

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Cost and Cost-Effectiveness of mHealth interventions for the prevention and control of Type 2 Diabetes Mellitus: A protocol for a Systematic Review
<b>AUTHORS</b>	Rinaldi, Giulia; Hijazi, Alexa; Haghparast-Bidgoli, Hassan

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Isabel de la Torre University of Valladolid, Spain
<b>REVIEW RETURNED</b>	03-Nov-2018

<b>GENERAL COMMENTS</b>	<p>The main objective of this paper is to systematically review and evaluate the cost and cost-effectiveness of interventions for prevention and controlling type 2 DM (Diabetes Mellitus). The topic is interesting but in its current status this paper cannot be published. The authors should improve several aspects such as:</p> <ul style="list-style-type: none"><li>- In abstract they should indicate the main contribution of this work. The different sections in the abstracts should be well-explained no mixing. After, keywords are in strengths and limitations, why?</li><li>- In Introduction, they must be more concise and add updating references.</li><li>- In methods section, Why did u use only 3 databases for searching? For example, they can also search in Science Direct, IEEE Explore, etc.</li><li>- Figure 1 should be more clear.</li><li>- Sumarizing Results should be Results only.</li><li>- I don't find conclusions and discussion in this work.</li><li>- References should be updated in all cases.</li></ul> <p>In general, all these aspects should be improved with quality for its publication.</p>
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<b>REVIEWER</b>	Sheyu Li West China Hospital, Sichuan University; Ninewells Hospital, University of Dundee
<b>REVIEW RETURNED</b>	21-Dec-2018

<b>GENERAL COMMENTS</b>	Thanks for letting me review this paper. Despite mobile health intervention for diabetes has been widely used in the clinical practice with promising effectiveness in improving the glucose control and self-management, the cost-effectiveness remains a big
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	<p>gap. The study is important and timely. However, I have some concerns about the study.</p> <p>Major:</p> <ol style="list-style-type: none"> <li>1. I would strongly recommend the authors to register their study in PROSPERO before submitting the protocol of systematic review.</li> <li>2. Unlike other interventions, the cost for the mHealth intervention may mean differently. It could be the cost for the users (subscribing fee), the health providers (system renting fee), the app developers (developing and maintaining cost) or other. Are the authors interested in all aspects of the cost, or only specific cost of the intervention?</li> <li>3. There seems two separate systematic reviews in the protocol, the cost, and the cost-effectiveness. May the authors wish to state the inclusion and exclusion criteria separately?</li> <li>4. The authors stated that they aim to include patients with diagnosed diabetes or at high diabetes risk. However, they seem to exclude the studies without showing the T2DM data according to figure 1. Could the authors kindly explain, please? Meanwhile, what does 'full EE' mean?</li> </ol> <p>Minor:</p> <ol style="list-style-type: none"> <li>1. As stated by the authors, the cost-effectiveness analysis could be conducted based on trial or modeling. May the authors wish to add a subgroup analysis based on it?</li> <li>2. 'App' and 'Application' may be helpful as keywords in the searching strategy. Meanwhile, the MeSH Term is strongly recommended in the searching strategy.</li> <li>3. A brief discussion to summarize the potential implementation, strength and limitation of the study in the design level may be necessary.</li> <li>4. 'not reporting any costing data' and 'Not evaluating mHealth interventions' may be duplicated with the inclusion criteria.</li> <li>5. May the authors explain why studies not being published in peer-reviewed journals are to be excluded, please?</li> </ol>
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<b>REVIEWER</b>	Paraskevas GKOLFAKIS Attikon University General Hospital, Athens, Greece
<b>REVIEW RETURNED</b>	18-Jan-2019

<b>GENERAL COMMENTS</b>	<p>Dear Editor,</p> <p>thank you for providing me to perform the statistical review of the manuscript entitled "Cost and Cost-Effectiveness of mHealth interventions for the prevention and control of Type 2 Diabetes Mellitus: A protocol for a Systematic Review".</p> <p>In their well-written protocol the authors describe their intention to perform a systematic review regarding the cost and cost-effectiveness of mHealth interventions for the prevention and control of type 2 Diabetes Mellitus. Their protocol follows the PRISMA-P guidelines and the authors define sufficiently the rationale for conducting this review, the endpoints, the methods to be used (specific exclusion and inclusion criteria to be applied during the literature evaluation, participants, intervention and outcome measures).</p>
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	<p>They also provide the search strategy to be followed allowing future repetition of the study.</p> <p>It is not clear if authors plan to also perform a quantitative analysis of their retrieved data. Acknowledging that not all systematic reviews lead to a meta-analysis authors' intention (or not) to undergo such an analysis should be stated in the protocol and respective methods should additionally be described (statistical tests to be used, estimation of outcome measure effect, heterogeneity investigation and sensitivity analysis).</p>
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## VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Isabel de la Torre

In abstract they should indicate the main contribution of this work. The different sections in the abstracts should be well-explained no mixing.

o Thank you for your comments. The abstract has now been revised to include the main contribution of this work.

o The different sections in the abstract have been divided into the three standard BMJ Open sections for abstracts; Introduction, Methods & Analysis and Ethics & Dissemination.

o A sentence has been added at the end of the “Methods & Analysis” to clarify how the results will also be analysed: “As we are predicting heterogenous results we will conduct a narrative and interpretive analysis of the data.”

After, keywords are in strengths and limitations, why?

o Dear reviewer, thank you for pointing out this. The have now removed the key words.

In Introduction, they must be more concise and add updating references.

o Dear reviewer, thank you for your comments. We have updated the references in the introduction to include the number of people living with diabetes in 2018, rather than 2014. We have also looked at and mentioned the global health expenditure towards diabetes in 2018. These new additions are in red color within the new manuscript version.

o Thank you also for suggesting we should make the introduction more concise. We have now acted upon this and removed several sentences from the introduction. We have been able to shorten the introduction to just one page.

In methods section, Why did u use only 3 databases for searching? For example, they can also search in Science Direct, IEEE Explore, etc.

o Dear reviewer, thanks for your comments. From our experience, Science Direct and IEEE Explore rarely yield new results once the prior three databases have been utilized. However, we have now included Science Direct in our database search.

Figure 1 should be more clear.

o Dear reviewer, thank you for your comments. We have now simplified the PRISMA flow-chart for our protocol. We have included this as PDF attachment in the re-submission.

Summarizing Results should be Results only

o We thank the reviewer for their comments. We have now removed any elements of discussion from our 'Summarizing Results' paragraph. This is now more concise and only addresses how we will summarize and present our results.

o We have included that we will summarize results according to Additional File 1. We will also convert results to 2017 international dollars using purchasing power parity conversion factors for each setting.

I don't find conclusions and discussion in this work.

o Dear reviewer, thank you for this suggestion. We have added a short "Discussion" and "Conclusion" paragraph. These paragraphs highlight the importance of this review and reiterate the main limitations we expect to encounter in our review.

References should be updated in all cases.

o Dear reviewer, thank you for your comment. We have updated the references to ensure that they are the most recent and up to date.

In general, all these aspects should be improved with quality for its publication.

We thank the reviewer for their extremely useful comments. We believe our manuscript has improved by changes suggested by your comments, and, those of Reviewers 2 and 3.

Reviewer: 2

Reviewer Name: Sheyu Li

Thanks for letting me review this paper. Despite mobile health intervention for diabetes has been widely used in the clinical practice with promising effectiveness in improving the glucose control and self-management, the cost-effectiveness remains a big gap. The study is important and timely. However, I have some concerns about the study.

Major:

1. I would strongly recommend the authors to register their study in PROSPERO before submitting the protocol of systematic review.

o Dear Reviewer, thank you for suggesting this. We have now registered the study protocol on PROSPERO. We have added the registration number (CRD42019123476) under the abstract in our Manuscript.

2. Unlike other interventions, the cost for the mHealth intervention may mean differently. It could be the cost for the users (subscribing fee), the health providers (system renting fee), the app developers (developing and maintaining cost) or other. Are the authors interested in all aspects of the cost, or only specific cost of the intervention?

o We thank the reviewer for their comments. We have now added the following sentence to the 'type of studies' section (page 6) to clarify what we mean by cost of intervention.

"All studies that report cost of the intervention, either from provider (e.g., design and implementation costs), patients (e.g., subscription fee, cost of changing behavior) or societal perspectives, will be included in the review." (page 6).

3. There seem two separate systematic reviews in the protocol, the cost, and the cost-effectiveness. May the authors wish to state the inclusion and exclusion criteria separately?

o We thank the reviewer for their comments. We have now made some revisions in the paper about the partial economic evaluation or cost of intervention studies. Specifically, we have clarified what we mean by cost of intervention studies and added a few sentences on how we assess quality of reporting in partial economic evaluation.

"Partial economic evaluations are defined as evaluations that provide the cost of the intervention but do not, however, compare the costs to an alternative intervention or to the outcomes of the intervention"

"For partial economic evaluations, we developed a modified tool using the relevant criteria in the CHEERS checklist and the tools used by previous researchers"

"The modified CHEERS checklist for partial economic evaluations or costing studies is a 16-item checklist (Additional file 3)."

o We have created a tool for evaluating partial economic evaluations and attached it in Additional File 3.

o We also slightly modified the exclusion criteria and we believe that this would capture all costing and cost-effectiveness/full economic evaluation studies.

4. The authors stated that they aim to include patients with diagnosed diabetes or at high diabetes risk. However, they seem to exclude the studies without showing the T2DM data according to figure 1. Could the authors kindly explain, please?

Dear reviewer, thank you for your comments. As per your own comments and those of Reviewer 1, we have now revised and simplified Figure 1. We will include a complete and summative version of Figure 1 in our final systematic review manuscript.

5. Meanwhile, what does 'full EE' mean?

o Dear Reviewer, thank you for highlighting this point. We have defined the difference between a partial and a full economic evaluation in our "Methods" section under "Types of Studies".

Minor:

1. As stated by the authors, the cost-effectiveness analysis could be conducted based on trial or modeling. May the authors wish to add a subgroup analysis based on it?

o Dear reviewer, thank you for this suggestion. We have now added this in our sub-group analysis.

2. 'App' and 'Application' may be helpful as keywords in the searching strategy. Meanwhile, the MeSH Term is strongly recommended in the searching strategy.

o Thank you, reviewer, we have now added these terms to our search strategy.

3. A brief discussion to summarize the potential implementation, strength and limitation of the study in the design level may be necessary.

o Dear reviewer, we appreciate your suggestion and we have now included a short “Discussion” paragraph to summarize the potential implementation and strengths and limitations of our review.

4. 'not reporting any costing data' and 'Not evaluating mHealth interventions' may be duplicated with the inclusion criteria.

o Dear reviewer, thank you for noticing this. To clarify the terms have now been made clearer to highlight the differences between them. They are now “Not addressing mHealth based interventions” and “not reporting any cost or cost-effectiveness data on the interventions”.

5. May the authors explain why studies not being published in peer-reviewed journals are to be to exclude, please?

o Dear reviewer, thank you for this suggestion. We included this criterion as a quality factor as the studies published in a peer-reviewed journal have already scrutinized for their validity, and originality and this process ensure they have a certain level of quality. However, we have highlighted this as one of the limitations of our review and the bias it can cause.

Reviewer: 3

Reviewer Name: Paraskevas GKOLFAKIS

Dear Editor,

Thank you for providing me to perform the statistical review of the manuscript entitled "Cost and Cost-Effectiveness of mHealth interventions for the prevention and control of Type 2 Diabetes Mellitus: A protocol for a Systematic Review".

In their well-written protocol, the authors describe their intention to perform a systematic review regarding the cost and cost-effectiveness of mHealth interventions for the prevention and control of type 2 Diabetes Mellitus. Their protocol follows the PRISMA-P guidelines and the authors define sufficiently the rationale for conducting this review, the endpoints, the methods to be used (specific exclusion and inclusion criteria to be applied during the literature evaluation, participants, intervention and outcome measures). They also provide the search strategy to be followed allowing future repetition of the study.

It is not clear if authors plan to also perform a quantitative analysis of their retrieved data. Acknowledging that not all systematic reviews lead to a meta-analysis authors' intention (or not) to undergo such an analysis should be stated in the protocol and respective methods should additionally be described (statistical tests to be used, estimation of outcome measure effect, heterogeneity investigation and sensitivity analysis).

o Dear Reviewer, thank you for highlighting this issue. We only plan to perform a narrative (descriptive) analysis of the results. This is because, based on our experience, the data will be too heterogeneous to be able to carry-out a quantitative meta-analysis. We have now highlighted this in the “Analysis” section.

## VERSION 2 – REVIEW

<b>REVIEWER</b>	Sheyu Li West China Hospital, Sichuan University
<b>REVIEW RETURNED</b>	25-Feb-2019

<b>GENERAL COMMENTS</b>	Thanks for the careful revision by the authors. I would endorse the publication of this protocol in BMJ Open.
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<b>REVIEWER</b>	Paraskevas GKOLFAKIS Hepatogastroenterology Unit, University general Hospital ATTIKON, Athens, Greece
<b>REVIEW RETURNED</b>	28-Feb-2019

<b>GENERAL COMMENTS</b>	Authors addressed all raised issues. Manuscript can be accepted in its current form.
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