

Correspondence

Is randomization of breast-feeding feasible?

To the Editor:

In the title of their recent article, Kull et al¹ state that breast-feeding (BF) reduces the risk of asthma during the first 4 years of life. In our opinion, the authors did show that prolonged BF is protective with respect to the development of asthma, but this is not the case for BF per se, because only 1.2% of the participating infants were not breast-fed. To defend the author's statement, a considerable number of participants should not have received BF at all. A randomized controlled trial (RCT) would be the study design of choice; however, this is considered by some unethical to perform.¹

We explored the feasibility of an RCT administering either BF or a hydrolyzed formula for the first 4 months of life to newborns at high risk to develop atopic disease. First, the Medical Ethics Committee of our hospital had the opinion that an RCT would be difficult to approve because of the equipoise or uncertainty principle as is written in the Declaration of Helsinki.² This holds that a subject may be enrolled in an RCT only if there is true uncertainty about which of the treatments is most likely to benefit the patient. Moreover, it would be necessary to show that another study design imposing a lesser burden on the participants could yield the same results. Clearly, the chances of bias in observational studies are larger than in experimental trials. Second, a power calculation showed that the number of required participants was 675 in each group, assuming that high-risk children have a risk of 21.2% to develop asthma, according to Chulada et al,³ and anticipating a reduction in the risk to develop asthma of 6% with 80% power and a significance level of .05. This would necessitate a very long inclusion period or many participating research centers. Moreover, to evaluate whether parents are willing to collaborate in a specific study, we sent a questionnaire to 156 adults who participated in other primary prevention trials. After 4 weeks, 79.4% of the questionnaires were returned, and only 10% of the high-risk parents said they would agree to participate in such a trial, indicating that inclusion would require approaching 10 times as many high-risk parents. Moreover, these 10% respondents are unlikely to be a random sample of all invitees. In summary, for this specific study, we would need to contact almost 14,000 high-risk parents to include the necessary 1400 participants, anticipating almost 4% withdrawal after randomization.

We conclude that such a study, although undoubtedly of importance, is at this moment almost impossible to perform for ethical and logistical reasons. However, this does not affect our point of view about the results of the study by Kull et al,¹ that they do not show a preventive effect of BF per se on the development of asthma in very young infants.

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Reply

To the Editor:

Hoekstra et al¹ call attention to the circumstance that in the Swedish birth cohort study, we did not assess the effect of any breast-feeding versus none.² Only 1.2% of the children in our study were not breast-fed at all, so such an analysis was not meaningful. Our results indicate that a certain period of breast-feeding is needed to reduce the risk of asthma. Furthermore, a sufficient duration of breast-feeding is desirable when studying the association between breast-feeding and allergic diseases.³ Obviously, there are several grounds to encourage breast-feeding, including the possibility to reduce the risk of allergic diseases.⁴

Hoekstra et al¹ also address the issue of a randomized controlled trial as the study design of choice. We agree that a randomized controlled study would be optimal when studying the association between asthma and breast-feeding. Nevertheless, randomization regarding breast-feeding is not feasible for ethical reasons. Consequently, the application by Hoekstra et al¹ for such a study was turned down by the medical ethical committee of their hospital because the principles of the Helsinki declaration would be put aside. This would most likely have been the answer of an ethical committee in Sweden as well.

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