COMMENTS AND RESPONSES

Response to Comment on: Besser et al. Lessons From the Mixed-Meal Tolerance Test: Use of 90-Minute and Fasting C-Peptide in Pediatric Diabetes. Diabetes Care 2013;36:195–201

We thank Dr. Chaudhary and colleagues (1) for their interest in our article (2). The authors raise some statistical questions about the analysis of the effects of age at diagnosis and fasting C-peptide on the time to insulin deficiency. We are happy that our analysis and results are correct but would like to clarify the assumptions made and to highlight a minor issue with the presentation of these results in Fig. 3 of our article.

The authors point out that Kaplan-Meier graphs should begin from unity at time zero (diagnosis). We can confirm that this was the case in our analysis, but we agree that this is not clear from the figure because the estimated survival function is not plotted before the first event time (3 months postdiagnosis). We have now produced revised figures showing estimated survival probabilities during the initial time interval to make this clear (see Supplementary Data). This change to the plot does not affect the results we describe or the conclusions we have drawn.

We note that one of the limitations of the data in this study is that we don't know the exact time of insulin deficiency, as 90-min C-peptide results were only available at specific intervals (referred to as interval censoring). In particular, we did not have C-peptide results to determine insulin deficiency at diagnosis, so we were restricted to the 3-month data. As required for application of standard survival analysis techniques, we made the assumption that there was no left censoring of the survival times (i.e., no patients were insulin-deficient before diagnosis). We have conducted a sensitivity analysis to assess the impact of assuming that patients who were insulin-deficient at 3 months were also deficient at diagnosis. This made little difference to the results and no difference to the medians that we report in the article, as one might expect. Other statistical approaches could be used to further investigate the impact of interval censoring (3), but we felt this was outside the scope of the article.

Chaudhary et al. (1) also suggest the use of the log-rank statistic to compare the survival distributions in our Fig. 3. We would like to point out that *P* values from the log-rank test were given alongside the median survival times for the two extreme groups. This was not explicitly stated in the RESEARCH DESIGN AND METHODS section of our article, and we acknowledge this was not clear from the way the results were presented. A limitation of the log-rank test is that it considers each risk factor separately. In addition to the Kaplan-Meier curves, we also presented the results of Cox regression analysis investigating the joint contribution of age at diagnosis and fasting C-peptide at diagnosis to the risk of decline in C-peptide from diagnosis. This analysis showed that C-peptide and age of diagnosis were both independent predictors of C-peptide decline.

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References

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