
Effects of breastfeeding on health outcomes in childhood: beyond dose-response relations

Dear Sir:

Kramer et al (1), whose report was published recently in the Journal, should be congratulated for their 6.5-y follow-up of nearly 14 000 participants in the Promotion of Breastfeeding Intervention Trial (PROBIT), the first randomized trial of a breastfeeding promotion intervention in healthy, full-term infants. Whereas they acknowledge that their findings may not apply to comparisons of breastfed and formula-fed children, they nevertheless conclude, “Previously reported beneficial effects [of breastfeeding] on these outcomes [measures of adiposity, stature, or blood pressure] may be the result of uncontrolled bias due to confounding and selection.” In our view, Kramer et al cannot draw this conclusion, because their study addresses only the effect of prolonging the duration of exclusive breastfeeding on anthropometric and blood pressure outcomes at 6.5 y of age.

It has been stated that evidence of a dose-dependent association between breastfeeding and health outcomes would be required to support the biological causality of the assumed beneficial effects (2). The potential consequences of prolonging the duration of breastfeeding, addressed by Kramer et al, therefore are certainly of relevance for the debate on the long-term health benefits of breastfeeding. A recent meta-analysis suggests that, for each additional month of breastfeeding, the risk of overweight would be reduced by 4% (2). Unfortunately, Kramer et al did not provide information on the mean number of weeks for which children in the intervention and control groups had been breastfed; that information would have allowed an estimation of the magnitude of the differences in outcomes that could have been expected. In addition, their attempt to reproduce the results of other observational studies by comparing infants completely weaned within the first month with those exclusively breastfed for >6 mo, to further illustrate the absence of an effect of extended breastfeeding, is misleading. Infants who have been exclusively breastfed for >6 mo often represent a relatively selected group (eg, in this case, only 1.5% of the PROBIT cohort), which is characterized by particular behaviors. Any consequences of this practice are likely to be associated with these behaviors rather than with breastfeeding per se. It has even been argued that these infants may receive nutritional intakes below requirements at this age (3), and the “catch-up” or accelerated growth that may follow such early undernutrition could result in unfavorable body-composition development in the long term.

Current evidence suggests that even the substantial extension of breastfeeding duration achieved in the PROBIT cohort could be expected to yield only modest effects on adiposity and blood pressure (2, 4). Therefore, the limited precision of the outcome measurements in the PROBIT cohort is of particular concern. The correlation coefficients presented to illustrate the validity and reproducibility of the data are of questionable value because they compare measurements made an average of 18 mo apart; the range is an astonishing 5.3–32.6 mo. They do not allow one to distinguish the quality of the measurements from the biological tracking of anthropometric variables or plausible deviations that may be expected over the course of 18 mo in growing children (5). Thus, imprecise measurements may well have masked the likely modest effects of breastfeeding prolongation on the health outcomes assessed.

Despite the importance of potential benefits associated with prolonging the duration of breastfeeding, it appears more relevant from a public health perspective to focus on the differences between formula-fed and breastfed children—ie, whether children who have been offered formula in place of human milk may experience adverse health effects in the longer term. The intervention study by Kramer et al does not, however, add any new evidence to this debate, although nonscientists and the general public could erroneously assume, from their overly general conclusion, that it does. Even if prolonging the duration of breastfeeding has only a limited (or no) benefit for health outcomes, breastfeeding per se—as opposed to formula feeding—could still be beneficial for these outcomes for the following 2 reasons.

First, benefits could stem primarily from breastfeeding in the first weeks of life, which is a potentially critical window for programming long-term health (6). Support for this proposal comes from a study investigating the offspring of diabetic mothers, in whom adjustment for the volume of breast milk ingested during the first week of life largely accounted for the associations between breastfeeding in the 2nd to 4th week (or its duration) and relative body weight or risk of overweight (7). Accordingly, a recent analysis by our group (8), using data from the Dortmund Nutritional and Anthropometric Longitudinally Designed Study, showed a protective effect of full breastfeeding on the development of percentage body fat throughout childhood, irrespective of whether full breastfeeding was defined as full breastfeeding for ≥2 wk or as full breastfeeding for ≥4 mo. In addition to this main finding, a modest dose-response relation between breastfeeding and adiposity was observed.

Second, breastfeeding could still be of relevance for subgroups of infants. In our recent analysis, only boys whose mothers were over-weight profited from being fully breastfed for the development of their percentage body fat between 0.5 and 7 y of age (8). Additive interactions of maternal prepregnancy BMI and breastfeeding for childhood overweight between 2 and 14 y of age were also seen in the 1996 National Longitudinal Survey of Youth (9). Changes in maternal weight after a pregnancy are common, and maternal overweight in later childhood, which was the variable used in these PROBIT analyses, will more likely be a marker of the child’s current behavioral environment than an indication of the fetal environment. Thus, it is perhaps not surprising that studies assessing maternal weight in later childhood could not corroborate an interaction between maternal overweight and breastfeeding (1, 10).

Admittedly, the study by Kramer et al contributes to the accumulating evidence that the overall effects of breastfeeding on later health outcomes are likely to be modest. The prolongation of exclusive breastfeeding may confer limited benefit for adiposity, stature, and blood pressure in later childhood. Future studies should, however, address whether breastfeeding per se, particularly in the first weeks of life, may nonetheless entail long-term health benefits for specific subgroups.

None of the authors had a personal or financial conflict of interest.

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Reply to AE Buyken et al

My colleagues and I thank Dr Buyken and her colleagues for their comments on the Promotion of Breastfeeding Intervention Trial (PROBIT). They claim that our study “addresses only the effect of prolonging the duration of exclusive breastfeeding.” That is inaccurate, however, because the breastfeeding promotion intervention we randomly assigned (based on the WHO/UNICEF Baby-Friendly Hospital Initiative) was designed to increase both the duration of any breastfeeding and the exclusivity of breastfeeding in the 1st 6 mo of life. Both of those goals were achieved in the experimental group in the 1st year of follow-up (2).

Buyken et al express their “particular concern” that “imprecise measurements may well have masked the likely modest effects of breastfeeding prolongation on the health outcomes assessed” at 6.5 y. Although random measurement errors and inter-polyclinic differences certainly did reduce the precision of the trial group differences for the triceps skinfold-thickness and blood pressure measurements, null effects with extremely narrow CIs were observed for body mass index (BMI; in kg/m²) and abdominal obesity. In an individual-subject data meta-analysis of observational studies, Owen et al (3) were able to control for confounding by socioeconomic status, maternal BMI, and maternal smoking during pregnancy in 11 studies. After such control, they found no significant reduction in mean BMI (−0.01; 95% CI: −0.05, 0.03) between breastfed and formula-fed infants, a result that is entirely consistent with our results comparing 2 randomly assigned groups differing in breastfeeding duration and exclusivity. Although my colleagues and I agree that our results cannot address the potential benefits of any breastfeeding, compared with no breastfeeding, in the first weeks of life, the results of the systematic review of Owen et al, comparing any breastfeeding with formula feeding, cast serious doubt on any claim of a “programming” effect of early breastfeeding that confers long-term protection against obesity.

Finally, my colleagues and I urge researchers and other readers to be skeptical about all reports of conditional effects. Many biostatisticians and clinical trialists have cautioned against subgroup analysis, even in properly randomized controlled trials (4, 5). In the face of an overall null result, it is inevitable that post hoc stratification by some baseline factor (even a factor such as an astrological sign) will yield a statistically significant result. Unless such conditional (subgroup) effects are hypothesized a priori and are replicated in other studies, however, they are highly likely to reflect type 1 errors—ie, chance findings. Thus, the observation by Buyken et al from an observational (nonrandomized) study that breastfeeding was protective only in boys of overweight mothers should be regarded with skepticism unless and until such results are reported in other studies.

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REFERENCES