The authors reply: Allen and Koplin hypothesize that the apparent protective effect in the Enquiring about Tolerance (EAT) trial in the per-protocol analysis could be explained by a higher rate of nonadherence among infants in the early-introduction group whose parents reported food-allergy symptoms than among infants in the early-introduction group whose parents did not report such symptoms. This was not the case. Although a higher rate of nonadherence did occur among infants whose parents reported symptoms, the rate of challenge-proven food allergy among participants in the early-introduction group who did not adhere to the protocol was almost identical to the rate among participants in the standard-introduction group who adhered to the protocol (Table S10A in the Supplementary Appendix of our article).

The introduction of peanut in the standard-introduction group between 7 and 12 months of age was minimal. Although egg did start to be introduced in the standard-introduction group after 6 months, the frequency of consumption in the early-introduction group remained significantly higher at every month between 7 months and 12 months (P<0.005 for all comparisons). The EAT trial showed that it is not just the introduction of allergenic food but the consumption of it in sufficient quantity that may induce a protective effect.

The prevalence of FPIES-like reactions in the early-introduction group was 7 of 652 participants (1.1%; 95% confidence interval, 0.4 to 2.2), not 7 of 486. No cohort study has systematically recorded the prevalence of FPIES with regard to multiple foods, and hence the true prevalence of FPIES is unknown. We state in the Supplementary Appendix of our article that the cases we observed were FPIES-like, because we did not undertake confirmatory challenges immediately for FPIES-like reactions (on safety grounds), hence the true rate of FPIES in our trial may have been somewhat lower.

It has been suggested that differences in reported foods causing FPIES might simply reflect cultural differences in how early they are introduced, with rice and grains being introduced early in the United States and fish early in Italy, with correspondingly more reports of FPIES with these foods in the respective countries. However, it is interesting to note that no FPIES-like reactions were reported for milk or fish in the early-introduction group. It remains to be seen what two other unpublished studies that are introducing egg early, the Beating Egg Allergy Trial and the Starting Time for Egg Protein trial (Australian New Zealand Clinical Trials Registry numbers, ACTRN12611000535976 and ACTRN12610000388011, respectively), will show.

Although we would not endorse the introduction of solid food from 1 month of age, we agree with Bobrow that the move away from the early introduction of solids was based on scant evidence as far as food allergy is concerned. Nevertheless, once this concept became entrenched in international infant-feeding guidelines, a state of equipoise existed that required a randomized trial to resolve. We believe that the body of evidence is moving toward the early introduction of allergens to prevent food allergies. Perhaps grandparents know best after all!

Michael R. Perkin, Ph.D.
St. George’s, University of London
London, United Kingdom

Gideon Lack, M.B., B.Ch.
King’s College London
London, United Kingdom
gideon.lack@kcl.ac.uk

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