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In Reply

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Velle-Forbord and colleagues raise concerns about reverse causation and differences in metabolic parameters among lactation groups. The longitudinal design in our study¹ (up to 7 examinations in 30 years) addressed reverse causation by measuring antecedent risk factors, including insulin resistance and dysglycemia before pregnancy, as well as other potential confounders in the lactation-diabetes association. Although biochemical measures reached statistical significance, the absolute values of differences among lactation groups were quite small (<2% to 5%) and fell within normal physiologic ranges, as expected for young and healthy women enrolled in CARDIA at ages 18 to 30 years. Thus, lactation groups exhibited clinically similar metabolic status (eg, median homeostatic model assessment for insulin resistance range of 1.5–1.9; mean fasting glucose range of 79–80). Nevertheless, inclusion of baseline insulin resistance or fasting glucose in multivariate models only minimally affected the strong, graded inverse associations for lactation duration with incident diabetes.

About 73% of incident diabetes arose among black women (50% of our sample), who are less likely to breastfeed regardless of socioeconomic status. Thus, cultural barriers for black women may exert stronger influences on lactation duration than maternal obesity or metabolism.^{2,3} For the general population of the United States, the most pervasive influences on lactation behaviors include cultural barriers (negative perceptions), social policy (paid maternity leave limited to 6–8 weeks), psychological constraints (body image discomfort, lack of family support),⁴ as well as adverse perinatal outcomes, and insufficient lactation education or support among women who are obese.⁵ High proportions of women who are overweight or obese and have gestational diabetes mellitus (GDM) are able to breastfeed successfully.⁶ Pregnant women treated for GDM report similar prevalence of delayed onset of lactogenesis (DOL) compared with those without GDM (33% vs 23% to 44%, respectively).⁷ This study by Matias et al⁷ found no association between GDM severity (no. of abnormal values on 3-hour glucose tolerance test) and DOL, except among a small subgroup (2% overall) treated with insulin.

The cluster-randomized PROBIT study⁸ mentioned by Velle-Forbord et al focused on breastfeeding support, thereby precluding comparison to unexposed (ie, nonlactating)

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women, potentially attenuating the true excess risk. Given this constraint, it is not surprising that average blood pressure and body mass index measured only once at 11.5 years postdelivery did not differ by intervention. Furthermore, PROBIT⁸ did not assess glucose tolerance before, during, or after pregnancy because pregnant women in Belarus were not routinely screened for GDM, and less than 0.1% of women reported GDM. The strength of the CARDIA study¹ is the temporality of biochemical measures before pregnancy and lactation, as well as validated GDM history, that previous studies have been unable to evaluate.

Our study¹ evaluated antecedent potential confounders, preserving the temporality for the observed strong gradient of higher lactation duration and lower relative hazards of incident diabetes. Our longitudinal design provides robust evidence for persistent health benefits, although one cannot completely rule out residual confounding, the magnitude of the protective associations reduce this possibility. However, randomization to lactation is neither desirable nor ethical, thus trials are unlikely to address the issue.

We appreciate the letter from Dr Gragnoli and colleagues who provide an expanded discussion of the potential role of prolactin as a biological mechanism related to genetic loci for the association we found. In the discussion section of our paper, we briefly highlighted potential mechanisms for the inverse association between lactation duration and incidence of diabetes. While we included mechanisms related to higher prolactin levels in lactating women—for example preservation of pancreatic β -cell mass and function—we regret that space limitations did not allow us to further elaborate.

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