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C-section and the Neonatal Gut Microbiome Acquisition: Consequences for Future Health

Silvia Arboleya[a, b] M. Suárez[c] N. Fernández[b, c] L. Mantecón[c] G. Solís[c] M. Gueimonde[a, b] C.G. de los Reyes-Gavilán[a, b]

[a]Department of Microbiology and Biochemistry of Dairy Products, Instituto de Productos Lácteos de Asturias (IPLA-CSIC), Villaviciosa, Spain; [b]Diet, Microbiota and Health Group, Health Research Institute of Principado de Asturias (IISPA), Oviedo, Spain; [c]Department of Pediatrics Service, Central University Hospital of Asturias (HUCA-SESPA), Oviedo, Spain

Key Messages

- The potential short- and long-term consequences of decisions about mode of birth may not be underestimated.
- The C-section rates recommended by WHO should be achieve over the world.
- C-section has significant impact on the microbiome development.
- More research is needed in order to decipher the specific impact of C-section on the microbiome and to develop nutritional strategies for minimizing it.

Keywords

Infant · Gut · Microbiota · C-section · Health · Restoration strategies · Delivery mode

Abstract

Background: The human gut microbiota is assembled during infancy with an increase in diversity and stability. The correct colonization and the establishment of this microbiome are linked to the early and future health status of the individual. It is known that caesarean delivery alters this optimal microbial foundation. C-section (CS) is a common obstetrician surgery; however, it is not without risk for the mother/infant dyad. The World Health Organization recommends not exceeding 10–15% of the total deliveries; nevertheless, this rate has been increasing rapidly worldwide in the last decades. ***Summary:*** This review discloses the clinical parameters for correct CS recommendation. Moreover, the major microbial changes in the infant gut microbiome acquisition as a consequence of delivery mode and medical practices surrounding it, as well as, the early and long-lasting effects for both mother and babies are discussed. In addition, some strategies for the gut microbiota restoration are analysed. The aim of this review is to show the need for the development of strategies for minimizing or limiting the impact of caesarean on the microbiome development, favouring future health.

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E-Mail karger@karger.com
www.karger.com/anm

Silvia Arboleya
Department of Microbiology and Biochemistry of Dairy Products, Instituto de Productos Lácteos de Asturias, Consejo Superior de Investigaciones Científicas (IPLA-CSIC), Paseo Río Linares, s/n, ES–33300, Villaviciosa, Asturias (Spain)
E-Mail Silvia.Arboleya@ipla.csic.es

Introduction

The intestinal microbiota is a key driver of the gut and immune system development; it also has an important effect on brain and behaviour. An increased body of evidence has shown that the early microbiota colonization exerts a strong influence on the later health status of the individual. The establishment of the gut microbiota at the beginning of life is a non-random process affected by many factors, among which the mode of delivery is of paramount importance. In the last 2 decades, caesareans have been on the rise worldwide, increasing rates by over 30% of deliveries in some countries. It has been observed that infants born by C-section (CS) have an altered microbiota with respect to vaginally delivered (VD) infants. Those differences in the microbial colonization may partly contribute to explain the risk of different non-communicable diseases observed in CS babies along life. The vertical mother-offspring microbial transmission, although not completely understood yet, seems to be less frequent in CS neonates than in VD babies. That is why, the so-called "first thousand days", represent a true window of opportunity for the microbiota reprogramming in a healthy direction through nutritional interventions aiming at the restoration of the normal microbial colonization pattern in the neonate.

Epidemiology and Clinical Parameters of CS

CS is one of the most frequent hospital surgical interventions both in developed and developing countries. The World Health Organization (WHO) considers a rate of 10–15% of total deliveries as optimal for caesarean sections [1]. The decision to undergo a CS to complete a gestation involves important sanitary and ethical factors due to the consequences that can affect the mother and the neonate in the short-, medium- and long-term [2].

Absolute maternal indications for CS include chorioamnionitis, maternal pelvis deformity, gross cephalo-pelvic disproportion, eclampsia or HELLP (Hemolysis, Elevated Liver enzymes, and Low Platelet count) syndrome, foetal asphyxia/acidosis, umbilical cord prolapse, placenta praevia, obstructing labour or uterine rupture. It can be considered relative indications: altered tococardiographic tracing, failure of labour progression and previous CS, although these 3 indications are arguable according to each labour [3]. As regarding neonates, CS would be indicated to complete gestation in some cases of large preterm babies [4], in certain diseases or foetal malformations detected in uterus, and for babies whose mothers presented active infections, such as human immunodeficiency virus (HIV) and genital herpes [5].

Maternity and perinatal morbi-mortality decrease when caesareans are correctly indicated; however, it is demonstrated that CS rates over 10–15% of total deliveries are not associated with significant reductions in mortality. Therefore, higher rates are suggestive of an unnecessarily used practice [1], involving a risk for both baby and mother.

In recent years, the concern about unnecessary caesareans has been rising and the current trend is to reduce these interventions as much as possible. In the United States, about 33% of deliveries were by CS in the last decades, and their incidence in recent times follows a slow but progressive trend to decrease according to the recommendations of international healthcare and scientific communities [6]. In other countries around the world, the rate is variable, with an incidence average of about 19% but with important differences between poor and rich countries [7]. In our region (Asturias, Spain), the Hospital Universitario Central de Asturias (HUCA) reached a CS rate of 15.5% from all deliveries at the end of the year 2017, while the average of the whole region was 17%.

The intrapartum antibiotic prophylaxis (IAP) is administered in all caesareans with the objective to avoid surgical infections. The current protocols seek to ensure a correct antibiotic concentration in blood, tissues and surgical wound during the whole process for as long as the incision is open, which involves the arrival of the antibiotic to the foetus before the section of the umbilical cord. The different administration protocols are based on the cost, shelf-life, safety and action spectrum of the antibiotic, and on the resistances that microorganisms may have acquired. Protocols using metronidazole, gentamicin, cefoxitin, cefazolin, and even meropenem are described [8]. At HUCA, most of the protocols use intravenous cefazolin (or vancomycin for pregnant women allergic to betalactamics) before the abdominal incision. A recent meta-analysis has concluded that the IAP should be recommended in all the caesareans as routine. Authors conclude that IAP reduces the infection incidence at surgical wound, endometritis and serious infections up to the 60–70%. Therefore, the use of prophylactic antibiotics is significantly beneficial in all the CS deliveries [8].

Last but not least, it should be taken into account that when antibiotics are administered before the clamping of the umbilical cord, an exposure of the newborn to the antibiotic occurs due to its passing through the placenta.

Breast milk can also be a way by which antibiotics pass from the mother to the infant. We do not currently know the consequences of this exposition in the neonate [8]. It could affect the correct establishment of the intestinal microbiota and increase the antibiotic resistance on gut microorganisms and even the correct immune system development, with transitional but not depreciable effects [8].

Development of Microbiome in CS Babies

The early gut microbial colonization lays the foundation for an adequate infant development and the physiological homeostasis later in life. However, it remains unclear whether the process commences during the pregnancy or during labour. In spite of this, it is currently well demonstrated that the delivery mode is one of the main drivers on the colonization and correct establishment of the gut microbiota. Several studies have confirmed different intestinal microbiota patterns between CS and VD babies; however, the source of microbial transmission is not wholly clear [9]. CS babies are not directly exposed to mother vaginal microbiota, so this first inoculum comes from other maternal localizations, such as skin or mouth, or from non-maternal sources like the surrounding delivery environment [10]. Dominguez-Bello et al. [11] showed that babies born by CS harboured, just after delivery, bacterial communities at different body sites (mouth, nasopharynges or meconium) similar to the mother's skin microbiota (*Staphylococcus* spp.), whereas the microbiota of VD infants was closer to the mother's vaginal microbiota (*Lactobacillus, Prevotella*, or *Atopobium* spp.). The authors link this observation with the higher susceptibility to certain pathogens in CS babies. Shi et al. [12] also observed lower microbiome and metabolic diversity in the meconium of CS babies compared with VD ones, with the levels of *Bacillus licheniformis* being higher in babies born by CS. Those studies disclose a different starting point of the microbial colonization depending on the delivery mode.

In a systematic review, Rutayisire et al. [13] concluded that CS is associated with a lower microbial diversity and lower abundance of Actinobacteria and Bacteroidetes phyla, *Bifidobacterium* and *Bacteroides* being the genera most affected. Moreover, these authors, in good agreement with Milani et al. [10], indicated that the phylum Firmicutes, mainly represented by *Clostridium* and *Lactobacillus,* is more increased in CS babies in comparison with VD neonates from birth to the third month of life. Rutayisire et al. [13] did not show differences in the microbiota due to the delivery mode at the age of 6 and 12 months, a fact that was indeed reported by other authors even until 7 years of life (although differences at this age between babies born by CS and VD were less pronounced than in neonates) [10, 14]. Discrepancies in the results obtained by different authors can be partially explained by different concurrent and confounding factors that are not always properly identified as neonatal exposures (such as the IAP), or adequately reported (such as race or geographical differences), or even due to factors related with the experimental techniques used (dependent- and independent- culture techniques, DNA extraction methods, etc.). Moreover, CS may reduce breastfeeding, which can contribute to the difficulty that generally arises during the lactation process in the first months of life [13]. However, it seems a common point that *Bacteriodes* are one of the most affected microbes by delivery mode. It was observed that *Bacteroides* was depleted or was present at low levels in full-term babies born by CS [15], even in the absence of antibiotic treatment to mothers before surgery [16], and in premature babies [17].

Early and Long-Lasting Effects of CS

It is important to remark that the abuse of CS is not without risk in terms of maternal and infant disease risk. It has been shown that women undergoing CS are more likely to develop urinary tract infections as compared with those giving birth by VD [18]. Indeed, CS delivery is the main risk factor for postpartum maternal infection [8]. Moreover, there is a risk of adjacent organs damage (intestine, bladder and ureters), an endogen risk derived from anaesthesia, and a potential need for transfusion or a thromboembolic complication. Negative consequences for future gestations could also be possible, such as delayed intrauterine growth, miscarriages, ectopic pregnancies, stillbirth, infertility and alterations in the position of the placenta [3], among others.

As a consequence of the increased risk of infection, these women receive antibiotics, introducing these antimicrobial agents in the perinatal period, which poses additional risk in terms of maternal and infant microbiota development. Moreover, the differences between CS and VD babies are not restricted to the gut microbiota; infants born by CS have been reported to present reduced levels of immune mediators such as cytokines [19], and an increment of neonatal respiratory distress, or even of mortality and disability at medium-long term has been observed.

In this context, it is not surprising that CS has been reported to have both short- and long-term implications for the infant, and has been associated with a poorest health outcome when compared with VD. Differences between CS and VD babies are already obvious and observable from the very early moments of life, as underlined by the differences found in the Apgar scores, which is a widely used measure of neonatal health [20]. Later on, a higher risk of different non-communicable diseases has also been observed in CS-delivered subjects, including allergic diseases [21, 22], celiac disease [23], obesity [24, 25], type-1 diabetes [26] and even hypertension in young adults [27].

Strategies for Shaping Gut Microbiota and Improving Health

Infants born by CS are deprived of exposure to maternal vaginal microbiota during birth. "Vaginal seeding" practice consists of externally spreading mother's vaginal fluids to infant with the purpose to transfer the maternal vaginal microbiota to newborns, thus favouring a proper microbial initial colonization. Only a pilot-study, with low number of infants, described a partial microbiota restoration by vaginal microbial transfer [28]; nevertheless, the risk of neonatal infection by unintended maternal pathogens exposure should not be neglected [29]. Therefore, current medical recommendations on the application of this practice are cautious, and highlight the need of more studies evaluating its safety and benefit [29].

There is a "window of opportunity" in early life, during which time aberrant changes in gut microbial colonization can result in immune dysregulation but during which time the composition of the intestinal microbiota can still be "re-programmed" through nutritional interventions. The beginning and end of this window are a matter of intense debate but likely coincides from conception until the age 2–3 years [30]. Breast milk is the best nutrition for infants and constitutes the best modulator for the correct establishment of the microbiota and maturation of the immune system through its microbial content, bioactive oligosaccharides and extracellular vesicles including diverse cargo, as mRNA, miRNA and proteins [31]. Nevertheless, in cases of special risk or when exclusive breastfeeding cannot be maintained, dietary intervention to mothers in the perinatal period or to infants constitutes a suitable strategy. Although some probiotic microorganisms have been proven to be efficient in preventing necrotizing enterocolitis and allergy in full-term infants, intervention studies aimed specifically at children born by CS are still scarce and focus specifically on the supplementation of infant formulas. So, a formula containing *Lactobacillus reuteri* DSM 17938 positively modulated the early development of the microbiota of infants born by CS towards the composition found after VD [32], whereas the addition of the strain *Bifidobacterium lactis* CNCM I-3446 positively affected the immune and gut functions of CS babies [33]. A recent multicentre study determined that supplementation with a synbiotic combination of galacto-oligosaccharides/fructo-oligosaccharides and a *Bifidobacterium breve* strain counteracted the delayed *Bifidobacterium* colonization in CS-delivered infants, emulating colonization patterns of VD babies [34].

Perspectives and Future Trends on the Research about the Relationship among CS, Microbiota and Later Health

Worldwide CS rates remain higher than those suggested by WHO recommendations [1]. Scientific and clinical evidences support the importance of the gut microbiota on the neonate development and health. However, the correct establishment and development of the intestinal microbiome is altered by several factors, among which "the caesarean" is of paramount importance. Although clear differences in the microbiota of babies born by CS or VD have been abundantly reported, the real effect of CS may be masked by several confounding factors, such as IAP (Fig. 1). Therefore, more studies are needed to decipher the microbial alterations specifically associated to the CS form of delivery.

In order of reverting the CS effects and recovering the intestinal microbiota composition, there was a certain excitement after the "vaginal seeding approach" followed by Dominguez-Bello et al. [28]; however, as previously stated, there is still a concern about the safety of this process. More studies with higher number of babies are necessary in order to evaluate the risk and consequences of this practice, not only over the gut microbiota but also regarding the present and future health of the individual. An interesting approach to overcome the associated risk of the vaginal seeding would be the use of selected cocktails of beneficial bacteria derived from the mother's vaginal microbiota, which needs for its design of an exhaustive knowledge of the first microbial founders of baby's skin and gut as well as of the vaginal microbiota.

Breastfeeding is recognized as the optimal nutrition for infants [31]. Previous studies have demonstrated that breast-milk or formula-milk provides a different recovery of the beneficial gut microbiota profile after its alteration

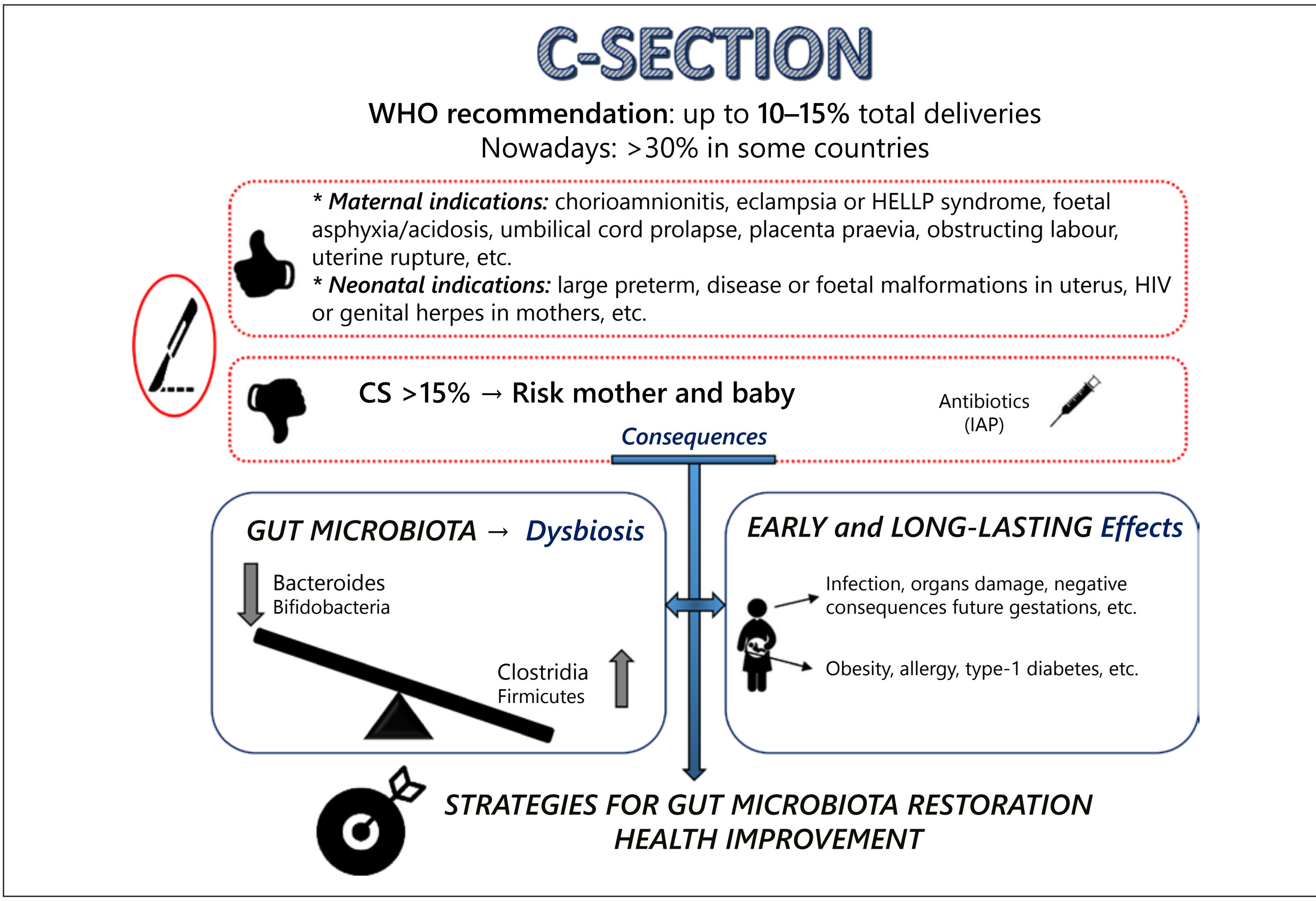

Fig. 1. CS and its implication on the neonatal gut microbiome acquisition. CS, C-section; HELLP, hemolysis, elevated liver enzymes, and low platelet count; HIV, human immunodeficiency virus; IAP, intrapartum antibiotic prophylaxis.

by antibiotic exposure of babies or their mothers [35]. It is then necessary to elucidate the effect that the feeding type could play in the gut microbiota restoration of newborns after caesarean delivery. Breastfeeding can be delayed after CS; thus, only the detailed knowledge about its influence on the gut microbiota establishment could favour the formulation of new health recommendations.

Weaning is another important stage, where the gut microbiota becomes more complex and diverse [9]. The timing and selection of the first solid foods are factors that have an important effect in the correct development of the gut microbiota. More research focused on the influence of those factors, not only in the assembly of the microbiome but also in the correction of the dysbiosis associated to CS is needed.

Nutritional intervention strategies aimed at gut microbiota modulation in dysbiosis states – such as the use of probiotics, prebiotics, synbiotics or long chain fatty acids – should be directed not only to restoring gut microbiota composition and function after CS but also on the correct brain development, as recently pointed out by Moya-Pérez et al. [36]. The Microbiota-Gut-Brain-Axis concept is gaining relevance and recent scientific evidences suggest an important role of the gut microbiota in brain processes. In this way, some works have linked the effect of CS with the incidence of neuropsychiatric disorders [36] or risk of behavioural problems [37]. More investigations are needed to confirm the relationship between CS, gut microbiota and brain function, in order to design nutritional strategies helping at the establishment of a correct microbiota-gut-brain axis connection in early life.

The evidence discussed in this review highlights the impact of the caesarean on the gut microbiota development and on the future maternal and offspring health.

The observations here presented emphasize the need to optimize CS rates and to develop intervention strategies for minimizing the impact of caesarean on the microbiome development.

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Disclosure Statement

The authors declare that they have no competing interests to disclose.

References

1 WHO/RHR/15.02: World Health Organization 2015. Statement on Caesarean section rates, 2015.
2 Signore C, Klebanoff M: Neonatal morbidity and mortality after elective cesarean delivery. Clin Perinatol 2008;35:361–371, vi.
3 Mylonas I, Friese K: Indications for and risks of elective Cesarean section. Dtsch Arztebl Int 2015;112:489–495.
4 Grabovac M, Karim JN, Isayama T, Liyanage SK, McDonald SD: What is the safest mode of birth for extremely preterm breech singleton infants who are actively resuscitated? A systematic review and meta-analyses. BJOG 2017;125:652–663.
5 Kennedy CE, Yeh PT, Pandey S, Betran AP, Narasimhan M: Elective cesarean section for women living with HIV: a systematic review of risks and benefits. AIDS (London, England) 2017;31:1579–1591.
6 Lagrew DC, Low LK, Brennan R, Corry MP, Edmonds JK, Gilpin BG, Frost J, Pinger W, Reisner DP, Jaffer S: National partnership for maternal safety: Consensus bundle on safe reduction of primary Cesarean births-supporting intended vaginal births. J Obstet Gynecol 2018;131:503–513.
7 Betran AP, Ye J, Moller AB, Zhang J, Gulmezoglu AM, Torloni MR: The increasing trend in Caesarean section rates: Global, regional and national estimates: 1990–2014. PLoS One 2016;11:e0148343.
8 Smaill FM, Grivell RM: Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section. Cochrane Database Syst Rev 2014;10:CD007482.
9 Meropol SB, Edwards A: Development of the infant intestinal microbiome: a bird's eye view of a complex process. Birth Defects Res C Embryo Today 2015;105:228–239.
10 Milani C, Duranti S, Bottacini F, Casey E, Turroni F, Mahony J, Belzer C, Delgado Palacio S, Arboleya Montes S, Mancabelli L, Lugli GA, Rodriguez JM, Bode L, de Vos W, Gueimonde M, Margolles A, van Sinderen D, Ventura M: The first microbial colonizers of the human gut: composition, activities, and health implications of the infant gut microbiota. Microbiol Mol Biol Rev 2017; 81:pii:e00036-17.
11 Dominguez-Bello MG, Costello EK, Contreras M, Magris M, Hidalgo G, Fierer N, Knight R: Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. Proc Natl Acad Sci U S A 2010;107:11971–11975.
12 Shi YC, Guo H, Chen J, Sun G, Ren RR, Guo MZ, Peng LH, Yang YS: Initial meconium microbiome in Chinese neonates delivered naturally or by cesarean section. Sci Rep 2018;8: 3255.
13 Rutayisire E, Huang K, Liu Y, Tao F: The mode of delivery affects the diversity and colonization pattern of the gut microbiota during the first year of infants' life: a systematic review. BMC Gastroenterol 2016; 16:86.
14 Salminen S, Gibson GR, McCartney AL, Isolauri E: Influence of mode of delivery on gut microbiota composition in seven year old children. Gut 2004;53:1388.
15 Backhed F, Roswall J, Peng Y, Feng Q, Jia H, Kovatcheva-Datchary P, Li Y, Xia Y, Xie H, Zhong H, Khan MT, Zhang J, Li J, Xiao L, Al-Aama J, Zhang D, Lee YS, Kotowska D, Colding C, Tremaroli V, Yin Y, Bergman S, Xu X, Madsen L, Kristiansen K, Dahlgren J, Wang J: Dynamics and stabilization of the human gut microbiome during the first year of life. Cell Host Microbe 2015;17:852.
16 Jakobsson HE, Abrahamsson TR, Jenmalm MC, Harris K, Quince C, Jernberg C, Bjorksten B, Engstrand L, Andersson AF: Decreased gut microbiota diversity, delayed Bacteroidetes colonisation and reduced Th1 responses in infants delivered by caesarean section. Gut 2014;63:559–566.
17 Gregory KE, LaPlante RD, Shan G, Kumar DV, Gregas M: Mode of birth influences preterm infant intestinal colonization with Bacteroides over the early neonatal period. Adv Neonatal Care 2015;15:386–393.
18 Gundersen TD, Krebs L, Loekkegaard ECL, Rasmussen SC, Glavind J, Clausen TD: Postpartum urinary tract infection by mode of delivery: a Danish nationwide cohort study. BMJ Open 2018;8:e018479.
19 Malamitsi-Puchner A, Protonotariou E, Boutsikou T, Makrakis E, Sarandakou A, Creatsas G: The influence of the mode of delivery on circulating cytokine concentrations in the perinatal period. Early Hum Dev 2005;81: 387–392.
20 Costa-Ramón AM, Rodríguez-González A, Serra-Burriel M, Campillo-Artero C: It's about time: cesarean sections and neonatal health. J Health Econ 2018;59:46–59.
21 Bager P, Wohlfahrt J, Westergaard T: Caesarean delivery and risk of atopy and allergic disease: meta-analyses. Clin Exp Allergy 2008; 38:634–642.
22 Thavagnanam S, Fleming J, Bromley A, Shields MD, Cardwell CR: A meta-analysis of the association between Caesarean section and childhood asthma. Clin Exp Allergy 2008; 38:629–633.
23 Decker E, Engelmann G, Findeisen A, Gerner P, Laass M, Ney D, Posovszky C, Hoy L, Hornef MW: Cesarean delivery is associated with celiac disease but not inflammatory bowel disease in children. Pediatrics 2010;125:e1433–e1440.
24 Pei Z, Heinrich J, Fuertes E, Flexeder C, Hoffmann B, Lehmann I, Schaaf B, von Berg A, Koletzko S: Cesarean delivery and risk of childhood obesity. J Pediatr 2014;164:1068–1073.e1062.
25 Mueller NT, Mao G, Bennet WL, Hourigan SK, Dominguez-Bello MG, Appel LJ, Wang X: Does vaginal delivery mitigate or strengthen the intergenerational association of overweight and obesity? Findings from the Boston Birth Cohort. Int J Obes 2017;41:497–501.
26 Cardwell CR, Stene LC, Joner G, Cinek O, Svensson J, Goldacre MJ, Parslow RC, Pozzilli P, Brigis G, Stoyanov D, Urbonaite B, Sipetic S, Schober E, Ionescu-Tirgoviste C, Devoti G, de Beaufort CE, Buschard K, Patterson CC: Caesarean section is associated with an increased risk of childhood-onset type 1 diabetes mellitus: a meta-analysis of observational studies. Diabetologia 2008; 51:726–735.

27 Horta BL, Gigante DP, Lima RC, Barros FC, Victora CG: Birth by caesarean section and prevalence of risk factors for non-communicable diseases in young adults: a birth cohort study. PLoS One 2013;8:e74301.
28 Dominguez-Bello MG, De Jesus-Laboy KM, Shen N, Cox LM, Amir A, Gonzalez A, Bokulich NA, Song SJ, Hoashi M, Rivera-Vinas JI, Mendez K, Knight R, Clemente JC: Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer. Nat Med 2016;22:250–253.
29 Cunnington AJ, Sim K, Deierl A, Kroll JS, Brannigan E, Darby J: "Vaginal seeding" of infants born by caesarean section. BMJ 2016; 352:i227.
30 Laursen MF, Bahl MI, Michaelsen KF, Licht TR: First foods and gut microbes. Front Microbiol 2017;8:356.
31 Le Doare K, Holder B, Bassett A, Pannaraj PS: Mother's milk: A purposeful contribution to the development of the infant microbiota and immunity. Front Immunol 2018;9:361.
32 Garcia Rodenas CL, Lepage M, Ngom-Bru C, Fotiou A, Papagaroufalis K, Berger B: Effect of formula containing Lactobacillus reuteri DSM 17938 on fecal microbiota of infants born by Cesarean-section. J Pediatr Gastroenterol Nutr 2016;63:681–687.
33 Baglatzi L, Gavrili S, Stamouli K, Zachaki S, Favre L, Pecquet S, Benyacoub J, Costalos C: Effect of infant formula containing a low dose of the probiotic Bifidobacterium lactis CNCM I-3446 on immune and gut functions in C-Section delivered babies: a pilot study. Clin Med Insights Pediatr 2016;10:11–19.
34 Chua MC, Ben-Amor K, Lay C, Neo AGE, Chiang WC, Rao R, Chew C, Chaithongwongwatthana S, Khemapech N, Knol J, Chongsrisawat V: Effect of synbiotic on the gut microbiota of Cesarean delivered infants: a randomized, double-blind, multicenter study. J Pediatr Gastroenterol Nutr 2017;65: 102–106.
35 Nogacka A, Salazar N, Suarez M, Milani C, Arboleya S, Solis G, Fernandez N, Alaez L, Hernandez-Barranco AM, de Los Reyes-Gavilan CG, Ventura M, Gueimonde M: Impact of intrapartum antimicrobial prophylaxis upon the intestinal microbiota and the prevalence of antibiotic resistance genes in vaginally delivered full-term neonates. Microbiome 2017;5:93.
36 Moya-Perez A, Luczynski P, Renes IB, Wang S, Borre Y, Anthony Ryan C, Knol J, Stanton C, Dinan TG, Cryan JF: Intervention strategies for cesarean section-induced alterations in the microbiota-gut-brain axis. Nutr Rev 2017;75:225–240.
37 Rutayisire E, Wu X, Huang K, Tao S, Chen Y, Tao F: Childhood emotional and behavior problems and their associations with cesarean delivery. Rev Bras Psiquiatr 2017;20:145–153.