Author’s response to reviews

Title: How diet, physical activity and psychosocial well-being interact in women with Gestational Diabetes Mellitus: An integrative review

Authors:
Leah Gilbert (leah.gilbert@chuv.ch)
Justine Gross (justine.gross@hospvd.ch)
Stefano Lanzi (stefano.lanzi@chuv.ch)
Dan Quansah (Dan.quansah@chuv.ch)
Jardena Puder (jardena.puder@chuv.ch)
Antje Horsch (Antje.horsch@chuv.ch)

Version: 1 Date: 20 Nov 2018

Author’s response to reviews:

20th November 2018

Leah Gilbert
GDM Service, – Office 6041
Lausanne University Hospital - CHUV
Avenue Pierre-Decker 2
CH-1011 Lausanne
Switzerland
leah.gilbert@chuv.ch
Dear Professor Yeyi Zhu,

Re: Manuscript ID Number PRCH-D-18-01018

Title: "How diet, physical activity and psychosocial well-being interact in women with Gestational Diabetes Mellitus: An integrative review"

Many thanks for the opportunity to revise and resubmit the above manuscript for publication in BMC Pregnancy and Childbirth.

We were delighted to receive your email dated 27th of October 2018 with the constructive suggestions of two reviewers. In this letter, we list each of the reviewers’ comments and point-wise demonstrate how we have addressed them. We are pleased to have addressed all of the concerns raised. In the manuscript and the tables, all changes are marked in the text by a yellow highlighting.

We very much look forward to hearing from you and thank you again for this chance to revise our manuscript, which we believe has now improved as a result of the reviewer’s comments and your suggestion to revise the English language.

Yours sincerely,

Leah Gilbert (on behalf of all co-authors: Justine Gross, Stefano Lanzi, Dan Yedu Quansah, Jardena Puder and Antje Horsch)
Dear Professor Yeyi Zhu,

Re: Manuscript ID

Number PRCH-D-18-01018- "How diet, physical activity and psychosocial well-being interact in women with Gestational Diabetes Mellitus: An integrative review"

Dear Mrs Gilbert,

Your manuscript "How diet, physical activity and psychosocial well-being interact in women with Gestational Diabetes Mellitus: An integrative review" (PRCH-D-18-01018) has been assessed by our reviewers. They have raised a number of points which we believe would improve the manuscript and may allow a revised version to be published in BMC Pregnancy and Childbirth.

Their reports, together with any other comments, are below. Please also take a moment to check our website at https://prch.editorialmanager.com/ for any additional comments that were saved as attachments. Please note that as BMC Pregnancy and Childbirth has a policy of open peer review, you will be able to see the names of the reviewers.

If you are able to fully address these points, we would encourage you to submit a revised manuscript to BMC Pregnancy and Childbirth. Once you have made the necessary corrections, please submit online at:

https://prch.editorialmanager.com/

If you have forgotten your password, please use the 'Send Login Details' link on the login page at https://prch.editorialmanager.com/. For security reasons, your password will be reset.

Please include a cover letter with a point-by-point response to the comments, describing any additional experiments that were carried out and including a detailed rebuttal of any criticisms or requested revisions that you disagreed with. Please also ensure that all changes to the manuscript are indicated in the text by highlighting or using track changes.

Please also ensure that your revised manuscript conforms to the journal style, which can be found at the Submission Guidelines on the journal homepage.

A decision will be made once we have received your revised manuscript, which we expect by 26 Nov 2018.
Please note that you will not be able to add, remove, or change the order of authors once the editor has accepted your manuscript for publication. Any proposed changes to the authorship must be requested during peer-review, and adhere to our criteria for authorship as outlined in BioMed Central's policies. To request a change in authorship, please download the 'Request for change in authorship form' which can be found here - http://www.biomedcentral.com/about/editorialpolicies#authorship. Please note that incomplete forms will be rejected. Your request will be taken into consideration by the editor, and you will be advised whether any changes will be permitted. Please be aware that we may investigate, or ask your institute to investigate, any unauthorized attempts to change authorship or discrepancies in authorship between the submitted and revised versions of your manuscript.

I look forward to receiving your revised manuscript and please do not hesitate to contact us if you have any questions.

Best wishes,

Yeyi Zhu
Associate Editor
BMC Pregnancy and Childbirth
https://bmcpregnancychildbirth.biomedcentral.com/

Response: Many thanks for providing us with an opportunity to revise the above manuscript for publication in BMC Pregnancy and Childbirth. We now had the manuscript corrected by an English native speaker and thus hope that the language use is appropriate.

Reviewer(s)' Comments to Author

Reviewer 1

A relatively new methodology and design. so please define what is the integrative review and its value. http://guides.temple.edu/c.php?g=78618&p=4260131 definition of GDM needs to be more clear.

Response: Thank you for your positive comments, we agree with your comment and have added a description of the guidelines we followed to elaborate our integrative literature review. Pages 7-8, Lines 163-176, highlighted in the manuscript in yellow and below:
Design

"This integrative review follows the guidelines elaborated by Whitemore and Knafl (2005) [69]. As we were investigating a new topic, we needed a design which would allow us to explore this topic in a broad manner and to produce evidence-based results. We followed Whitemore and Knafl’s design firstly by identifying variables of interest and elaborating specific research questions. We then used computerized databases to augment efficiency as well as the scope of our review. Secondly, we defined inclusion and exclusion criteria that guided the decision to exclude irrelevant articles, and we evaluated the quality of each original article. When analysing data, we categorized, summarized and ordered our data extracted from primary articles and organized the results according to subgroups. Whitemore and Knafl (2005) also recommend creating data displays; thus, we summarized our findings in tables (see additional file 1) and created a conceptual model integrating all of our results (see Figure 2). Finally, we specified the implications for clinical practice, as recommended by the authors."

We also added additional information to the description of GDM that we extracted from the American Diabetes Association, which was originally described lower down in the manuscript. Page 5, Lines 98-103, highlighted in the manuscript in yellow and below:

Introduction

"Gestational Diabetes Mellitus (GDM) is diagnosed when a woman has glucose intolerance during pregnancy that does not fulfil the criteria for the diagnosis of diabetes [1, 2]. It usually resolves after childbirth [1, 2], although it carries pre-, peri-, and postnatal risks of adverse outcomes in the mother and the child [3]. For example, up to 40% of women with GDM are known to have pre-diabetes in the early postpartum period [4]. Globally, the prevalence of GDM is approximately 17.8% to 23.1% [5, 6], and 10.8% in Switzerland [7]."

We would like to thank you again for your comments and we hope our answers are satisfactory.

Reviewer 2

This is a systematic literature review investigating 1) how physical activity, diet and psychosocial well-being "interact" in women with GDM and in their offspring; 2) how effective interventions that address more than one domain of interest are in reducing risk factors such as anthropometry, metabolic laboratory control, delivery and other clinical features. Two observational studies and 15 interventional studies including at least two domains of interest (diet, physical activity and psychosocial well-being) were included. The observational study
found that psychosocial well-being was positively associated with dietary quality and physical activity. The interventional study found that interventions combining diet and physical activity lead to increased physical activity and diet and lower stress perception; many of them also led to reduced BMI, improvements in some metabolic outcomes, reduced risk of type 2 diabetes after pregnancy and inconsistent birth outcomes. No intervention study has a psychosocial component.

However, the conclusion regarding the "interactions" of psychosocial well-being with diet and physical activity and the recommendation of integrating psychosocial well-being in interventions were only vaguely supported by 2 observational studies and 1 or 2 intervention studies.

Response: Thank you for your comment, with which we agree. We thus toned down our conclusions regarding the associations between diet, physical activity and psychosocial well-being. Below and you will also find these changes highlighted in the revised manuscript.

Page 4, Lines 75-79.

Abstract

"Conclusion. This integrative review showed that psychosocial well-being interacted with diet as well as with physical activity in women with GDM. We recommend that future studies consider integrating psychosocial well-being in their intervention, as observational studies demonstrated that social support and self-efficacy helped with adopting a healthy lifestyle following GDM diagnosis"

…

Page 22, Lines 537-539.

Discussion

"Moreover, it summarized the effectiveness of interventions addressing more than one lifestyle domain, including diet and physical activity on anthropometric, metabolic, delivery and other clinical outcomes."

…

Page 22, Lines 543-546.

"Results from this review indicated that the interaction between lifestyle domains produced desirable outcomes. The two observational studies integrated in this review demonstrated that psychosocial well-being such as social support and self-efficacy were important factors that were associated with adherence to a healthy lifestyle."
"Overall, evidence from this integrative review suggests that lifestyle interventions including a psychosocial intervention during pregnancy could augment the women’s adherence to diet and physical activity, which in turn might have complementary and interactive effects on the physiological and psychological health of women with GDM."

Clinical implications

"On the other hand, this review showed that psychosocial well-being, such as self-efficacy and social support may be important when adopting a healthy diet and physical activity habits. Thus, we propose that any intervention focusing on behavioral change, should evaluate and consider integrating psychosocial well-being as part of the intervention components, as this might add to the lack of research in this domain."

"Future studies that plan to adopt psychosocial interventions should focus on self-efficacy and/or social support, as both elements are associated with diet and physical activity habits."

"Thus, future interventions may focus on the psychosocial well-being of women with GDM to help alleviate and/or ameliorate stress symptoms [126]."
Conclusion

"Given that psychosocial well-being, such as social support and self-efficacy, are associated with physical activity and healthy dietary choices, we recommend that future intervention studies consider integrating psychosocial well-being in a combined diet and physical activity intervention to investigate the role of self-efficacy and social support on GDM." 

Of equal importance, the study never addressed the question of whether combined intervention has better effects on the outcomes compared to interventions addressing a single domain - which is necessary to justify any combined intervention in the first place.

Response: Thank you for this comment. However, we believe there might possibly be a misunderstanding. Our integrative review is the first step in looking at the effect of combined interventions and we always compare the findings to the control groups or the baselines found in the original papers. Thus, there is a comparison between combined interventions and interventions addressing a single domain or even no domain, or with before the treatment started. The next step then would be to investigate whether combined interventions are more effective than single interventions. This is mentioned at the end of our introduction Page 7, Lines 154-158 and below:

Introduction

"Therefore, this integrative review explored how physical activity, diet, and psychosocial well-being interact in women with GDM and in their offspring by analyzing and synthetizing observational and intervention studies. In addition, we investigated how effective interventions that address more than one domain of interest are in reducing risk factors associated with GDM."

Other major comments:

1. The term "interact" is vague and misleading. Upon reading the word, I thought the study examines whether diet, physical activity and psychosocial wellbeing have synergistic effects on health outcomes (i.e., statistical interaction), where in fact it examined whether the three domains are correlated. A clearer term is needed.

Response: Thank you for this valuable feedback and opportunity to clarify. Indeed, we were not looking at statistical interactions, as this is not the aim of an integrative literature review (Whitemore and Knafl, 2005) [68]. In order to clarify our concept of interaction, we chose to add a description in the introduction Page 6, Lines 137-141, highlighted in the manuscript in yellow and underlined below.
Introduction

"Many modifiable risk factors that relate to GDM also interact with each other. In this review, the term “interaction” covers correlations or associations, found in the original papers, between our domains of interest [diet (including breastfeeding), physical activity and psychosocial well-being (including depression, anxiety, stress, sleep, self-efficacy and social support)]."

2. The "clinical outcomes" needs to be prespecified in the inclusion criteria (page 8, line 162). Also, different outcomes were reported in different articles, thus there is a potential for publication bias - only significant findings were reported, as the author noted.

This problem is augmented by the paper's lack of clearly prespecified outcomes - thus any significant results reported in the articles were captured in the review. Maybe a formal test for publication base can be used.

Response: Thank you for this comment. However, there might possibly be a misunderstanding regarding the methodology of the integrative review (Whitemore and Knafl, 2005) we chose to use. Your comment would have corresponded to the methodology of a systematic review. However, the aim of an integrative literature review, like ours, is to integrate as many findings as possible that concern the research questions and answer inclusion criteria to allow data to be as broad as possible. This is because an integrative review is usually a first step to investigate a new topic of interest. Indeed, Whitemore & Knafl’s recommendations (used in our review) are to analyze all of the data first and then to order, code categorize and summarize them into an integrated conclusion (please see pages 7-8, Lines 163-176 for a summary of these recommendations).

However, we agree that our second research question was broad: “What should be the ingredients of an interdisciplinary lifestyle intervention to counter the negative impacts of GDM?” We realized that we had mentioned clinical outcomes in the research questions in the introduction, which may have caused confusion; therefore, we changed it. Page 7, Lines 156-158., highlighted in the manuscript in yellow and below you will find what we added.

Introduction

"In addition, we investigated how effective interventions that address more than one domain of interest are in reducing risk factors associated with GDM."
3. Are the interventions during pregnancy or postpartum? This distinction has important implications and perhaps should be discussed separately. This point wasn't clear in the paper.

Response: Thank you for this useful comment. Indeed, this was not clear and the intervention period of the studies has been added in the methods. Page 13 Lines 308-311, highlighted in the manuscript in yellow and below.

Methods - Lifestyle interventions investigated

"All outcome variables were tested either during pregnancy [80, 83, 89] or in the postpartum period [74-88]. In intervention studies, the interventions started either during pregnancy [76, 79, 80, 82, 83, 89] or in the postpartum period [77, 78, 81, 84-88] (for details, please refer to Tables 1 and 2 in additional file 1)."

We also proceeded to clarify the intervention period (starting during pregnancy or starting during the postpartum period) in the additional file 1 by adding a sentence in the “intervention” column in the tables of additional file 1. Moreover and following your comment about clarity, we also proceeded to mention each time if the results were compared to the control group or compared to the baseline in the “major findings in intervention group” column of additional file 1. We believe this allows the reader to identify rapidly the starting period (pre- and post-partum) of each study as well as if the results are compared to a control group or to the baseline.

4. There is one study that compared women in the lifestyle intervention group to those without GDM (page 11, line 231-232). This study should not be included as the comparison does not demonstrate the effects of lifestyle interventions on GDM.

Response: Many thanks for spotting this mistake; we excluded this study from our review and made changes accordingly throughout the manuscript and removed it from the tables (additional file 1), as well as from the flow chart.

5. For outcomes reported in sufficient number of articles, meta-analysis may be used to synthesis the findings in a more formal way.

Response: Thank you for your comment. However, our methodology is that of an integrative review (Whitemore and Knafl, 2005), and conducting a meta-analysis is not part of an integrative review. Please refer to previous response above (point 2).
6. Although over adverse perinatal outcomes have been associated with the lifestyle interventions in the reviewed articles (page 21, line 473-479), this was never discussed as a potential downside to these interventions in the discussion.

Response: Many thanks for this comment. Indeed, this should have been done in the previous version of the manuscript. However, following your major comment 4, we proceeded to take out the only study reporting negative perinatal outcomes in the infant. Indeed, both of the other studies investigating delivery outcomes demonstrated no change or improvements in the intervention groups compared to the control group.

7. There were large heterogeneities in the study intervention and follow-up period across studies, making interpretation of the findings difficult. The author may try to explain some of the differences in results in relation to this heterogeneity.

Response: Thank you for this point, we added this as the first point in the limitations (discussion section) and as mentioned in your major comment 3, we proceeded to clarify if the intervention was compared to control group or baseline in the tables (additional file 1). Page 28, Lines 689-697, highlighted in the manuscript in yellow and below.

Discussion – Strengths and limitations

"Firstly, conducting an integrative literature review lead to integrating studies with large heterogeneities regarding the intervention and follow-up periods across studies, as well as in the types of lifestyle interventions used in each individual studies. Thus, our results need to be interpreted with caution."

Minor comments:

1. Page 5, line 77: this is not how GDM was defined. Please check for the standard definition.

Response: Many thanks for your comment; we have now added some information concerning the standard description of GDM extracted from the American Diabetes Association, which was originally described lower down in the manuscript. Page 5, Lines 98-103, highlighted in the manuscript in yellow and with the added information underlined below.
Introduction

"Gestational Diabetes Mellitus (GDM) is diagnosed when a woman has glucose intolerance during pregnancy that does not fulfil the criteria for the diagnosis of diabetes [1, 2]. It usually resolves after childbirth [1, 2], although it carries pre-, peri-, and postnatal risks of adverse outcomes in the mother and the child [3]. For example, up to 40% of women with GDM are known to have pre-diabetes in the early postpartum period [4]. Globally, the prevalence of GDM is approximately 17.8% to 23.1% [5, 6], and 10.8% in Switzerland [7]."

2. Page 5, line 79-80: should this be prevalence or incidents? Among whom? Also, the percentage seems high than what I know.

Response: Thank you for your comment. Indeed, we can confirm that this is the prevalence of GDM. For example, one of the studies we cite regarding the prevalence in Switzerland made the following statement: “The prevalence of GDM in our population was 10.9%, much lower than in the UAE (37.7%), in China (22.7%) and in the HAPO cohort (16.1%) [1, 2].” Please refer to the last page of this document to find the full references.

3. Page 8, line 154: why does the updated search in 2018 yield fewer articles than the older search in 2016?

Response: Thank you for this comment. We have proceeded to add the following sentence explaining why the second literature search yielded fewer articles. Page 8, Lines 194-196, highlighted in the manuscript in yellow and below.

Search strategy

"The second literature search yielded fewer articles than the first one because we were able to exclude the time period related to our first search in Pubmed, thus avoiding the exclusion of duplicates in this database."

4. Page 8, line 172: only dietary interventions, but not observational studies on dietary supplements were not excluded?

Response: We thank you for noticing this typo. Indeed, we proceeded in the same way for observational studies and thus changed the following sentence. Page 9, Lines 207-212, highlighted in the manuscript in yellow and below.
Exclusion criteria

"We excluded study protocols, conference abstracts, recommendation papers, guidelines, qualitative studies and review articles. Articles that exclusively investigated women with type 1 and type 2 diabetes were excluded. Intervention studies that only tested pharmacological interventions were also excluded, as were genetic, epigenetic and genomic studies. Studies on diet, which focused only on dietary supplements were also excluded. Animal research and papers addressing exclusively the microbiome were also excluded."

5. Is the JBI's checklist for analytical cross-sectional studies appropriate for the prospective cohort study? There are other checklists such as STROBE statement for observational studies. What's the difference between JBI's checklist for RCT and the CONSORT statement?

Response: Thank you for this comment. We re-evaluated the quality of the prospective cohort study according to the JBI checklist for cohort studies and we also chose to re-evaluate the non-RCT studies in accordance with another checklist for quasi-experimental studies, to improve the assessment of quality in all studies. All the changes have been made throughout the manuscript and in the tables. You will find the changed evaluations of articles in the manuscript highlighted in yellow and the changes made below:

Page 10, Lines 228-231.

Methods – Data extraction and quality appraisal

"The quality of included studies was assessed with the JBI critical appraisal Checklist for Randomized Controlled Trials [70], Checklist for quasi-experimental studies (non-randomized experimental studies) [71], Checklist for Analytical Cross Sectional Studies [72] and Checklist for Cohort studies [73]."

Pages 21-22, Lines 517-531.

Results - Quality of studies reviewed

"Authors (LG & DYQ) rated the majority of included articles to be of good quality based on the Joanna Briggs Institute Appraisal Tools (2017) [74-84, 86-89] (see tables 1 and 2 in additional file 1). The checklist for analytical cross-sectional studies [72] was used for the cross sectional
observational study [74], the checklist for cohort studies [73] was used for the prospective cohort study [75] whereas for intervention studies, the checklist for randomized controlled trials [70] was employed for the randomized controlled trials [76, 78, 79, 81, 82, 84, 87-89]. For the remaining intervention studies [77, 80, 83, 85, 86], we used the checklist for quasi-experimental studies [71]. Studies rated as having a good quality described in detail the design and methodology used, the process of recruiting participants, study setting, gave clear and detailed presentation of findings and had study limitations that were unlikely to affect the reliability and validity of study findings. The only study rated as having poor quality [85] did not explain the reasons for drop out in participants and did not conduct analysis to compare the drop outs to the participants remaining in the study. It thus had limited information on data analysis a small sample size, both of which could lead to a high risk of bias and a poor generalizability of the study."

Used to be on Page 28, Line 692.

Limitations

"Furthermore, some of the integrated studies lacked of quality."

To answer the second part of your question, we chose the Joanna Briggs Institute (JBI) instruments, as the JBI checklist is a well-known evidence-based instrument to evaluate healthcare research in nursing, midwifery, medicine and allied health, which was exactly the scope of our review. Indeed, we chose not to use the CONSORT statement, as it is more generally used for randomized controlled trials. Finally, we wanted to use one tool only (JBI) to evaluate all included studies for ease of comparison; this is the reason why we did not use CONSORT for RCTs and then JBI for observational studies.

6. Page 10, line 209: "most" should be more than half.

Response: Many thanks for this comment, we have now changed the sentence. Page 11, Lines 248-249, highlighted in the manuscript in yellow and below.

Characteristics of the included studies

"The 14 intervention studies took place in seven different countries, with the highest number of them conducted in the USA (n=5/14) [74-78] and China (n=3/14) [79-81]."
7. Page 10, line 214: what is "intervention trials"? Does it have randomization and/or comparison group? Better specify it.

Response: Indeed, this was not described, so we added a description, which has been highlighted in the manuscript in yellow and below you will find the information we added.

Page 11, Lines 252-255.

Results - Characteristics of the included studies

"Of these intervention studies, the large majority were randomized controlled trials (RCTs) (n=9/14) [76, 78, 79, 81, 82, 84, 87-89] and the remaining studies were intervention trials (n=5/14), with two of them (n=2/5) containing a control group [80, 83] and the other three (n=3/5) using a pre/post-test design [77, 85, 86]."

Pages 11-12, Lines 268-275.

"An exception remains for three studies (n=3/14) that were designed differently. Indeed, one study compared the lifestyle intervention group at the end of the study (one year) to the baseline of that same lifestyle intervention group and thus did not contain a control group (n=1/14) [86]. For the second study, the authors used a single-group pre-post design and measured the effect of the intervention across time [77]. Finally, the last study was a single arm pilot before and after intervention study [85]. For these studies, these design details will always be mentioned in our results section."

For the two additional studies which we have now described more clearly, all results corresponding to these studies have also been modified. Although we chose not to add those modifications here in our response letter in the interest of readability, we guarantee this has been changed throughout the manuscript.

8. Page 22, line 497: depression, anxiety and sleep were searched but no article contain such information.

Response: Thank you for noticing this; we added this in the discussion. Pages 28-29, Lines 694-697, highlighted in the manuscript in yellow and below.

Discussion - Strengths and limitations
"Moreover, although we had also searched for terms, such as depression, anxiety and sleep in the psychosocial well-being domain, no results were found for these outcomes. This might be due to the fact that, as mentioned, psychosocial well-being was only present in two observational studies and as an outcome in two intervention studies."

9. Page 22, line 504-505: this again implies that the three domains have synergistic effects on health outcomes, which this study did not investigate.

Response: Following your first major comment, we described the term “interaction” in the introduction in order to avoid misunderstandings; please see our answer to Major comment 1.


Response: We thank you for noticing this typo; we changed the sentence as follows. Pages 22-23, Lines 546-548, highlighted in the manuscript in yellow and below.

Discussion

"Indeed, the observational studies demonstrated that social support and self-efficacy were associated to positive changes in diet and physical activity."

11. Page 27, line 641-643: this claim is not supported

Response: Thank you for your helpful comment. We have now modified the statement to make it more in line with the results of our integrative review. Page 28, Lines 676-678. highlighted in the manuscript in yellow and below.

Discussion

"After all, the success of a combined diet and exercise intervention may also depend on the mothers’ psychosocial well-being (depression, stress, self-efficacy and social support) during pregnancy."

12. Page 28, line 656-657: the RCT design per se addresses internal validity, but not generalizability.
Response: We agree with your comment and have thus taken this sentence out (not shown here, as it was simply removed).

Additional modification

When improving the tables, we realized that we had forgotten one result for one of the RCTs integrated in the review (O’Dea et al. 2015) concerning two-hour glucose after OGTT. Thus, we added this result and this changed the following parts of the manuscript and prompted us to regroup the results concerning glucose in our result section (changes not shown below for the grouping of results to improve readability). Below you will find the added terms, we have also proceeded to highlight these changes in yellow in the manuscript.

Pages 18-19, Lines 446-451

Results - Metabolic outcomes

"Concerning other glucose-related values (n=3/7), all of these values were reduced in the intervention groups (n=3/3), demonstrating lower one-hour glucose after OGTT at study end (6 weeks) (n=1/1) [79], lower two-hour glucose after OGTT at the one year follow-up of a three-month intervention [87] and lower 2-hour postprandial blood glucose at the end of an eight-week intervention (n=1/1) [89]."

…

Page 20, Lines 475-478

"In summary, the majority of the studies that included metabolic outcomes revealed a decrease in total and LDL cholesterol, triglycerides, and in glucose values. Results in HbA1c and HDL cholesterol were inconsistent and the other outcomes were not measured in enough studies to draw conclusions."

Page 24, Lines 578-580

Discussion

"Regarding metabolic outcomes, the intervention studies led to a decrease in total cholesterol, LDL cholesterol, triglycerides and glucose values compared to the control groups, although results for HbA1c and HDL cholesterol were inconsistent."
"Our results are in line with these findings, as three interventions measured glucose values and two studies lead to improvements in two measured glucose values. The third study lead to improvements in 2-hour glucose after OGTT and to similar results in fasting plasma glucose."

"Indeed, previous research has shown that regular exercise increases insulin action by stimulating glucose uptake in the muscle through glucose transport proteins (GLUT4) that mediate insulin-dependent glucose uptake [105], and our results showed improvements in 2.5/3 of the studies analyzing glucose as an outcome."

On behalf of our team, we thank you again for your very helpful and insightful comments, which we believe have highly improved the quality of our paper. We hope we answered your questions appropriately.

Bibliography for Reviewer 2: minor comment 2:
