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Commentary: breastfeeding and obesity—the 2011 Scorecard

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The last decade began with high hopes that increasing breastfeeding rates would be one solution to the mushrooming obesity epidemic.[1] Now, 10 years later, have we figured out that these hopes were ephemeral? Getting to the right answer is crucial for public health and also teaches us about causal inference.

Why should breastfeeding lower obesity risk? First, plausible mechanisms exist. Breast milk contains hormones such as leptin, adiponectin and ghrelin, which might help determine long-term appetite signalling.[2] To a greater extent than bottle-fed infants, infants who are nursing typically let their mothers know when they are full by coming off the breast, which could lead to better self-regulation of energy intake as they grow.[3]

A second rationale involves infant growth patterns. After the first 3–4 months of life, breastfed infants gain less weight than formula-fed infants.[4] Gaining less weight in infancy predicts lower rates of obesity and its complications later in childhood and into adulthood.[5,6]

Third, nutrient-based interventions are suggestive. Infant formulae contain more protein than breast milk. In individual-randomized controlled trials, protein-enriched formulae (with or without increased calories) among preterm, small for gestational age (SGA) or term infants produce faster weight gain, increased adiposity and some adverse cardio-metabolic consequences in childhood and adolescence.[7–9]

Fourth, many cohort studies show an association. Meta-analyses published several years ago showed moderate reductions in obesity risk associated with having been breastfed or with longer duration of breastfeeding.[10–12]

With this litany of supportive evidence, why are we now circumspect? The concerns relate to confounding, reverse causality, generalizability and misclassification.

From early on, concerns have existed about confounding because in nearly all of the study populations reviewed in the meta-analyses, breastfeeding and obesity were socially patterned in the same direction. 'Tricks of the trade' to overcome such confounding include adjustment for social and economic factors, sib-pair analyses, performing studies where the confounding structure is different, exploration of mechanisms, and perhaps best of all, randomized controlled trials of breastfeeding (rather than manipulation of nutrient content of formulae).

What have we learned from these approaches? No one method of controlling for confounding is perfect. The meta-analysis of breastfeeding and mean BMI of Owen *et al*.[13] showed that adjusting for social and economic factors nullified an otherwise modest effect, although many of the reviewed studies did not have sufficient covariate information to include in the adjustment procedure.

Within-family studies minimize confounding because siblings typically grow up in similar socioeconomic circumstances. The few published studies suggest that differences in breastfeeding duration between sib pairs are related to substantial differences in later obesity.[14–16] However, power is limited even in relatively large studies because sibs tend to be breastfed for similar durations.

Studies among populations with different confounding structures can be informative. The report of Brion *et al*.[17] in this issue is especially useful because they invoked two cohorts with differing social patterning of breastfeeding and of obesity, and two distinct outcomes. Longer breastfeeding duration was associated with higher IQ in both cohorts. In contrast, it predicted lower BMI only in the British but not the Brazilian cohort, in which breastfeeding was not demonstrably socially patterned and the socioeconomic–BMI association was in the opposite direction. The authors rightly conclude that these findings argue for confounding in the British context, although it would have instructive if they had analysed breastfeeding well beyond 3 months, when breastfed infants still tend to be at least as heavy as formula-fed infants.

To explore mechanisms biomarker studies are tempting, but to date they are hampered by

Table 1 The '2011 Scorecard'

	Supports protective effect of breastfeeding?		
Type of Study	Yes	Maybe	No
Cluster randomized controlled trial of breastfeeding promotion			No effects on anthropometric outcomes at 6.5 or 11.5 years of age, but observational data within the cohort show no (or slightly +) association
Cohort studies, mostly White European descent	Three pooled meta-analyses of (dichotomous) obesity show modest associations, but limited confounder control		One individual-level meta-analysis of mean BMI shows no effect after confounding control, but limited number of studies with sufficient data
Cohort studies in developing countries and racial/ethnic minorities			Many are null, but in some misclassification of exposure may exist
Sib-pair analyses in cohort studies		Three studies suggest effect, but low power	
Comparison of cohorts with different confounding structure			One study suggests that confounding explains observed associations
'Reverse causality?'		A few studies suggest this phenomenon, but could be in opposite direction to hypothesis	
Biological effects of breast milk		Conflicting data on adipokines	
Biological effects of formula	RCTs of high vs low protein (+/− energy) result in more adiposity and related outcomes		
Behavioural effects of nursing	Short-term studies suggest less self-regulation in bottle- vs breast-fed infants		
Ecological analysis			Breastfeeding rates have gone up along with emergence of the obesity epidemic, but that does not rule out inverse individual-level effects

Summarizing evidence for and against the hypothesis that having been breastfed reduces the risk of obesity.

difficulties in measuring breastmilk components directly, questions about how well the infant gut can absorb large molecules like adipokines, and to what extent static blood levels can inform relevant pathways.[18]

The Promotion of Breastfeeding Intervention Trial (PROBIT) is the paragon of randomized controlled trials. In this experiment of breastfeeding promotion in the Republic of Belarus, Kramer *et al*.[19,20] showed no effect on mean BMI, skinfold thicknesses or obesity at the age of 6.5 years, and preliminary data show similar findings at the age of 11.5 years. These results are in spite of large intervention–control differences in duration and exclusivity of breastfeeding. One caveat is that all mother–infant pairs initiated breastfeeding, so if the first days of life are critical for the infant feeding–obesity link, this study would miss it. Additionally, an observational analysis of the 6.5-year outcomes showed that longer duration of breastfeeding was actually associated with slightly higher BMI and skinfold thicknesses, thus raising the question of whether this trial can serve to overcome residual confounding observed in other studies.

What about reverse causality? We do not really mean that a child's obesity caused him or her to have been breastfed less! The concern is that more rapid weight gain in infancy induces breastfeeding cessation, and that the faster weight gain itself entrains later obesity. If that were the case, it would only *appear* that shorter breastfeeding duration causes obesity. In an observational analysis within the PROBIT trial, however, Kramer *et al*.[21] showed that among breastfed infants at the beginning of each 1- to 3-month interval, it was actually the smaller infants who were more likely to wean by the next visit. Thus, although those findings indicate some

element of reverse causality, they would imply that shorter duration of breastfeeding leads to lower, rather than higher, obesity risk.

Nearly all of the participants in the existing meta-analyses emanate from populations of White European descent. What can we make of the fact that many recent studies in the developing world and in racial/ethnic minorities in the USA do not show associations between infant feeding and later obesity? One possibility is results are not generalizable, i.e. that only among White Europeans does longer breastfeeding reduce obesity risk. Given that the biology should be similar across populations, this inference seems implausible. Is confounding to blame? The findings of Brion *et al*.[17] in this issue would argue for that explanation. On the other hand, the confounding structure is similar among racial/ethnic minorities and Whites in the USA. Another possibility is misclassification. In the USA, blacks and Hispanics are more likely than Whites to resort to a combination of formula and breastfeeding early after birth, but only among Whites is this combination associated with reduced overall breastfeeding duration.[22] Some parents put cereal or other solid foods in the bottle, and early introduction of solid foods itself—perhaps especially among formula-fed babies—is associated with higher risk of obesity.[23] As epidemiologists who are balancing feasibility and participant burden with the desire for large sample sizes, we are often limited to asking relatively simplistic questions about infant feeding. An anthropological approach may be needed to understand in more depth the variation in infant feeding styles, thus informing a next generation of epidemiological inquiry.

Although the collective evidence (Table 1) suggests that breastfeeding—initiation, longer duration or exclusivity— may very well exert a modest protective effect on childhood and adolescent obesity, it no longer appears to be a major determinant. Nevertheless, because breastfeeding also reduces infection and allergy-related outcomes and probably increases IQ, World Health Organization recommendations for 6 months of exclusive breastfeeding remain a just and justifiable policy around the world.

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