Author's response to reviews

Title: Efficacy of Internet-based Interventions for Children, Youth, and Young Adults with Anxiety and/or Depression: A Systematic Review and Meta-Analysis

Authors:

Xibiao Ye (xye@wrha.mb.ca)
Sunita Bayyavarapu Bapuji (sbaapujii@wrha.mb.ca)
Shannon Winters (swinters@wrha.mb.ca)
Ashley Struthers (astruthers@wrha.mb.ca)
Melissa Raynard (Melissa.Raynard@umanitoba.ca)
Colleen Metge (cmetge@wrha.mb.ca)
Sara Kreindler (skreindler@wrha.mb.ca)
Catherine Charette (ccharette2@wrha.mb.ca)
Jacqueline Lemaire (jlemaire@afm.mb.ca)
Margaret Synyshyn (MSYNYSHYN@matc.ca)
Karen Sutherland (KSUTHERLAND@matc.ca)

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Author's response to reviews: see over
Responses (in blue, *italic*) to Reviewer’s Comments (MS: 7187887861164581)

**Reviewer 1:**

**Discussion**

1) Pg 10 “The effect of internet-based interventions may be explained by: (i) enhanced participant knowledge and coping skills introduced by the internet-based self-help content; (ii) more interaction between participants and therapists; (iii) enhanced parental or teacher guidance to cope with anxiety and depression; and/or (iv) the interactions among the three components.” – while it is fairly evident why (i) is a likely mechanism, it is less clear how (ii) and (iii) might operate. Can the authors please elaborate? Did the authors of the included papers discuss this issue?

*The statements have been deleted.*

2) Pg 10 The authors’ comments about finding significant effects for anxiety but not depression are contrary to the transdiagnostic approach to treatment of these disorders. Can the authors please comment? Also, it seems that Keller 2010 is the only study that showed significant positive effects on both anxiety and depression symptoms, whereas Reid 2011 and Storch 2011 were ineffective for both. Any comments on these observations? Given that one of the intended advantages of online interventions is its scalability, a transdiagnostic approach is clearly desirable. It would be important to highlight specific considerations for the design of future internet interventions, so comments in that regard in the context of this review would be valuable.

*We have replaced the statement “However, it is well recognized that, even if a CBT intervention is effective in reducing anxiety or depression symptoms, the intervention might not work for the other comorbid condition [1]. This indicates that the development of internet-based CBT interventions needs to consider the two disorders’ unique features.” with the following discussion:*

“Transdiagnostic CBT, an approach bringing therapeutic elements from disorder-specific CBTs together to treat diagnostically mixed patients, may offer several advantages but there is no sufficient evidence supporting the efficacy or effectiveness of this approach versus control.[2] Few studies have found that internet-based trans diagnostic CBT improved patient outcomes when compared to control.[3] However, it is unclear whether transdiagnostic CBT performs better than disorder-specific CBTs.[4] Previous studies have indicated that even if a CBT intervention was effective in reducing anxiety or depression symptoms, the intervention might not work for the other comorbid condition [1]. Therefore, more research is needed to compare internet-based diagnostic CBT vs. disorder-specific CBT for anxiety and depression.”

**Title**

1) Is the review of effectiveness or efficacy? The title should be amended accordingly.

*All studies are RCTs. “Effectiveness” has been changed to “Efficacy.”*
2) Likewise, the authors set out to evaluate cost-effectiveness, but since there is no data on that, the title should not include reference to it.

*The term “cost-effectiveness” has been removed from the title.*

Background
3) First sentence--please specify whether this is lifetime or 12-month prevalence.

*The term “each year” has been inserted.*

Method
4) Why did the subgroup analysis by quality rating include only studies with strong vs. moderate quality but not those with weak quality? It should be made clear in the Data Analysis section that weak quality studies would be excluded, before stating ‘We undertook a subgroup analysis by quality rating (strong vs. moderate).’ In fact, it should be specified in the Critical Appraisal section how the ‘global quality rating’.

*We believe that including weak studies into the pooled analysis is not appropriate as these studies are seriously biased. The sentence “We included high or moderate quality studies in the meta-analysis.” has been added to the Data Analysis section.*

*The criteria for global quality rating are now described in the Critical Appraisal section.*

5) The authors should specify in the Data analysis section:
   a) How they would use the heterogeneity statistics to determine the quality of evidence, e.g. I²<25% = high quality evidence; citing a relevant source.

   *The sentence “I² <30% and I²=30-50% were considered the presence of minimal heterogeneity (high quality evidence) and moderate heterogeneity (moderate quality evidence), respectively.” has been added.*

   b) What sensitivity analyses they would run.

   *This sentence has been inserted:*
   “To test the robustness of the pooled effect estimates, we rerun the models by using anxiety/depression outcomes measured by alternative instruments (each study assessed anxiety/depression symptoms using multiple instruments simultaneously).”

Results
6) Table 1 –instead of the reference number in the left-most column, using the Author, Year format like that used in the forest plots will improve the readability of the Table.

*Revised accordingly.*
7) Figure 1 should be done in PRISMA format. The key missing information are the reasons for “Records excluded after full-text screening” and other stage labels in the process of study inclusion.

*PRISMA flow diagram template has been applied (Figure 1)*

8) Pg 8: “All studies but one [13] explicitly stated that cognitive behavioral therapy (CBT) was applied in the interventions.” Can the authors briefly state what the one study used?

*The sentence “Intervention group participants in this study used a mobile phone based tool to self-monitor their mood, stress, and alcohol and cannabis use daily and received SMS and phone call supports from psychologists [5]” has been inserted.*

Discussion

9) Pg 10-11 “Second, the findings may not apply to patients with severe anxiety/depression disorders since all participants from the included studies had mild or moderate symptoms” This is unsurprising, but on a positive note has implications for indicated prevention. The authors should note this briefly.

*The statement has been changed to “Second, the studies included in this analysis involved patients with mild or moderate anxiety/depression symptoms [5-8]. While the analysis indicates that internet-based intervention can improve symptoms in those patients, the interventions may not affect patients with severer symptoms.” to reflect the positive effect.*

10) Pg 11, first paragraph—the limited extant findings also suggest that augmentation of the internet interventions are required to maintain the positive effects.

*The suggested sentence has been added to the first paragraph in the Discussion section.*

11) Pg 11, last paragraph—“this type of intervention”—please specify which type

*“this type of intervention” has been changed to “internet-based intervention”.*

12) Pg 12 Inventory names should have the first letters capitalised.

*Revised accordingly.*

13) The authors should comment somewhere in the Discussion about how their findings (and included studies) differ from the two published narrative reviews. Relevant comments from those reviews should also be referred to, especially if they relate to other studies that were not included in this meta-analysis, or commented on similarities or differences in existing intervention programs.

*The sentence “The finding supports the observations in the two previous narrative reviews where the majority of studies showed positive effects.” has been added.*
Reviewer 2

1. Although I understand the word count concerns inherent to writing any manuscript, it seems unusual that earlier reviews of this literature cited were not discussed in any detail as to their findings.

_The sentence “The finding supports the observations in the two previous narrative reviews where the majority of studies showed positive effects.” has been added to reflect previous review findings._

2. I question the sensibility of excluding CD-ROM based interventions from the review. Although they are not ‘internet-based’, they are ‘computer-based’. By excluding these studies, the number of studies was so very small for each disorder, that it was not really worth doing a ‘meta-analysis’. Also, both Camp-Cope-a Lot (Kendall et al) and Cool Teens (Wuthrich et al., 2012) are two of the major contributors to the computer-based therapy literature (as well as BRAVE-ONLINE which IS internet-based and is included in the review). It seems very strange not to include these major contributions just because they are not technically ‘internet-based’. I also wonder why the Spence et al (2006) study conducted on BRAVE-ONLINE was not included.

_Two main reasons why we decided to not include CD-ROM studies: a) The primary purpose of this research grant was to examine the evidence for internet-based intervention as an innovation improving access to mental health services in young people (findings reported in this manuscript are part of research results). Connection and easy access are the most important features of internet-based intervention which CD-ROM intervention does not have. b) There have been systematic reviews particularly focusing on CD-ROM studies._

_The Spence et al (2006) article used a subset of all participants in the Spence 2011 article and was considered a duplicate._

3. On page 9 it was not clear (in the first paragraph) what the last sentence was about. Was this conducted in the study under review or in previous studies? It was not clear which.

_“in this analysis” has been inserted to the sentence._

4. The authors claim on page 9 that only one study followed participants for longer than 12 weeks after the intervention. However, this is not true. March et al followed up participants at 6 months and Spence et al followed up participants at 12 months.

_The March and Spence studies followed only participants in the control groups at 6 months and 12 months, respectively. The statement has been changed to “Only one study followed participants in both intervention and control groups for 12 months after the intervention [14] and showed no intervention effect at this time point.”_

5. I question the utility of even talking about cost-effectiveness given that there were no studies conducted on this issue. I can understand it being placed in the discussion as a suggested area for
future research, but I fail to see the point of (particularly) placing it in the title and discussing it at length elsewhere in the manuscript.

The term “cost-effectiveness” has been dropped from the title.

6. On page 10 in the first paragraph, the authors put forward four explanations for the effects of internet interventions. However, there is no rationale for these four listed explanations and no references to back them up.

The statements have been deleted.

7. There was no discussion of the fact that, in at LEAST the cases of the BRAVE-ONLINE studies, treatment effects were significantly ENHANCED at follow-up compared to post-treatment. This would seem an important omission.

The sentence “Two studies followed control group participants but not intervention group participants 6 months and 12 months after the interventions, respectively, and found the improvement (compared to pre-intervention) retained [8, 11].” has been added to reflect this.

Reviewer 3

Was there a protocol written for this study? If there was, it should be mentioned at the beginning of the Methods.

Protocol registration information is now provided in Abstract and the first paragraph of Methods.

Below the inclusion and exclusion criteria heading, there is no mention of the intervention (internet-based interventions for depression and anxiety). Even though it looks obvious, you need to address it because all the other components of the PICOS framework are mentioned. Also, it should be more explicit the type of studies used for inclusion.

The following sentences have been inserted:

“Interventions of interest were those targeting anxiety and/or depression symptoms and were delivered via the Internet (fixed or mobile internet). We considered both parallel comparisons (randomized or non-randomized controlled trials), pre-/post-intervention comparison studies, and observational studies.”

Add a Title of “Study Selection” before mentioning how the articles were screened.

Title “Critical appraisal” has been changed to “Study appraisal and selection”
How the full text screening was done should be mentioned in the methods part.

The sentence “Full-text articles that did not provide sufficient information on the P.I.C.O.S. framework elements or did not meet the inclusion criteria as defined using the framework were considered irrelevant and were thus excluded.” has been inserted to reflect the full-text screening process.

The last sentence below the Critical appraisal title (“Figure 1 describes the process the process and the number of studies reviewed…”) should be in the results section.

Revised accordingly.

Under the Results, there is a sentence that says: “All interventions included online self-help sessions; six supplemented online self-help with therapist support via email, short text message (SMS), and/or phone call (one of the six studies also included family support [16]); one included school-based group support and teacher support”. It is unclear when you are talking about the “intervention” or about the “studies” (you are numbering both).

The sentence has been changed to:
“Interventions in all studies included online self-help sessions; six studies supplemented online self-help with therapist support via email, short text message (SMS), and/or phone call (one of the six studies also included family support [6]); one study included school-based group support and teacher support [12].”

In Table 1, under the column of Reference it should appear the name of the first author as well as the year instead of the number of the reference.

Revised accordingly.

One of the last paragraphs in the results section should be moved to the discussion: “This suggests that the effect might not be maintained over a long period of time.”

This sentence has been removed from the Results section and discussion about this issue is included in the Discussion section.