

# Comment on Halken et al

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## **Title:**

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*To the Editor*

We read with great interest the European Academy of Allergy and Clinical Immunology (EAACI) guideline on prevention of food allergy (FA) (1). In particular, recommendation 3.1.2 states: “The EAACI Task Force suggests introducing well-cooked hen’s egg, but not raw egg or uncooked pasteurized egg, into the infant diet as part of complementary feeding to prevent egg allergy in infants.” The authors declare in advance that only Intention-To-Treat (ITT) analyses were considered and they cite, in support of the aforementioned recommendation, four studies (2-5).

However, according to the ITT analysis, the first two studies (2, 3) find no evidence that consumption of hen’s egg prevents hen’s egg allergy. The third study (4) reports an efficacy in this regard, but the authors: a) enrolled children with eczema, therefore a category at increased risk of developing FA; b) have associated aggressive eczema treatment, and it is not possible to establish the weight of one and the other treatment on the final outcome; c) excluded from the final analysis of the data about 18% of randomized patients, and it is difficult for statistical significance to be maintained if the worst-case scenario analysis were applied. Moreover, we consider technically difficult for a parent to be able to weigh 50 mg of cooked egg powder to be given to their child, as Natsume et al (4) suggest. At the end, the authors (4) evaluated the effectiveness of their preventive strategy with an oral food challenge with 7 g of heated whole-egg powder, and therefore the study in question cannot tell us anything about the possible effectiveness in the prevention of allergy to raw or undercooked egg. The fourth study (5) cited by the EAACI Task Force (1), is based on a subgroup analysis that did not benefit from a specific randomization. The previously unplanned subgroup analysis, in the absence of specific randomization, is well used for formulating hypotheses to be tested with a specifically planned study, but is less adequate to support a recommendation contained in a guideline.

In short, it seems to us that recommendation 3.1.2 (1) cannot be issued. Moreover, no times and doses are indicated to start the possible administration of well-cooked egg, and even this definition seems a bit vague (“well cooked” means baked? Or hard boiled?). Contrary to our objection, other position papers of very authoritative scientific societies (6-10) substantially agree with recommendation 3.1.2 of the EAACI Task Force (1). However, even in these documents, the supporting evidence does not seem sufficient. In particular, table IV by Fleischer et al (7), which effectively summarizes the evidence available until 2021 on this topic, is very clear in this regard. Examining it, in fact, it is clear that we do not have the availability of methodologically valid studies that allow us to argue that the introduction of cooked egg during the complementary feeding, as the only intervention, reduces the likelihood of hen’s egg allergy, neither in infants at increased risk of developing FA nor in those at normal risk.

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