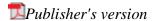


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THE AUTHORS REPLY: Vuillermin and Allen suggest that our analysis of the outcome of the pilot study of the Trial to Reduce IDDM in the Genetically at Risk (ClinicalTrials.gov number, NCT00570102) was flawed. We wish to emphasize that we followed the intention-to-treat principle faithfully, since all children with available autoantibody data remained in their randomized group in the initial analysis, irrespective of whether or not they were exposed to the study formula. The statement that diabetes-associated autoantibodies probably developed in those three children randomly assigned to the hydrolysate group who had progression to diabetes remains a speculation in the absence of samples that could be analyzed. As shown in Table 1 of our article, the adjustment for the difference in the duration of exposure to the study formula did not appreciably change the hazard ratios and P values for the seroconversion rates.

Kim and Chae point out that autoantibodies can be present transiently and that such antibodies may not increase the risk of type 1 diabetes. We agree with that notion, and we have repeatedly shown that positivity for a single autoantibody is often transient, whereas children who are positive for two or more autoantibodies in most cases remain persistently positive.1,2 Table 2 in the Supplementary Appendix of the article (available at NEJM.org) shows that one of the eight children in the hydrolysate group who underwent seroconversion to positivity for two autoantibodies at the age of 12 months turned autoantibody-negative by 4 years of age and remained so up to the end of the follow-up. None of the 17 children with multiple autoantibodies in the control group turned autoantibody-negative during follow-up. Twelve of the 99 children (12% randomly assigned to the casein hydrolysate group and 26 of the 109 children (24%) randomly assigned to the control group remained persistently autoantibody-positive during their follow-up. Accordingly, the consideration of only persistently autoantibody-positive children would rather increase than decrease the effect of weaning to a highly hydrolyzed formula on the appearance of signs of beta-cell autoimmunity.

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Since publication of their article, the authors report no further potential conflict of interest.

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