. Is there data for "not at all" pre and post? A number of participants seem to get worse?
Needs comment? Figure data are descriptive, interesting, but these drops are not individually significant?

We have included a detailed table (please see response to Reviewer 1 above)

The study is reported as a quality assurance activity.

I think the content of this paper is important. However, I think the issues raised above need to be addressed before publication.
In short, the study does establish that suicide ideation drops. However, the effects cannot be attributed to the online intervention. The central conclusion that inclusion of patients with suicide ideation into these services is not contra-indicated is reasonable, however, there is no comparision with pre post rates established in other services.

No other reports of iCBT detail the changes in suicidal ideation

Reviewer: Jo Robinson
Research Fellow
Orygen Youth Health Research Centre
University of Melbourne
Australia

1. Is this study nested in a bigger RCT? If so this should be clearly stated 2. The authors state that "They were advised to exclude people who were ‘actively suicidal", however 54% of patients were reported to being suicidal. Can the authors please explain this more clearly? It also appears that they have only included data here for those people who completed the program - could the authors please explain this fully, included rates of adherence / attrition for the overall study? A participant flow diagram and clear inclusion / exclusion criteria may be helpful here.
3. It would also be helpful to know what other treatment patients were receiving at the time.

4. "Clinicians are advised to contact patients at least twice during the course" - more information is needed here - e.g. what was the nature of this contact? Was it the same for all participants? How was it recorded?
5. Leading on from my point above - what safety measures were in place for participants? Were there any withdrawal criteria for the study?
6. Were participants only followed up post-intervention or was a longer follow-up period included? Were assessments conducted face-to-face or on-line and by whom?
7. Were possible adverse effects assessed in any way?

This is not an RCT but 'post marketing surveillance' using measures included as a routine to increase patient safety and ensure that standards are maintained. Automated reports of these measures are supplied to the patient's own clinician for this purpose. Investigators did not know the identity of these patients and there were no investigator initiated measures specific to this report, hence the limitation on what this reviewer would have liked us to ask. All patients give consent for their scores on the K10 and the PHQ-9 to be used for quality assurance purposes.

1. It would be of interest to know what happened to the depression scores of this sample over the treatment period. The authors state in the conclusion that these reduced over time but this is not reported in the results.

The results section in the original manuscript contained data on reductions in the PHQ-9.

2. What were the overall rates of adherence / attrition for the study?
Not applicable

3. The authors state that neither age nor gender were predictors of SI at follow-up. Did they test for any other potential predictors (e.g. depression scores / level of SI at baseline)?

1. A participant flow diagram would be helpful - this may also go some way to addressing my first comment above.
2. Did the study receive ethical approval? This seems to be more than QA to me - especially as they are seeking to publish their findings in the peer-reviewed literature and if it is part of a bigger RCT.

See above

I think this paper addresses an important topic. Hopefully the comments made above will help strengthen the findings.

VERSION 2 – REVIEW

REVIEWER	Jo Robinson Orygen Youth Health Research Centre
REVIEW RETURNED	01-Aug-2012

THE STUDY	The authors have still not addressed the question raised previously regarding the fact that 'They were advised to exclude people who were 'actively suicidal' - how do they define 'actively suicidal'? It is important to know who this sample are.
RESULTS & CONCLUSIONS	I think the authors should be more cautious in their conclusion that "this is the first study to show that an internet CBT course for depression reduces suicidal ideation" - I'm not sure that this can be concluded from the research conducted. Whilst suicidal ideation decreased we still do not know whether this was a result of the iCBT

	intervention or not. Whilst the limitations of the study design are now better reported, I still think that caution is required in the discussion and conclusions sections of the paper, including the abstract.
REPORTING & ETHICS	No mention of ethics is made in the paper, the authors however state that this was conducted as part of a QA process thus implying that no ethical approval is required. To my knowledge this still requires ethical approval even if it falls into the category of a minimal risk application, especially as they are seeking to publish the findings in the peer reviewed literature. However this may not be the case at St Vincents. I will leave this to the editor to determine.

VERSION 2 – AUTHOR RESPONSE

Reviewer: Jo Robinson
Orygen Youth Health Research Centre

Thank you for re-sending this manuscript and thanks to the authors for their revisions.

However a few concerns remain.

Firstly the authors have still not addressed the question raised previously regarding the fact that 'They were advised to exclude people who were ‘actively suicidal’ - how do they define 'actively suicidal'? It is important to know who this sample are.

I think the authors should be more cautious in their conclusion that "this is the first study to show that an internet CBT course for depression reduces suicidal ideation" - I'm not sure that this can be concluded from the research conducted. Whilst suicidal ideation decreased we still do not know whether this was a result of the iCBT intervention or not. Whilst the limitations of the study design are now better reported, I still think that caution is required in the discussion and conclusions sections of the paper, including the abstract.

No mention of ethics is made in the paper, the authors however state that this was conducted as part of a QA process thus implying that no ethical approval is required. To my knowledge this still requires ethical approval even if it falls into the category of a minimal risk application, especially as they are seeking to publish the findings in the peer reviewed literature. However this may not be the case at St Vincents. I will leave this to the editor to determine.