Reviewer's report

Title: Early Life Opportunities for Prevention of Diabetes in Low and Middle Income Countries

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Reviewer: Juliana Chan

Reviewer's report:

This is a generally well written article summarizing the emerging evidence regarding the importance of in utero and perinatal environment on the future risk of offspring developing diabetes and other NCD. The authors argued that both clinical and experimental data supported the concept of biological mismatching through interactions between epigenetic changes during in utero development and adult environment in driving the epidemics of gestational diabetes, childhood obesity and young-onset diabetes. Based on these premises, the authors advocated the introduction of a multipronged strategy with particular emphasis on promoting health literacy in children and young women, especially in low and middle income countries, to curb this epidemic of diabetes begetting diabetes.

The topic is relevant and its publication should contribute to the dissemination of knowledge to inspire more research and prevention programs in this field. A major weakness is the lack of description of this evidence despite the citing of a large number of references. In its current format, the article is more akin to an advocacy document.

Minor essential revisions

1. A table summarizing the major clinical and experimental data will increase the objectivity of the article and serves as a quick reference to non-experts.

2. Similarly, the article mentions a broad range of prevention strategies including weight management before pregnancy, nutritional intervention during pregnancy, breast feeding after pregnancy, avoidance of childhood obesity and community-based program to enhance health literacy. A schematic diagram showing the optimal stages when these strategies can be introduced, illustrated by some examples, and their potential benefits on both mother and offspring will be useful.

3. This reviewer found figure 1 difficult to interpret - what do the peaks and troughs represent for these trajectories? It is useful to state explicitly that the y axis represents the risk of NCD in the offspring while the boxes in the graph represent the maternal stresses during her life course and effects on pregnancies. The author also has to explain more clearly how each subsequent pregnancy will drive the risk of the offspring on an upward trajectory (p.9).

4. The authors have not mentioned the growing importance of emotional
deprivation during perinatal period and psychological stress during pregnancy on perinatal programming.

5. There are several examples where a broad statement was made without explanation or specific details, e.g.
P16, What is cardiovascular Q test and bleep test?
P8, Recent animal data now also raise the possibility of paternal transmission of diabetes risk between generations [29] - what next?.
P9, Experimentally feeding pregnant animals a high fat diet gives rise to offspring who become overweight and who demonstrate a range of metabolic and functional disorders similar to the human metabolic syndrome and which are also associated with epigenetic changes [32] - there are many epigenetic mechanisms and a brief description is needed for completeness for non-experts
It will be useful to replace some of these general statements with more details.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare I have no competing interests