Author’s response to reviews

Title: Mobile Health in the Management of Type 1 Diabetes

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Author’s response to reviews:
Declare RE: BEND-D-18-00220R1, entitled "Mobile Health in the Management of Type 1 Diabetes, A systematic review"

Dear Editor:

We really appreciate your great effort in reviewing our manuscript and provide us an opportunity to improve the quality of our paper. According to the reviewers’ suggestions, we have carefully revised and improved our manuscript including abstract, background, methods, results, discussion, etc. In addition, we invited a native speaker, Jennifer Barrett (PhD), who helped us to
edit and modify our manuscript. All authors declared that they have no competing interests. We have highlighted the changes in the manuscript.

Your comments and suggestions really helped us a lot. We have put great efforts on them. We wish it can be satisfactory. If there is any information I can provide, please don’t hesitate to contact me.

Thank you again for your time and patience. Look forward to hearing from you.

Sincerely yours,

Maolin

Technical Comments:
You provide a completed PRISMA checklist but have not made any changes to the title to indicate that this is a systematic review/meta analysis. Please ensure that this is done and check that all of the other points raised in the PRISMA checklist are included/reported in the paper

Response: Thanks reviewer for the comment. We revised the title of the paper, and corrected the errors in the checklist.

Please enlist the assistance of a biostatistician to assist with the analysis in your paper.

Response: In the course of revising the article, we invited statistical experts to verify the article.

Reviewer reports:
Rachel Miller (Reviewer 1): The objective of this study was to perform a systematic review and meta-analysis of mobile health interventions on glycemic control in type 1 diabetes. The authors report that among 8 studies representing 602 participants, there was a significantly greater decrease in mean HbA1c associated with mHealth intervention compared to standard care. This study addresses an important topic and its major strength is that it provides a nice systematic review of mHealth interventions in type 1 diabetes. However, there are several issues that need to be addressed:
Major comments:

1. In the abstract and throughout the text, the authors refer to "glycemic index" to mean "glycemic control". This is incorrect terminology and should be changed throughout.

Response: We revised the manuscript in accordance with the reviewers’ comments. We have corrected incorrect terminology (Abstract, Line 3, Page 3; Background, Line 17, Page 6).

2. In the exclusion criteria, it says that studies were excluded if they included patients with diabetic complications. This does not seem to be true, as for example the study by Rossi et al. includes patients with retinopathy and neuropathy, as shown in their Table 1. So does this mean that studies including patients with minor complications were included? More detail is needed to clarify this point. Which specific complications were considered exclusion criteria and how many studies were excluded for this reason should be described. Excluding participants with complications also affects the generalizability of these results.

Response: Thank you very much for your advice. We checked the literature carefully. Our exclusion criteria are not accurate enough. Patients in this study were included in the study with missing patients with diabetic complications. We have also re-checked the excluded articles and found no literature excluded for this reason. We revised the article Inclusion and exclusion criteria (Methods, Line 3-4, Page 8).

3. In the statistical analysis section, it seems that the authors started with the fixed effects model and then performed a test for heterogeneity. Because this test was not statistically significant, they determined that the random effects model should not be used. While this is a commonly used approach, it is better to begin with the random effects model especially because we would assume that there is likely variability across these studies which were carried out in very different populations. As one of the goals of meta-analysis is to determine variability of effect sizes across studies, the random effects model is likely to be more appropriate regardless of the result of the test of heterogeneity. If the fixed effects model is used when the random effects model should have been used, this can result in invalid estimates of the means, standard errors, and significance tests. More detail regarding the modeling would help to clarify the approach and justify the use of the fixed effects model. Were random effects models also fit? Did the estimates change when using random effects versus fixed effects?

Response: Thank you for your comments. Statistical analysis of this study was conducted using Review Manager Version 5.3 for Windows (The Cochrane Collaboration, Software Update, Oxford, UK). According to the Corcoran handbook, If P > 0.10 and I2 < 50%, the results of homogeneity were considered good, and the fixed effects model was used for analysis. Otherwise, the random effects model was used. So we use the fixed effect model. Of course, we have tried to use the random effects model for analysis. There was no difference between the
results of the two models and that of the fixed effect model (I²=12%, P=0.34; the mean of HbA1c (95% confidence interval) is (-0.025 [-0.43, -0.007]; P= 0.006). So we chose the fixed effects model.

4. The p-values are currently presented as >0.05 or <0.05. Exact p-values should be presented.

Response: Thanks reviewer for the opinions. We revised the content of the article and gave the Exact p-values (Abstract, Line 16, Page 3; Results, Line 1-7, Page 11; Results, Line 3-4, Page 12; Results, Line 9-11, Line 6-8, Page 12).

5. There are a few sections of the discussion that contain statements that are not substantiated by references. For example, on Page 14 it is stated that "compared with adults, teenagers have a poor understanding of the use and content of mobile phones". This is a puzzling statement and there is no reference to support it. Additionally, there are several sentences on Page 15, beginning with "Text messaging interventions were associated with lower costs and increased ease of operation…", which are not supported by references.

Response: Thanks reviewer for the comment. We revised the article and supplement relevant references (Discussion, Line 18-20, Page 14; Line 6-7, Page 15).

Minor comments:

1. In the inclusion criteria, it says "To be included in this study, the patients had to have reading and writing skills necessary to complete their medical histories and the questionnaires independently". It is not clear how is was assessed in each study. Was an age cut-off used to choose which studies to include? More details are needed.

Response: Thanks reviewer for the comment. All included patients should acquire reading and writing skills so that they could fill the anamnesis and psychological questionnaires independently. We also noted the age of the patient in screening the literature.

2. The 6003 citations described on Page 10 does not match the total of 5302 in the Figure.

Response: Thanks reviewer for the question. I'm terribly sorry, this is a slip of the pen. We corrected the error in our article (Results, Line 3, Page 10).

3. It would help to improve readability if subheadings were added to the results section for each of the subgroup analyses (e.g. age, intervention method, etc.)
Response: Thanks reviewer for the recommendations. We added the subheadings in results section for each of the subgroup analyses (Results, Line 21, Page 11; Line 5, Page 12; Line 13, Page 12).

4. What age cut-off was used to define the youth and adult groups?

Response: Thanks reviewer for the question. According to the average age (median age) provided in the literature, we grouped younger than 19 as the adolescent group and older than 19 as the adult group.

5. Adding a brief summary of the contents of the various interventions included in this analysis to the results section would be helpful to the reader.

Response: Thanks reviewer for the recommendations. We add the relevant summary in the results section (Results, Line 17-20, Page 11).

Reviewer 2 (Reviewer 2): PEER REVIEWER COMMENTS: To view the full report from the academic peer reviewer, please see the attached file.

REVIEWER COMMENTS FROM REPORT: This paper provides evidence in the form of a systematic review as to the effectiveness of mHealth interventions for glycaemic control in patients with type 1 diabetes. This answers an interesting and novel question and the methodology for extracting and analysing the data is of a good standard. The manuscript is structured appropriately and presents data in a clear manner, however I find some sentences a little hard to read and there are instances where statements are not supported by evidence or citations (as pointed out below).

REQUESTED REVISIONS:

I have a handful of comments that would improve the overall readability of the paper and communicate an appropriate justification for the study and interpretation of the results:

Title: It might be helpful to indicate in the title of the paper the study design (A systematic review and meta-analysis).

Response: Thanks reviewer for the comment. We revised the title of the article, added the study design (Title Page, Line 1-2, Page 1).
P5,L2-4: The first two statements need citations and on Line 4 there is a typographical error '...adolescents. with...'

Response: Thanks reviewer for the comment. We supplement relevant references based on the content (Background, Line 2-4, Page 5).

P5,L10: this is not a clear sentence - perhaps the word 'includes' is missing before failure but I am not sure?

Response: Thanks reviewer for the comment. We revised the article (Background, Line 10, Page 5).

P5,L13: it would be nice if you could give evidence in support of the statement that T1DM incurs an economic burden - what are the stats on this?

Response: Thanks reviewer for the comment. We supplement relevant references based on the content (Background, Line 13-14, Page 5).

P5,L15-20: You mention Studies have shown... but do not tell the reader which studies. Please add appropriate citations to support all of your claims here.

Response: Thanks reviewer for the comment. We supplement relevant references based on the content (Background, Line 15-20, Page 5).

P6,L3-4: this sentence needs revising to make more sense.

Response: Thanks reviewer for the comment. We revised the article (Background, Line 3-6, Page 6).

P6,L4-8: A definition of what exactly is meant by mobile health (mHealth) would be useful here. I would also change the phrase well documented as the evidence you cite is not conclusive - change to 'A number of studies have shown...' perhaps?

Response: Thanks reviewer for the comment. We revised the article (Background, Line 3-8, Page 6).

P6,L17: It would be helpful to stick to one term so as not to confuse the reader (e.g. Glycaemic index control, HbA1c, glycated haemoglobin).

Response: We revised the manuscript in accordance with the reviewers’ comments. We have corrected incorrect terminology (Abstract, Line 3,5, Page 3; Background Line 17, Page 6).

P7,L13: Justify why interventions greater than 3 months was selected as a criteria.

Response: Thanks reviewer for the opinion, HbA1c is not affected by daily blood sugar fluctuations, exercise or food. Glycosylated hemoglobin (HbA1c) provides objective criteria of
metabolic control over the most recent 8–12 weeks. So, we chose the literature where the intervention lasted at least three months. We have added relevant references (Methods, Line 13-15, Page 7).

P7,L16: Justify why patients had to have the literacy to complete measures independently.

Response: Thanks reviewer for the comment. All included patients should acquire reading and writing skills so that they could fill the anamnesis and psychological questionnaires independently.

P8,L5: Could you elaborate or rephrase what is meant by (5) consisted of previously published literature [do you mean no secondary data analyses were included?]

Response: Thanks reviewer for the comment. In the process of screening the literature, we found that part of the research from different angles published a number of studies. But the data used is the same. So we need to rule out duplicate publications. We revised the article (Methods, Line 6, Page 8).

P8,L11 This sentence needs modifying - delete 'they used' at the start.

Response: Thanks reviewer for the comment. We revised the article (Methods, Line 14-15, Page 8).

P8,L13-14: you do not need to include this again, it would be better to say 'included studies that met our inclusion criteria'.

Response: Thanks reviewer for the comment. We revised the article (Methods, Line 15-16, Page 8).

P8,L17-18: Could you be clearer about what 'redundant publications' means?

Response: Thanks reviewer for the comment. The republished articles are consistent with those previously published. All refer to articles on different topics published using the consolidated database.

P10,L10: does not read very well, change to something like "...completed the respective intervention studies, of which there were..."

Response: Thanks reviewer for the comment. We revised the article (Results, Line 11-12, Page 10).

P11-12: throughout the results section please state the exact p value rather than P< 0.05. Also tell the reader that the results you report are the mean difference and 95% CI(at least in the first instance).
Response: Thanks reviewer for the comment. We added the exact P values, and related definitions in the text (Results, Line2-4, Line 5, Line 7, Line 20, Line 3-4, Line 10-11, Line 16-17, Page 12).

P11,L1: You need a citation to support the statement "t1DM is managed differently in different groups"

Response: Thanks reviewer for the comment. We supplement relevant references based on the content (Results, Line 19, Page 11).

P11,L18: again stick to reporting HbA1c not 'glycated haemoglobin'

Response: Thanks reviewer for the opinion. We have corrected the terms of the full text (Results, Line 19, Page 11; Line 2, Line 10, Line 15, Line 17, Page 12. Discussion, Line 20, Page 13; Line 5-6, Page 16).

P13,L10: Rephrase this sentence as it does not quite make sense..."...meta-analysis showed that using mHealth interventions reduced HbA1c relative to no mHealth control groups

Response: Thanks reviewer for the comment. We revised the article (Discussion, Line 15-16, Page 13).

P13,L17: tell us which study you refer to here

Response: Thanks reviewer for the comment. We revised the article supplement relevant references based on the content (Discussion, Line 20-21, Page 13).

P14,L2-5: this needs rewriting to be more clear for the reader what the point is you are making.

Response: Thanks reviewer for the comment. We revised the article (Discussion, Line 7-8, Page 14).

P14,L15-16: Please include a citation giving evidence to support the claim that teenagers have a poor understanding of the use and content of mobile phones compared with adults. Also elaborate on how these factors affect glycaemic control (next sentence).

Response: Thanks reviewer for the comment. Compared with adults, adolescents' self-management ability is poor, and their understanding of health education is not clear enough. We revised the article and supplement relevant references (Discussion, Line 18-20, Page 14).

P14,L20: delete the word 'our' and change 'accepted' to something like 'has potential but needs to be refined' in accordance with the rest of your argument.

Response: Thanks reviewer for the comment. We revised the article (Discussion, Line 1-3, Page 15).
P15,L6;L10: what studies - need citations!

Response: Thanks reviewer for the comment. We supplement relevant references based on the content (Discussion, Line 20-12, Line 14-15, Page 15).

P15,L12-14: delete the word 'our' and expand to include reference to mHealth as this was the subject of your study

Response: Thanks reviewer for the comment. We revised the article (Discussion, Line 17-18, Page 14).

P15,L17: this has flagged up that from your table and tables and the text that we do not know if intervention duration is defined as the time the experimental group used the mHealth programme or to a follow-up measurement period that occurred after the intervention had stopped. Please clarify where relevant

Response: Thanks reviewer for the comment. We are checked the inclusion of literature, the intervention duration refers to the duration of continuous intervention. We revised the article (Methods, Line 13-15, Page 7; Discussion, Line20- 21, Page 15).

P16,L14: I would suggest putting the sub group comment after the sample size limitation as this is part of that original point you raise.

Response: This should really be explained in the limitations of sample size. We revised the article (Limitations, Line 12-13, Page 16)

P16,L17-20: It isn't clear what you mean here, do you mean rather than the mHealth programme itself? please rephrase to clarify.

Response: Thanks reviewer for the comment. HbA1c is the gold standard for measuring blood sugar control, but it is not affected by the fluctuation of blood sugar every day, nor is it affected by exercise or food. Therefore, long-term intervention is needed to reduce HbA1c. The existence of shorter intervention time in this study may have an impact on the findings. This is inevitable. We have also revised the content to make the meaning clearer (Discussion, Line 21 Page 16,Line 1-3 Page 17).

Table 1 and Table 2: Pick a better term than 'intervention way'. You call it intervention type in the text, which is better but should be defined in the legend (i.e. what the difference between text message and application is by your definition).

Response: Thanks reviewer for the suggestion. Yes, it is more appropriate to use the intervention type. In addition, we added the definition of the two intervention methods to footnotes in the form(Table 1).