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‘Vaginal seeding’ after a caesarean section provides benefits to newborn children:

FOR: Does exposing caesarean-delivered newborns to the vaginal microbiome affect their chronic disease risk? The critical need for trials of ‘vaginal seeding’ during caesarean section

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According to the World Health Organization, caesarean section is medically necessary in 10–15% of pregnancies; however, this mode of delivery exceeds 60% in some populations (e.g. Brazil) and is increasing globally. Although caesarean section can be life-saving, it also creates an unnatural exposure for the newborn. Caesarean-delivered babies are extracted from the sterile womb, bypassing exposure to the vaginal canal and the natural first microbiota exposure to the newborn. Over 20 studies have zfound that acquisition and development of the microbiome in caesarean-born infants is different from that in vaginally born infants, and the differences may persist for up to 4 years of age (Fouhy et al. *Nat Commun* 2019;10:1517). Even if transient, impacts to microbiome development during early-life critical periods of immune and metabolic programming have been shown to have lasting health consequences (Cox et al. *Cell* 2014;158:705–21).

Substantial evidence from epidemiologic and experimental studies with mice has documented that caesarean delivery is associated with an increased risk in the offspring of developing a range of chronic health conditions, including obesity, allergies, asthma and neurodevelopmental outcomes. At least three meta-analyses of observational studies have confirmed that caesarean delivery is associated with higher risk in the offspring becoming overweight and developing obesity, and a large longitudinal study found that among siblings

Disclosure of interests

Dr Dominguez-Bello has a patent, US Patent 10357521. Completed disclosure of interest forms are available to view online as supporting information.

born to the same mother, vaginal birth after caesarean section decreases offspring risk of developing obesity in childhood, adolescence and adulthood by 31% (Yuan et al. *JAMA Pediatr* 2016;170:e162385). Importantly, an experimental study in mice indicates that caesarean section causes excessive weight gain in the absence of antibiotics (Martinez et al. *Sci Adv* 2017;3:eaao1874), a factor that has been raised as a potential confounder in observational studies. The critical issue now is determining whether mother-to-newborn transfer of vaginal microbes is causally associated with health outcomes in humans.

Swabbing of caesarean-born babies immediately after birth with the mother's vaginal secretions, a practice coined 'vaginal seeding', is a means of transferring the mother's vaginal microbiome to the newborn. Importantly, this procedure provides a means to test whether it is possible to restore microbes that colonise during vaginal birth. Evidence from a small pilot study indicated that vaginal seeding partially restores the microbiome of caesarean-delivered neonates (Dominguez-Bello et al. *Nat Med* 2016;22:250–3) but larger, more rigorous studies are needed to assess the effect of vaginal seeding on microbiome trajectories and health outcomes. Well-designed trials are urgently needed in light of the rise in caesarean deliveries worldwide, increasing requests from mothers asking clinicians for vaginal seeding and mothers seeding their babies themselves. Despite potential health benefits, there are also potential risks, such as infections (e.g. group B streptococcus).

In conclusion, caesarean section impacts the offspring microbiome and is associated with risk of microbiome-related diseases, even in studies that have accounted for potentially confounding factors such as intrapartum antibiotics and maternal indications for caesarean delivery. At this point, additional observational studies in humans and interventional studies in animals will not be sufficient to guide policy in humans. Randomised trials of vaginal seeding in caesarean-delivered newborns are needed, both to determine whether restoration of the vaginal microbiome exposure changes infant microbiome development trajectories and, more importantly, to determine whether changes in the microbiome alter the risk of caesarean section-associated diseases.

Supplementary Material

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