THE AUTHORS REPLY

We thank Smits and Hukkelhoven (1) for their insight into the positive, linear association between interpregnancy interval and the risk of cleft palate in Sweden and their comments on our recent paper (2). We categorized the interpregnancy interval a priori, according to our previous study (3) on pre-pregnant weight change and adverse pregnancy outcomes. We would not have sufficient statistical power to examine the association between interpregnancy interval and cleft palate in finer categories, and we did not intend to test such a hypothesis; our finding was unexpected (2).

The notion that very short interpregnancy intervals could be associated with increased risk of cleft palate through depletion of maternal micronutrient reserves (4) is an intriguing one. If we were to categorize interpregnancy intervals into 3-month periods as suggested in the letter by Smits and Hukkelhoven (1), the birth prevalences of isolated cleft palate per 1,000 livebirths in our population would be 0.68 (<3 months), 0.17 (3–<6 months), 0.31 (6–<9 months), and 0.25 (9–<12 months) for women with intervals of less than 12 months. It might seem like the birth prevalence of these defects in women with the shortest interpregnancy intervals (<3 months) would indeed be higher than those of women with longer intervals. Nevertheless, we must note that the number of defects in each of those categories was 1, 1, 4, and 5, respectively, which severely hampers the possibility of making statistical inferences. In addition, a greater prevalence of cleft palate was not observed consistently throughout intervals shorter than 6 months in our data, contrary to the critical timing for depletion proposed in Smits and Essed’s hypothesis (4).

We agree that the maternal depletion hypothesis is an interesting proposition, with potentially practical implications, that deserves testing in future studies.

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REFERENCES


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