Commentary: Assessing the impact of breastfeeding on child health: where conventional methods alone fall short for reliably establishing causal inference

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Given the strong social patterning of both breastfeeding and child health in high-income countries (HICs), there is a high probability of observing associations that are confounded by broader socio-economic factors rather than being due to any biological effects of breastfeeding. Even where extensive adjustments for confounders are made, residual confounding remains a persistent problem. As the exact nature of the relationship between socio-economic position (SEP) and health-related characteristics and disease are complex and not entirely understood, it is difficult to fully capture this in analyses and comprehensively control for confounding by SEP. As such, conventional observational methods, relying on the adjustment of associations for measured confounders, will likely be, on their own, insufficient for reliably establishing causal inference. This is evident, for example, from recent antioxidant trials failing to replicate the results of large-scale observational studies reporting protective effects that were independent of a wide range of confounders. This is the most likely attributable to the presence of residual confounding in the observational studies.

With respect to the association between breastfeeding and child obesity, various observational studies have reported decreased risk on child obesity associated with breastfeeding in infancy; however, a meta-analysis indicated that this may be largely due to publication bias and confounding. In contrast, family studies using siblings discordant for breastfeeding duration to control for social, familial and environmental confounding, suggest that associations may not in fact be completely confounded by these factors. Thus, the picture in terms of causal effects of breastfeeding on child obesity is unclear. Ideally, a randomized trial would provide the gold standard for causal inference. However, a trial randomizing mothers to breastfeed or not breastfeed would clearly be unfeasible and unethical. A recent trial of breastfeeding promotion in Belarus has been carried out. This trial resulted in a large increase in exclusive breastfeeding in the intervention group (43.3 vs 6.4%) and a higher prevalence of any breastfeeding at all ages ≤12 months, but mean adiposity and levels of obesity were similar by randomized group, suggesting that breastfeeding is not causally related to child obesity.

It is thus becoming increasingly apparent that combining conventional approaches with additional methods of testing causal inference are required to establish the long-term effects of breastfeeding and other developmental exposures on later life outcomes. Various new methods for improving causal inference in observational studies in general have been advanced, including new statistical approaches, maternal–paternal comparisons, sibling comparisons, Mendelian randomization and other genetically informed studies. However, not all of these will be applicable to breastfeeding, being, for example, specific to prenatal exposures or, where genetic variants are used, it is not clear if an appropriate genetic variant relating to breastfeeding will be available.

The study by Kwok et al. using the children of 1997 cohort in this issue of the IJE takes advantage of differences in the confounding structure of breastfeeding and child obesity in Hong Kong compared with Western/European countries (where the majority of existing studies reporting associations on breastfeeding have been carried out) to explore causal inference. As the authors discuss, in high-income populations, individuals of higher SEP are more likely to breastfeed and less likely to have obese children. In contrast, in non-Westernized countries child obesity tends to be less clearly socially patterned and, in Hong Kong in particular, sustained exclusive breastfeeding is more common in less-educated women. This means that if the inverse associations of breastfeeding with adiposity, reported in studies of Western populations, are largely explained by
socio-economic confounding, whereby infants of more highly educated and higher SEP families are more likely to be breastfed and, as a result of this higher SEP, more likely to engage in activities that protect against obesity (better diet, more physical activity and less sedentary behaviour), than in a population where the association of SEP with breastfeeding is either non-existent or in the opposite direction (less-educated and less-affluent mothers more likely to breastfeed), then we would expect the associations in these populations to be non-existent or in the opposite direction (depending also on knowledge of how SEP affected other obesity risk factors). Indeed, in the study from Hong Kong, there was no association between breastfeeding and child BMI or overweight. Thus, the protective associations previously observed in studies from high-income/Western settings may be due to confounding by SEP and related maternal, environmental and familial characteristics. Further studies characterizing differences in the factors related to breastfeeding between Western and non-Western populations may improve our understanding of what specifically drives this association, if it is not due to biological effects of breastfeeding per se.

An added complication in making causal inference using comparisons of populations where confounding structure of breastfeeding differs is considering the role of weaning, its composition and the variation in populations in the nature of the solids and liquids breastfed and non-breastfed babies are being given. As Kwok et al.⁹ state, in Hong Kong it is common for breastfed infants to be given glucose drinks, which could account for the lack of protective effects of breastfeeding on later risk of obesity. Furthermore, there are also differences between HICs and low- or middle-income countries (LMICs) in what breast milk is being substituted for in non-breastfed infants, with formula being the principle replacement in HICs and cow’s milk in LMICs.¹⁰ Thus, there may be differences between HICs and LMICs in the nutritional composition of the breast-milk substitute as well as in the overall dietary composition of breastfed and non-breastfed infants (over and above the breast milk and breast-milk substitute themselves). This may result in differences in the ability to detect the ‘true’ effects of breastfeeding or differences in the extent to which breastfeeding may confer beneficial effects in certain populations; i.e. breastfeeding may confer greater beneficial effects in populations where there are important differences in the nutritional composition of breastfed and non-breastfed infants compared with populations where the nutritional quality of breastfeeding and non-breastfeeding diets are approximately the same.

The study by Kwok et al., as stated by its authors, demonstrates the role of studies from different socio-historical contexts in clarifying associations observed in long-term economically developed populations. Studies such as these constitute new approaches for improving causal inference in relation to the effects of breastfeeding on child health and are useful additional methods that can be used to build on the conventional approach adopted in observational epidemiology. It is likely that no single method alone will address all issues, and thus numerous different approaches in conjunction, each with its own advantages and limitations, should ideally be explored in order to arrive at more reliable conclusions regarding the causal effects of breastfeeding on later health and disease.

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**References**