

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	The Short-Term Health and Economic Burden of Gestational Diabetes Mellitus in China: A Modeling Study
<b>AUTHORS</b>	Xu, Tingting; Dainelli, Livia; Yu, Kai; Ma, Liangkun; SilvaZolezzi, Irma; Detzel, Patrick; Fang, Hai

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Tim Dall IHS Markit, USA
<b>REVIEW RETURNED</b>	23-Aug-2017

<b>GENERAL COMMENTS</b>	<p>The technical aspects of this manuscript are generally well written and the methods and assumptions appear to be sound. My major concern is that the manuscript needs thorough editing by a native English speaker. Some sentences are phrased awkwardly and this makes it difficult to understand.</p> <p>If 2.9 million pregnant women suffer from GDM, then the QALY loss estimate of 1 million seems very high. Are we saying that the average GDM pregnancy is associated with about a third of a QALY? (This estimate comes primarily from Reference #27). Is the 0.65 QALY associated with maternal diabetes (Table 2) relative to having a normal pregnancy, or having maternal diabetes compared to not being pregnant? That is, is the 0.65 just related to GDM or does it include the reduced QALY associated with pregnancy in general?</p> <p>Table formatting needs to be fixed in some instances. For example, in Table 2 the far right column should drop the decimals because the numbers are large.</p> <p>Overall, it's a good paper but needs substantial editing.</p>
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<b>REVIEWER</b>	P.I.Lenoir-Wijnkoop Utrecht University, The Netherlands
<b>REVIEW RETURNED</b>	06-Sep-2017

<b>GENERAL COMMENTS</b>	<p>Interesting topic, relevant in current and future maternity health care context.</p> <p>The reviewer also provided a marked copy with additional comments. Please contact the publisher for full details.</p>
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## VERSION 1 – AUTHOR RESPONSE

### Reviewer 1:

1) The technical aspects of this manuscript are generally well written and the methods and assumptions appear to be sound. My major concern is that the manuscript needs thorough editing by a native English speaker. Some sentences are phrased awkwardly and this makes it difficult to understand.

Response: We thank Reviewer 1 for positive comments on our manuscript. We invited two native English-speaking colleagues to improve the quality of the English throughout our manuscript in the revision.

2) If 2.9 million pregnant women suffer from GDM, then the QALY loss estimate of 1 million seems very high. Are we saying that the average GDM pregnancy is associated with about a third of a QALY? (This estimate comes primarily from Reference #27). Is the 0.65 QALY associated with maternal diabetes (Table 2) relative to having a normal pregnancy, or having maternal diabetes compared to not being pregnant? That is, is the 0.65 just related to GDM or does it include the reduced QALY associated with pregnancy in general?

Response: We thank Reviewer 2 to point out this important issue; there was a mistake. The health loss reported refers to the difference between a normal pregnancy and a pregnancy with GDM. We calculated it in several steps:

- first we took the QALYs from the reported literature (e.g. Maternal diabetes 0.65);
- we calculated the health loss subtracting from 1 (full health) the QALY reported (following the example  $1-0.65=0.35$  QALY);
- since QALYs refer to a year period and our paper to 3 months only, we divided this figure by four ( $0.35/4=0.0875$  QALY);
- we finally multiplied these health losses by the appropriate number of women, which corresponds to:
  - a) 2.8 million (those suffering from GDM, equal to  $17.5\%$  prevalence\*16 million deliveries) for the Maternal Diabetes;
  - b) the 20% of the 2.8 million suffering from GDM using insulin (577,000 women) for the Insulin Injection;
  - c) the number of women with GDM (2.8 million) weighted by the difference in probability between GDM and non GDM group for the pre-term birth, the caesarean section and hypertensive disorders. For example, the probability of having a Pre-term birth is equal to  $6.35\%$  for GDM women and to  $3.47\%$  for non-GDM women, for a difference of  $3.88\%$ . Therefore, the pre-term incremental burden due GDM was calculated on the following number of women:  $2.8 \text{ million} * 3.88\%$  (112,000 women). We hope these steps are now clear. Table 2 and text (pages 8-9) were revised accordingly.

### Reviewer 2:

1) We thank Reviewer 2 for all the editorial edits and comments, and we had revised our manuscript accordingly. In addition, we also invited two native English-speaking colleagues to improve the quality of the English throughout our manuscript in the revision.

2) Page 2, Line 49. The original manuscript stated one limitation: "In order to extend our results to a national level, we assumed equal medical facility quality in urban and rural areas across China, while in reality healthcare system is not homogeneous." Reviewer 2 suggested "This should be approached in a proportional manner, in particular since most of the costing data probably come from the more specialized hospitals."

The assumption has to be based on the ratio of low resource settings/hospitals/specialized hospitals and the number of deliveries in each setting for 2015 for reaching a reasonable extrapolation on national level”.

Response: We thank Reviewer 2 for this helpful comment. We considered the cost differences by the levels medical institutions (low resource settings/hospitals/specialized hospitals and the number of deliveries in each setting for 2015) in our study, but it was not clearly stated in the previous version. The prices and costs of all medical treatments were obtained from 7 provincial Chinese Price Bureaus (representative 7 diverse regions in China) and literatures, and were also adjusted based on the different expenses in different level of medical institutions by calculating the average unit prices. Therefore, our results could be regarded as a national average. We clearly stated these strengths in the section of “Strengths and limitations of this study” and the section of Methods on Page 4 (Line 91-100).

3) Page 10, Line 223-224. GDM lifestyle interventions, including diet, exercise, and health education were very effective. Reviewer 2 requested references to support this statement.

Response: Two references (#15 and #36) were provided.

4) Page 10, Line 230-235. Reviewer 2’s comments: “This indication is mainly regarding to out-of-pocket costs for the concerned subjects. It would make more sense to compare with a health concern that is more representative for using health care resources.” “A comparison with data 15 years old should be avoided. Also, injuries in USA are not representative for other parts of the world”.

Response: We agree with Review 2 that these comparisons were not appropriate and we changed them To quantify the magnitude of this loss, the health loss due to GDM was about 1/4 of 1,180,260 QALYs loss caused by squamous cell carcinoma (one lung cancer type), or 1/18 of QALYs loss caused by all types of lung cancers in China. [37,38]

5) Figure 3, please check whether this input parameter of neonatal encephalopathy was used in the analyses and correct in the manuscript where needed.

Response: The neonatal encephalopathy has been analyzed in the study as one neonatal complication. It has been used in the Table 1 as one input parameter. We corrected the error in the text.

6) Appendix Figure 2 should use the same vertical scale for all the 4 small figures.

Response: We revised Appendix Figure 2 and used the same vertical scale for all the 4 small figures.

## VERSION 2 – REVIEW

<b>REVIEWER</b>	Irene Lenoir-Wijnkoop Utrecht University, The Netherlands
<b>REVIEW RETURNED</b>	02-Nov-2017
<b>GENERAL COMMENTS</b>	Thank you for answering the issues raised and related the modifications made to the manuscript initially answered. Concerns have been treated appropriately