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16 May 2016

Jin-Xin Kong  
Science Editor, Editorial Officer  
*World Journal of Diabetes*

Dear Dr Kong,

**Re: Resubmission of Manuscript ID 24775**

On behalf of my coauthors, I am pleased to submit to the *World Journal of Diabetes* our revised manuscript, entitled

*The relationship between depression and diabetes in pregnancy: a systematic review*

Thank you for your positive and constructive feedback on the original submission (your email dated 20 April 2016). We have responded to each of the reviewers' comments (please see attached tables) and revised the manuscript accordingly.

We thank you for your willingness to consider a revised version of the manuscript and look forward to your earliest response.

Sincerely,

Dr Ian Gallen

## Response to Comments from Peer-Review

Question or Comment #	Comment	Response
<b>Reviewer 1</b>		
1-1	This manuscript is a systematic review of the literature about the relationship between depression (post-partum depression in particular) and diabetes in pregnancy. After reviewing almost 1200 articles on the subject, the authors included in the review only 48 of them as they were the only pertinent to the topic. The assessment of the articles indicated overall poor study quality as many studies were observational and often lacked stringent, objective criteria to support a diagnosis of clinical depression. Based on these limitations, no clear consensus emerged from the literature review, as well as limited guidance for clinicians. The main conclusion of the authors is that high quality research with stringent criteria and assessable parameters is needed to establish specific guidelines for management of pregnant women with depression and gestational diabetes.	We thank the reviewer for this positive feedback.
<b>Reviewer 2</b>		
2-1	The article: "The relationship between depression and diabetes in pregnancy: a systematic review" is an analysis about the prevalence of depression among women with gestational diabetes that ranged from 4.1 to 80% in 16 studies. The analysis of the review was focused to exam whether diabetes and pregnancy was a risk factor for depression or depression was a risk factor for diabetes in pregnancy. The results are confuse because there was no clear consensus for the relationship and also there are no guides for the management of both situations in pregnancy. The analysis is interesting and data are valuable for clinicians because the presence of both situations are frequent.	We thank the reviewer for this positive feedback.
<b>Reviewer 3</b>		
3-1	The submitted review article "The	We thank the reviewer for this positive

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	<p>relationship between depression and diabetes in pregnancy: a systematic review” summarizes the recent and comprehensive published material on this subject. The article focuses on the current literature and represents an extensive and very broad and systematic overview of the issue. In the introduction the main issues are addressed: gestational diabetes, pre-existing or newly detected type 1, type 2 diabetes or any form of diabetes and depression prior, during pregnancy or postpartum, the issue that depression could be a risk factor for the development of type 2 diabetes and the lacking advice regarding care for these patients. In the method section literature search results and study characteristics are well described. Depression is often not fully developed in the sense of a ICD-10 or DSM-IV diagnosis, subclinical forms which are reported in depression questionnaires could lead to missing signs of worsening of mental states are not ignored. To summarize the paper gives a very complete state of the art view of the current knowledge of the relationship between depression/depressive symptoms and diabetes in pregnancy.</p>	<p>feedback.</p>
3-2	<p>There are some small issues to take into consideration: Please explain why the studies that reported depressive symptoms on measures of anxiety or bipolar disorder are excluded.</p>	<p>Although some scales designed to assess symptoms of anxiety or bipolar disorder include questions related to depression, we excluded studies that used these scales in order to focus our review on depression alone. Anxiety and bipolar symptoms can represent separate comorbid diagnoses according to ICD-10 and DSM-IV without meeting the criteria for depressive disorders. By excluding studies that used anxiety and bipolar disorder scales, we aimed to minimize the false-positive incidence of depression.</p>
3-3	<p>Considering study quality the selection bias (p 9,) and other biases (p 19) should be characterized in more details.</p>	<p>We appreciate the reviewer’s request for more detail regarding the potential biases inherent in the studies included in the review. However, because of the large number of studies and the generally poor reporting of many of the articles, we have not assessed the quality of individual studies. Instead, we have described the overall study quality and have acknowledged the limitations associated</p>

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		with different study designs (eg, prospective vs retrospective studies). Additional text regarding study quality has been added to the Discussion on page 20.
3-4	P 10 the abbreviation RCT was used for the first time without specification.	The abbreviation RCT is first used, with definition as “randomized controlled trial,” on page 10 in the section “Literature search results”.
3-5	The review is limited by the bidirectional nature between diabetes in pregnancy and depression before and during pregnancy and postpartum. Longitudinal studies are missing to clarify in particular the impact of depression on diabetes. The aspect of the shared underlying mechanism between depression and diabetes should be explained in more details.	We appreciate the reviewer’s comments regarding the mechanisms underpinning the bidirectional relationship between diabetes in pregnancy and depression. As mentioned in the manuscript Introduction, this relationship is well-established in non-pregnant patients, but little is known about the link between these diseases in pregnancy. However, even among non-pregnant patients, the mechanisms are not fully understood. We have now added a paragraph to the Discussion (page 19) that briefly discusses possible mechanisms linking diabetes with depression.
3-6	Article category: why this paper is presented under “Allergy”?	The designation of the article category as “Allergy” was unintentional and mistakenly occurred during submission. Given its multidisciplinary nature, the article could fall under several categories, including Endocrinology and Metabolism, Obstetrics and Gynecology, and Psychiatry.
3-7	Keywords: it seems that the keywords are not separated meaningfully	The keywords are presented in alphabetical order.
3-8	References: DSM-IV and ICD-10 are used without references	Reference 60 is the DSM-IV, which is cited in the Methods section on page 10 under “Definition of depression.”  The ICD version used varied among the studies depending on what was current when the data for the study was collected. Thus, we did not include a specific reference for ICD codes. However, we have added the website for ICD-10 ( <a href="http://www.who.int/classifications/icd/en/">http://www.who.int/classifications/icd/en/</a> ) as a reference (cited on page 11).
3-9	Figures: N and n is not consistently used	As per the American Medical Association Manual of Style, a capital N is used to denote the total sample size, whereas a lower-case n is used to denote the size of any subgroup, eg, women with gestational diabetes.

Question or Comment #	Comment	Response
<b>Reviewer 4</b>		
4-1	Authors are requested to give a possible explanation about the link between depression and diabetes mellitus, although work on this topic is not conclusive.	We thank the reviewer for this suggestion and have addressed this request by adding a paragraph to the Discussion, as described in reply to Reviewer 3's similar comment (see 3-5 above).
<b>END</b>		