COMMENTS AND RESPONSES

Response to Comments on: Rowan et al. Metformin in Gestational Diabetes: The Offspring Follow-Up (MiG TOFU): Body Composition at 2 Years of Age. Diabetes Care 2011;34:2279–2284

Barbour et al. (1) have advised caution about overinterpretation of the Metformin in Gestational diabetes: The Offspring Follow-Up (MiG TOFU) study findings. The aim of our article was to present a biologically plausible explanation for the differences we found in our study; we were concerned not to overinterpret our findings. Ongoing follow-up of these children with appropriate studies is vital to see if differences persist and if they are clinically relevant.

Barbour et al. comment that 46% of women treated with metformin had supplemental insulin, which we had expected in our population (2). Metformin was continued in these women, and the fetus was still exposed. If supplemental insulin has any effect, this would presumably reduce the differences between the groups.

We noted the limitations with the follow-up numbers. We were careful to report the small differences from the original MiG cohort and showed that the treatment groups had similar baseline characteristics. We further adjusted the results for baseline factors that could have influenced our findings, and differences became stronger. The children that had bioimpedance and dual-energy X-ray absorptiometry measures were representative of the larger follow-up group.

Our hypothesis was that there would be less central fat in metformin-exposed children, which was not demonstrated by our results. The central fat measures were similar between the treatment groups. However, these measures all included subcutaneous plus visceral fat, which is why we were unable to demonstrate whether there was less visceral fat or not in the metformin group. In addition to the articles referenced, Framingham data show that BMI and waist circumference do not accurately assess the degree of visceral fat and metabolic risk (3). We acknowledge that data are lacking in children.

We agree that maternal BMI correlates with offspring body fat, and our data are consistent with that. Adjusting for maternal BMI did not change our findings.

We do not think our findings suggest that metformin-exposed children have increased adiposity. Our data are novel, and the results required us to think about different fat depots and hypotheses that needed to be examined. Assessment at 2 years of age is only the beginning of the story, and the importance of further follow-up is reiterated. Any tangible improvements in child health would clearly be contingent on these results. It was our intention to be cautious with our conclusions and highlight the need for ongoing research. We stand by our conclusion that these data are reassuring for clinicians using metformin.

In response to Lau (4), skinfolds were increased not decreased in the metformin group. Assessors were unaware of treatment allocation. It is possible they were sometimes told by the mothers; if so, we believe any bias would have been toward smaller skinfold measurements in the metformin-treated women. We do plan to report diet and activity, as stated in our methods. The metformin follow-up group was similar to the original cohort with respect to numbers being treated with supplemental insulin (71/154 [45.8%] vs. 168/363 [46.3%]), which we would expect as, apart from small differences outlined in the article, the group was representative of the original cohort. Again, as metformin crosses the placenta and insulin does not, the focus of our follow-up was to compare the children exposed to metformin with those not exposed.

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