

## Formula Feeding Exposure Not Homogenous

All breastfeeding research faces the age-old challenge of innate selection bias. Girard et al<sup>1</sup> recently used advanced quasi-experimental techniques to mimic randomization in combination with a large contemporary cohort, making a novel contribution to the field.

This study has received significant press attention, mainly because the findings contradict previous researchers who reported positive relationships between breastfeeding and offspring cognitive development and/or performance. However, there is a crucial lack of discussion about a potentially critical contributing factor to these conflicting results: the exposure (formula-fed) group is not homogeneous. Infant formula feeding options are incredibly vast and differ between cultures. Combining all formula-fed infants into one single exposure diminishes researchers' ability to make clean comparisons. Furthermore, formula options and formulations are constantly changing, making it difficult to draw conclusive insights from compiled historical breastfeeding research that spans decades.

The conductors of the famous Promotion of Breastfeeding Intervention Trial used cluster randomization to study the impact of breastfeeding-support interventions in Belarus between 1996 and 1997. At 6.5 years, the intervention group exhibited significantly higher Wechsler Abbreviated Scales of Intelligence, ranging between 2.9 to 7.5 points.<sup>2</sup> In this current article, Girard et al studied infants born between 2007 and 2008 in Ireland. The difference in exposure between breastfed versus formula-fed infants in the Girard study is likely vastly different from that of infants

born over a decade earlier in Belarus. A similar principle can be applied to the well-publicized 2015 study that revealed that breastfeeding is associated with higher adult IQ (averaging 3.8 points), education, and income in a 1982 Brazilian birth cohort.<sup>3</sup> Although these older studies remain impactful, it is noteworthy (and often ignored) that infant formula options have since evolved and advanced, making comparisons with the Girard study difficult.

We can further observe results from a recent, well-conducted meta-analysis of 18 cohort studies that revealed significantly higher performance on adult intelligence tests among breastfed offspring, averaging 2.6 higher IQ points.<sup>4</sup> This meta-analysis included birth cohorts that spanned almost 4 decades (1968–2006). The authors provided no discussion of the inevitable heterogeneity in the formula fed group(s), both within cohorts and across decades. Neither did they attempt to control for either of these factors.

Although breast milk is undeniably the ideal feeding choice, advances in infant formula nutrition continue to shrink the gap in many infant outcomes. Continuing with our example of cognitive development, infants randomly assigned to receive an experimental formula supplemented with bovine milk fat globule membrane from 0 to 6 months exhibited 6 points higher Bayley scale scores at 12 months, similar to breastfed controls.<sup>5</sup> This difference in Bayley scores is noteworthy because it is similar in nature to the differences in IQ between breastfed versus formula-fed infants from the historical studies noted above.

Moving forward, researchers in the field need to acknowledge that formula feeding is not a homogeneous exposure.

Researchers need to begin characterizing the differences in formula exposure and incorporating these differences into studies of infant outcomes. We also need to acknowledge that insights from historical comparisons lose relevance as time passes, and infant formula continues to evolve at a faster pace than research is conducted.

Bridget E. Young  
Assistant Professor of Pediatric Nutrition, School  
of Medicine, University of Colorado  
E-mail: [bridget.young@ucdenver.edu](mailto:bridget.young@ucdenver.edu)

**CONFLICT OF INTEREST:** The author has indicated she has no potential conflicts of interest to disclose.

### REFERENCES

1. Girard LC, Doyle O, Tremblay RE. Breastfeeding, cognitive and noncognitive development in early childhood: a population study. *Pediatrics*. 2017;139(4):e20161848
2. Kramer MS, Aboud F, Mironova E, et al; Promotion of Breastfeeding Intervention Trial (PROBIT) Study Group. Breastfeeding and child cognitive development: new evidence from a large randomized trial. *Arch Gen Psychiatry*. 2008;65(5):578–584
3. Victora CG, Horta BL, Loret de Mola C, et al. Association between breastfeeding and intelligence, educational attainment, and income at 30 years of age: a prospective birth cohort study from Brazil. *Lancet Glob Health*. 2015;3(4):e199–e205
4. Horta BL, Loret de Mola C, Victora CG. Breastfeeding and intelligence: a systematic review and meta-analysis. *Acta Paediatr*. 2015;104(467):14–19
5. Timby N, Domellöf E, Hernell O, Lönnerdal B, Domellöf M. Neurodevelopment, nutrition, and growth until 12 mo of age in infants fed a low-energy, low-protein formula supplemented with bovine milk fat globule membranes: a randomized controlled trial. *Am J Clin Nutr*. 2014;99(4):860–868

doi:10.1542/peds.2017-1918