

## Letter to the Editor

# In reply to letter to the editor from S. Y. Chu, S. Y. Kim and J. Lau

We thank Dr Chu, Dr Kim and Dr Lau for their interest and comments regarding our systematic review on maternal body mass index (BMI) and gestational diabetes.

Besides the three main aspects they pointed out, our systematic review differed from theirs on other relevant aspects: (i) our critical evaluation of the quality of the included studies on the basis of criteria proposed by acknowledged international reference groups; (ii) the presentation and analysis of heterogeneity of all pooled odds ratios (OR); (iii) subgroup and sensitivity analysis including eight different variables; (iv) the detailed presentation of 21 studies with adjusted OR and the pooled adjusted OR derived from these studies; (v) the evaluation of an additional BMI category (moderate obesity) and (vi) the linear regression graph assessing the mean change in the risk of gestational diabetes mellitus (GDM) for each BMI unit change.

We believe that these additions are an important added value to the review, enhancing the validity of the results. In meta-analysis of observational studies, confounding and selection bias are likely to distort results (1–3). We acknowledged these limitations by critically assessing the quality of the primary studies regarding known sources of bias and by examining and reporting of heterogeneity. We also understand that it is critical to separately analyse studies presenting adjusted OR recognizing the value of adjusting in the first place as a way to reduce spurious results.

It is true that most of the included studies in our review define severely obese women as those with BMI > 35, while three out of five studies included in Chu's review used BMI > 40 to define that category. But we deliberately excluded two of these three studies (Callaway 2006 and Grossetti 2004) because the authors reported selective screening for GDM in their populations. We understand that including studies that did not offer screening for GDM to all women, but only to a group selected based on the presence of risk factors, could be an important source of bias. Therefore, we cannot be certain that Chu's higher pooled OR for severely obese women (their OR = 8.56, 95% confidence intervals 5.07–16.07 vs. our OR = 5.55, 95% confidence intervals 4.27–7.21) is due to their inclusion of more studies that used a higher BMI cut-off or to their inclusion of studies with selective screening for GDM.

The two large studies included by Chu *et al.* (Rosenberg 2003 and Robinson 2005) represent over one-third of their total population (302 247/844 295). We deliberately excluded these two studies as well as other similar studies, because we did not think it is correct to combine different measures of obesity in a single pooled OR. We selected BMI as the only measure to define exposure in order to reduce heterogeneity and because it appears to be reliable and superior to maternal weight for identifying risk for gestational diabetes (4). However, our review included 55 additional studies not included in their original review. Although bigger is not necessarily better, as smaller studies can devote more attention to characterizing confounding factors than larger studies (5), we do not agree with the statement made by Chu *et al.* that most of our additional studies were based on small populations. In fact, five of our additional studies had over 10 000 participants, seven had populations between 5000 and 10 000, and 31 included between 500 and 4999 women. Additionally, contrary to the information mentioned under their Table 2, we presented the results for all the 70 included studies (not only on 59 cohorts). In the text and supplementary material of our article, we present additional comparisons not made by Chu *et al.* (therefore not mentioned in their Table 2) such as moderately obese vs. normal women, obese general vs. non-obese general (BMI > 30 vs. BMI < 30) and overweight general vs. non-overweight general (BMI > 25 vs. BMI < 25) as well as studies that provided only adjusted OR and separate pooled OR for case-control studies.

Ultimately, the results from our systematic review reinforce the results obtained by Chu *et al.*, and as they mention, differences in the pooled OR are minor. More importantly, we share Chu's concern about the public health implications of the escalating problem of obesity worldwide. In our opinion, female obesity is especially worrisome as it can lead to increase in both maternal and perinatal adverse outcomes. However, as it is a modifiable risk factor, the dissemination of information about the significant increase in pregnancy risks caused by high maternal BMI (along with the implementation of lifestyle modification programmes) can contribute to reduce the burden of maternal obesity.

## References

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