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CESAREAN DELIVERY AND THE DEVELOPMENT OF THE INFANT GUT MICROBIOTA: EARLY-LIFE ALTERATIONS, HEALTH CONSEQUENCES, AND POTENTIAL STRATEGIES FOR MICROBIOTA MODULATION

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ABSTRACT

The establishment of the intestinal microbiota during early life is a dynamic developmental process that contributes to maturation of the gastrointestinal tract, immune system, metabolic pathways, and intestinal barrier. Mode of delivery is among the earliest factors associated with differences in microbial colonization. Infants born by cesarean delivery commonly demonstrate delayed acquisition of selected maternal-associated microorganisms, particularly *Bacteroides* and *Bifidobacterium*, as well as altered microbial succession during the first weeks and months of life. At the same time, cesarean-associated microbiota alterations cannot be attributed exclusively to the absence of exposure to the maternal vaginal microbiota. Perinatal antibiotic exposure, breastfeeding, gestational age, indication for cesarean delivery, duration of labor, maternal health, and environmental factors interact with delivery mode and may substantially influence microbial development.

This structured narrative review summarizes current evidence concerning the development of the infant gut microbiota following cesarean delivery, potential health consequences of altered early-life microbial trajectories, and available strategies for microbiota modulation. Particular attention is given to probiotics, prebiotics, synbiotics, breastfeeding, vaginal seeding, and maternal microbial transfer. Current evidence indicates that microbiota differences associated with cesarean delivery are most pronounced during early infancy and may partially diminish with maturation. Epidemiological associations between cesarean delivery and allergic, respiratory, gastrointestinal, and metabolic outcomes are biologically plausible but do not establish a microbiome-mediated causal pathway. Nutritional interventions can modify microbial composition, especially by increasing *Bifidobacterium*, but evidence for long-term clinical benefits remains limited. Vaginal seeding and other forms of maternal microbial transfer demonstrate potential for modifying microbial profiles but remain experimental because efficacy, safety, and long-term clinical relevance have not been adequately established. Future research should use longitudinal, standardized, multi-omics and clinically oriented approaches to determine whether targeted modulation of the infant microbiome can improve health outcomes following cesarean birth.

KEYWORDS

Cesarean Delivery, Infant Gut Microbiota, Neonatal Microbiome, *Bifidobacterium*, *Bacteroides*, Probiotics, Vaginal Seeding, Maternal Microbial Transfer

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1. Introduction

The human gastrointestinal tract is colonized by a complex and dynamic microbial ecosystem consisting of bacteria, viruses, fungi, archaea, and bacteriophages. The composition and functional activity of this ecosystem change continuously throughout life; however, the first months and years represent a particularly important developmental period. During infancy, microbial communities are established while the intestinal epithelium, mucosal barrier, metabolic pathways, and immune system are simultaneously undergoing maturation. Consequently, early-life microbial exposures may influence physiological processes that extend well beyond the neonatal period.

The gut microbiota contributes to multiple aspects of host physiology. Microorganisms participate in the metabolism of otherwise poorly digestible dietary components, synthesize or modify bioactive compounds, interact with the intestinal epithelial barrier, compete with potentially pathogenic microorganisms, and influence innate and adaptive immune responses. Microbial metabolites such as short-chain fatty acids (SCFAs), bile acid derivatives, and tryptophan metabolites can act as signaling molecules and influence epithelial integrity, immune regulation, and systemic metabolism. The early microbiota is therefore increasingly regarded as an active component of human development rather than a passive collection of microorganisms inhabiting the intestine.

The establishment of the infant microbiota is influenced by numerous maternal, perinatal, nutritional, and environmental factors. These include maternal microbiota, gestational age, mode of delivery, intrapartum and neonatal antibiotic exposure, breastfeeding, formula feeding, introduction of complementary foods,

contact with siblings, household environment, and geographical location. The relative importance of each factor varies according to developmental stage. Nevertheless, mode of delivery is one of the earliest identifiable exposures associated with differences in neonatal microbial colonization (Zimmermann & Curtis, 2018).

During vaginal birth, the infant is exposed to microorganisms originating from the maternal vaginal, perineal, fecal, and skin microbiota. In contrast, infants delivered by cesarean section do not pass through the birth canal and are initially exposed to a different microbial environment, including maternal skin microorganisms, healthcare-associated organisms, and microorganisms from the surrounding environment. Early work demonstrated that delivery mode influences microbial acquisition across several neonatal body sites, providing a biological basis for subsequent investigations of the intestinal microbiota (Dominguez-Bello et al., 2010).

The intestinal consequences of this difference have been repeatedly investigated. A systematic review of studies conducted during the first year of life found that cesarean delivery was associated with differences in the abundance and colonization of major bacterial groups. In particular, *Bifidobacterium* and *Bacteroides* were generally more abundant or more frequently detected in vaginally delivered infants, whereas differences were most apparent during the first months of life (Rutayisire et al., 2016). These findings suggest that delivery mode may influence the trajectory of microbiome establishment rather than determine a permanent microbial state.

More recent longitudinal research has provided a more detailed picture. Shao et al. (2019) analyzed 1,679 fecal microbiota samples from 596 full-term infants and demonstrated that cesarean delivery was associated with disrupted transmission of maternal *Bacteroides* strains and increased colonization by opportunistic microorganisms associated with the hospital environment, including *Enterococcus*, *Enterobacter*, and *Klebsiella*. The effects were less pronounced among vaginally delivered infants exposed to maternal antibiotic prophylaxis and among infants who were not breastfed, highlighting the contribution of factors other than delivery mode to early-life gut microbiota development.

These observations have led to the hypothesis that altered microbial colonization following cesarean delivery could contribute to later health outcomes. Epidemiological research has identified associations between cesarean birth and several conditions, including asthma, allergic disease, obesity, gastrointestinal disorders, and some immune-mediated diseases (Liu et al., 2024). However, the interpretation of these associations is challenging because cesarean delivery frequently occurs in the context of maternal or fetal characteristics that may independently affect offspring health. In addition, antibiotic exposure, breastfeeding, gestational age, and socioeconomic or environmental factors can act as confounders.

The term “dysbiosis” is therefore problematic if used indiscriminately (Van Hul et al. 2024). A microbial community that differs from that of vaginally delivered infants is not necessarily abnormal or harmful. Human microbiota composition varies considerably between healthy individuals, and there is no single microbial configuration that can currently be defined as universally optimal (Marco et al., 2026). It is more scientifically appropriate to describe many findings as cesarean-associated alterations in microbiota composition, colonization, or succession, reserving the term dysbiosis for contexts in which there is evidence of an ecologically or functionally adverse microbial state (Marco et al., 2026; Tiffany & Bäuml, 2019).

The possibility of modifying the microbiota after cesarean delivery has generated considerable scientific and clinical interest. Breastfeeding, probiotics, prebiotics, synbiotics, and maternal microbial transfer have all been investigated. Vaginal seeding, in particular, has attracted attention because it attempts to reproduce part of the maternal microbial exposure that occurs naturally during vaginal delivery. However, the evidence regarding its efficacy and safety remains insufficient for routine clinical implementation. A 2024 systematic review of vaginal seeding found changes in selected bacterial groups but inconsistent effects on overall microbial diversity, while a 2026 systematic review concluded that the ability of maternal microbial transfer to modify neonatal microbiota and improve clinically beneficial manners remains uncertain (Wang et al., 2024; Jurgiel et al., 2026).

The aim of this review is therefore to synthesize current knowledge regarding the relationship between cesarean delivery and infant gut microbiota development, examine possible health consequences of cesarean-associated microbial alterations, and critically evaluate strategies intended to modulate the infant microbiome during early life.

2. Methodology

2.1. Review design

This article was developed as a structured narrative review of the scientific literature concerning cesarean delivery, infant gut microbiota development, associated health outcomes, and microbiota-modulating interventions. A narrative approach was selected because the available literature encompasses multiple study designs, including longitudinal observational studies, cohort studies, randomized controlled trials, systematic reviews, meta-analyses, and mechanistic investigations. These studies differ substantially in population characteristics, microbiome sampling methods, sequencing techniques, intervention protocols, and outcome measures; quantitative pooling was therefore not undertaken within the scope of the present review.

The review was structured around the major conceptual areas of the topic: establishment of the infant gut microbiota, influence of delivery mode, modifying perinatal factors, potential health consequences, and strategies for microbiota modulation.

2.2. Literature identification

Relevant literature was identified through targeted searches of PubMed/MEDLINE, supplemented by examination of reference lists of relevant reviews and primary studies. The search focused on peer-reviewed publications addressing infant or neonatal gut microbiota, cesarean delivery, mode of birth, breastfeeding, antibiotic exposure, probiotics, prebiotics, synbiotics, vaginal seeding, and maternal microbial transfer.

The search strategy combined terms such as “cesarean delivery,” “caesarean section,” “infant gut microbiota,” “neonatal microbiome,” “*Bifidobacterium*,” “*Bacteroides*,” “delivery mode,” “breastfeeding,” “antibiotics,” “probiotics,” “prebiotics,” “synbiotics,” “vaginal seeding,” and “maternal microbial transfer.”

Particular attention was given to contemporary evidence published between 2016 through 2026, while earlier landmark studies were retained where they provided essential conceptual or methodological foundations.

2.3. Eligibility and evidence synthesis

Studies were considered relevant when they investigated at least one of the following: (1) gut microbiota development in infants according to mode of delivery; (2) microbiota-associated differences following cesarean delivery; (3) the contribution of antibiotics, breastfeeding, gestational age, or other perinatal variables to microbiota development; (4) associations between cesarean delivery, microbiota, and health outcomes; or (5) interventions intended to modify the microbiota of cesarean-born infants.

Systematic reviews and meta-analyses were prioritized when available. However, primary longitudinal studies and randomized controlled trials were also considered essential because aggregated findings from microbiome reviews may obscure important differences in sampling time, microbial taxa, and intervention protocols.

The evidence was synthesized qualitatively. Particular emphasis was placed on consistency across studies, biological plausibility, temporal relationships, methodological limitations, and the distinction between microbiological outcomes and clinically meaningful health outcomes.

3. Results

3.1. Development of the Infant Gut Microbiota

The establishment of the gut microbiota is a dynamic process that begins around birth and undergoes substantial transformation throughout infancy. Immediately after delivery, the neonatal gastrointestinal tract is colonized by microorganisms originating from maternal and environmental sources. Early microbial communities subsequently change as oxygen availability decreases, host immune responses mature, and nutritional substrates change.

Initial colonizers can influence the ecological environment in which later microbial populations become established. Facultative anaerobic bacteria may initially tolerate relatively oxygenated conditions and subsequently contribute to an environment favorable to obligate anaerobes. As this process progresses, *Bifidobacterium* and *Bacteroides* become increasingly prominent, while other anaerobic bacterial groups, including members of the Lachnospiraceae, Ruminococcaceae families, become more prominent with microbiome and dietary diversification.

The infant microbiome should not be considered a miniature version of the adult microbiome. It is developmentally distinct, characterized by substantial temporal variability and influenced strongly by milk feeding. The composition of breastfed infants differs from that of formula-fed infants because human milk contains a complex mixture of nutrients and bioactive compounds that selectively influence microbial growth.

Among the most important early bacterial groups are bifidobacteria. Human milk oligosaccharides (HMOs) provide substrates that are preferentially utilized by selected *Bifidobacterium* species. This relationship illustrates the importance of microbial function rather than taxonomic composition alone. A bacterial species becomes beneficial not merely because of its presence, but because of its ability to perform functions within a particular ecological and nutritional context.

Bacteroides species are also important early-life colonizers. They contribute to complex carbohydrate metabolism and may participate in microbial cross-feeding networks. Their delayed acquisition following cesarean delivery has been repeatedly documented and may partly reflect differences in maternal microbial transmission, although other perinatal factors, including antibiotic exposure, may also contribute.

The first year of life is characterized by rapid microbial maturation. The systematic review by Rutayisire et al. (2016) found that cesarean delivery was associated with differences in the abundance and diversity of major bacterial phyla during the first three months of life, including lower representation of Actinobacteria and Bacteroidetes in several studies, as well as the detection of *Bifidobacterium* and *Bacteroides*. Importantly, the magnitude of differences varied over time, supporting the concept that early microbial differences may be partially transient.

The microbiome is also influenced by microbial strain inheritance. Bacterial transmission is not limited to genera or species. Maternal strains can be transferred to infants and may establish long-term lineages. Consequently, the question of whether cesarean delivery changes microbial development involves not only which taxa are present but also whether specific maternal strains successfully colonize and persist (Podlesny&Fricke, 2021; Shao et al., 2019).

3.2. Impact of Cesarean Delivery on Early-Life Gut Microbiota

The relationship between cesarean delivery and infant microbiota has been investigated using culture-based techniques, targeted molecular methods, 16S rRNA sequencing, and whole-genome metagenomics (Shao et al., 2019; Stewart et al. 2017).

One of the earliest influential studies by Dominguez-Bello et al. (2010) demonstrated that delivery mode influenced the initial microbial communities acquired by newborns. Vaginally delivered infants acquired microorganisms resembling maternal vaginal communities, whereas cesarean-born infants showed greater similarity to maternal skin microbiota. Although this study did not establish the long-term functional consequences of these differences, it provided a foundation for subsequent microbiome research.

The gastrointestinal effects associated with delivery mode were examined in greater detail in longitudinal investigations. Shao et al. (2019) reported reduced transmission of maternal *Bacteroides* strains in cesarean-born infants and increased colonization by opportunistic pathogens associated with healthcare environments. Their study was notable for its size and use of whole-genome shotgun metagenomics, which allowed investigation of strain-level transmission rather than only genus-level abundance.

These findings suggest that the microbiological effect of cesarean delivery may involve two simultaneous processes. The first is a reduction or delay in the acquisition of some maternal-associated commensals. The second is increased exposure to microorganisms that are more characteristic of the healthcare environment. Collectively, the available evidence suggests that the microbiological effects associated with cesarean delivery may involve both reduced or delayed acquisition of particular maternal-associated microorganisms and increased acquisition of alternative microorganisms associated with the healthcare environment (Shao et al., 2019; Podlesny&Fricke, 2021).

However, the effect is not uniform. Some studies have reported limited or transient differences, while others have demonstrated substantial changes. Stewart et al. (2017), for example, reported no major sustained impact of delivery mode on overall microbiome development in a cohort of exclusively preterm infants, illustrating the heterogeneity of findings across populations and clinical settings.

Differences between studies may arise from multiple methodological factors. These include gestational age, the timing of stool collection, breastfeeding rates, antibiotic exposure, geographical location, sequencing technology, taxonomic databases, and differences in maternal microbial communities (Shao et al. 2019; Podlesny&Fricke, 2021; Singleton et al., 2026).

Longitudinal studies are particularly important because a single stool sample provides only a snapshot of a rapidly changing microbial ecosystem. A bacterium that is absent at day three may become abundant at week three, and a difference observed at one month may no longer be detectable at one year (Shao et al., 2019; Rutayisire et al., 2016).

The evidence therefore supports a model in which cesarean delivery modifies the **trajectory** of early microbial succession rather than permanently determining the infant microbiome (Shao et al., 2019; Podlesny&Fricke, 2021; Singleton et al. 2026).

3.3. Maternal Microbial Transmission

An important concepts emerging from contemporary microbiome research is strain-level maternal transmission (Podlesny&Fricke, 2021; Sinha et al., 2026).

The microbiota acquired during birth does not consist simply of generic bacterial taxa. Specific maternal strains can colonize the infant and persist over time. The likelihood of maternal strain transmission successful transmission may be influenced by delivery mode, environmental exposure, feeding, antibiotic treatment, and ecological compatibility with the developing infant gut (Podlesny&Fricke, 2021; Sinha et al., 2026).

The reduced transmission of maternal *Bacteroides* strains observed after cesarean delivery is particularly relevant (Shao et al., 2019). *Bacteroides* species can perform important metabolic functions and participate in complex microbial networks. Reduced or delayed acquisition of these bacteria may therefore influence subsequent ecological succession.

However, maternal microbial exposure continues after cesarean delivery through multiple postnatal routes, including breastfeeding, maternal skin contact, and the shared household environment. Recent strain-resolved evidence suggests that the maternal gut microbiome represents an important reservoir for infant gut strains, whereas transmission from vaginal and breast milk microbiomes appears to occur less consistently. Consequently, cesarean delivery does not eliminate maternal microbial exposure but may alter the timing and routes through which maternal microorganisms are acquired (Sinha et al., 2026).

This observation is important for interpreting the “bacterial baptism” hypothesis. The hypothesis proposes that exposure to maternal vaginal microorganisms during vaginal delivery provides an important early microbial inoculum. Although vaginal exposure clearly represents one route of microbial acquisition, current evidence indicates that it is only one component of a broader maternal–infant microbial exchange (Mueller et al., 2015; Sinha et al. 2026).

3.4. Role of Perinatal Antibiotics

Antibiotic exposure is one of the most important confounders in studies investigating cesarean-associated microbiota.

Cesarean delivery is commonly accompanied by prophylactic maternal antibiotics intended to reduce postoperative infectious complications. In addition, infants may receive antibiotics for suspected or confirmed neonatal infections. Antibiotics can substantially alter microbial abundance and community structure, particularly during a period when microbial communities are still being established.

The interaction between cesarean delivery and antibiotics is complex. Shao et al. (2019) observed microbiome alterations associated with cesarean delivery but also noted effects of maternal antibiotic prophylaxis and lack of breastfeeding. This highlights why the delivery mode should not be interpreted independently of perinatal medication exposure.

At the same time, evidence does not support a simple assumption that every antibiotic exposure causes an additional and equivalent disruption of the microbiota. Dierikx et al. (2022) investigated the timing of maternal antibiotic administration during cesarean delivery and found no significant differences in infant microbial colonization between administration before skin incision and after cord clamping, although both cesarean groups differed from vaginally delivered controls during the first month of life. This suggests that the timing of prophylactic antibiotic administration may not fully explain the microbiota differences observed after cesarean delivery.

The effect of antibiotics likely depends on the specific drug, dose, timing, duration of exposure, and characteristics of the developing microbial community. Future research should therefore report antibiotic exposure in detail rather than treating it as a binary variable.

Recent evidence has also highlighted the importance of maternal microbiota. A 2025 systematic review examining perioperative antibiotic prophylaxis during cesarean delivery found only three eligible studies involving 286 mothers and substantial methodological heterogeneity. Although findings regarding taxonomic diversity findings were inconsistent, functional diversity appeared to be sensitive to antibiotic exposure, suggesting that microbial function may be affected even when conventional diversity measures show limited changes (Feles et al., 2025).

3.5. Influence of Breastfeeding

Breastfeeding is one of the strongest postnatal factors influencing the development of the infant gut microbiota.

Human milk contains proteins, lipids, immunoglobulins, antimicrobial factors, HMOs, and microorganisms. HMOs are particularly relevant because they provide selective substrates for bifidobacteria and contribute to the establishment of a microbial environment distinct from that of formula-fed infants (Lordan et al., 2024; Kijner et al., 2022)

The relationship between breastfeeding and cesarean-associated microbiota alterations is therefore highly relevant. Breastfeeding may nevertheless influence gut microbiota through human milk oligosaccharides, bioactive compounds, and potentially microbial exposure, even in infants born by cesarean delivery.

Shao et al. (2019) reported that lack of breastfeeding was associated with some of the same microbial alterations observed after cesarean delivery. This suggests that breastfeeding may partially attenuate some microbiota differences associated with delivery mode.

However, breastfeeding should not be viewed as a complete “correction” of cesarean-associated microbiota. The effects of human milk on developing microbiota are complex and cannot be reduced to the presence of a single bacterial genus (Shao et al., 2019)

Furthermore, breastfeeding rates themselves may differ according to delivery mode. Pain, delayed initiation of lactation, maternal postoperative recovery, separation of mother and infant, and clinical complications can influence breastfeeding success after cesarean delivery (Beake et al., 2016; Ulfa et al., 2023). Consequently, differences in early feeding may contribute to the microbiota alterations observed between infants born by cesarean and vaginal delivery (Shao et al., 2019)

3.6. Elective and Emergency Cesarean Delivery

Cesarean delivery is not a biologically uniform exposure. Planned cesarean delivery before the onset of labor differs from non-elective cesarean delivery performed after labor has begun. These circumstances may differ with respect to duration of labor, rupture of membranes, timing of antibiotic administration, and the timing and extent of maternal–infant microbial exposure.

The distinction between cesarean delivery before and after the onset of labor may therefore be relevant when interpreting differences in infant gut microbiota. The acquisition and persistence of maternal microbial strains are influenced by multiple perinatal and postnatal factors, and delivery mode represents only one component of this process (Shao et al., 2019; Podlesny & Fricke, 2021).

Evidence from longitudinal studies also indicates that the microbiota associated with cesarean delivery is not determined by delivery mode alone. For example, Shao et al. (2019) identified effects associated with maternal antibiotic prophylaxis and breastfeeding in addition to delivery mode, while strain-level analyses have demonstrated that maternal microbial transmission can vary according to birth mode and other environmental and perinatal factors.

This distinction is important when interpreting both microbiome and epidemiological studies. Combining planned and non-elective cesarean deliveries into a single exposure category may obscure clinically relevant differences between these groups. Future research should therefore consider labor status, indication for cesarean delivery, antibiotic exposure, and other relevant perinatal factors separately whenever study design and sample size allow.

3.7. Health Consequences of Cesarean-Associated Microbiota Alterations

The possibility that early microbiota differences contribute to later disease is biologically plausible but difficult to prove.

The developing microbiota interacts with the intestinal epithelial barrier and immune system during a critical period. Microbial products can influence the development of regulatory T cells, antigen-presenting cells, innate immune responses, and epithelial integrity.

SCFAs represent one potential mechanistic pathway. Acetate, propionate, and butyrate are produced through bacterial fermentation of dietary substrates and can influence epithelial cells and immune regulation. Alterations in the microbial communities responsible for these metabolic pathways could therefore influence host physiology.

However, microbial composition and microbial function are not equivalent. A taxonomic difference does not necessarily imply a functional difference, and conversely, functional differences can occur without major changes in conventional diversity measures (Feles et al., 2025).

Epidemiological studies have repeatedly reported associations between cesarean delivery and allergic diseases (Liu et al., 2024)

A 2024 comprehensive systematic review and meta-analysis found associations between cesarean delivery and asthma, allergic rhinitis or conjunctivitis, atopic dermatitis or eczema, food allergy, and allergic sensitization in children (Liu et al., 2024). These findings are important because they support a population-level association, but they do not demonstrate that cesarean-associated microbiota alterations are responsible.

Several confounding and modifying factors may contribute to these associations. Maternal atopic disease, antibiotic exposure, breastfeeding, and environmental factors may independently influence offspring health and therefore complicate the interpretation of associations attributed to delivery mode. The microbiome may therefore represent one component of a multifactorial pathway rather than a single mediator.

Cesarean delivery has also been associated with childhood overweight and obesity in some observational studies. Several mechanisms have been proposed, including altered microbial energy metabolism, bile acid signaling, inflammatory pathways, and intestinal permeability. However, maternal obesity is a major confounder because it increases the likelihood of cesarean delivery and is independently associated with obesity in offspring. Therefore, current evidence does not currently justify the conclusion that cesarean-associated microbiota alterations cause childhood obesity.

The gastrointestinal tract represents an especially relevant target because the microbiota directly interacts with intestinal epithelial and immune systems. Associations between cesarean birth and several gastrointestinal outcomes have been reported, including infantile colic, gastroesophageal reflux, food allergy, celiac disease, and inflammatory bowel disease. However, the strength of evidence varies substantially among individual conditions.

A key limitation is that many gastrointestinal outcomes occur frequently in infancy and have multifactorial causes. For example, infantile colic can be influenced by feeding, temperament, maternal factors, and gastrointestinal development. Microbiota differences may contribute but are unlikely to be the sole determinant.

The finding of increased colonization by opportunistic pathogens after cesarean delivery raises an additional concern. Shao et al. (2019) identified increased abundance of healthcare-associated microorganisms and detected clinically relevant virulence factors and antimicrobial resistance genes in some organisms. This does not mean that cesarean-born infants are destined to develop infections. Rather, it indicates that early microbial exposure may influence the composition of the infant microbial reservoir and the presence of organisms carrying traits associated with opportunistic infection.

The clinical significance of these findings requires further investigation, particularly because neonatal infections are influenced by gestational age, hospitalization, invasive procedures, immune status, and antibiotic exposure.

3.8. Microbiota Modulation Strategies

The possibility of modifying the microbiota following cesarean delivery has led to several intervention strategies.

The main approaches include:

1. promotion of breastfeeding;
2. probiotic supplementation;
3. prebiotic supplementation;
4. synbiotic supplementation;
5. maternal dietary and microbiota interventions;
6. vaginal seeding;
7. broader maternal microbial transfer.

The available evidence varies substantially among these approaches, with differences in study design, intervention protocols, microbiological outcomes, and clinical endpoints. Importantly, changes in microbial composition do not necessarily translate into clinically meaningful health benefits. Therefore, microbiota-modulation strategies should be evaluated not only according to their ability to alter bacterial composition but also according to their safety, durability, and potential effects on infant health.

3.9. Probiotics

Probiotics are live microorganisms administered with the intention of providing a health benefit. Their effects are strain-specific and cannot be generalized across all microorganisms belonging to a particular genus.

Several randomized controlled trials have investigated probiotic supplementation in cesarean-born infants. Carpay et al. (2022) reviewed 12 randomized controlled trials involving term infants born by cesarean section or exposed to early antibiotics. Seven studies investigated probiotics and three investigated synbiotics. Supplementation generally increased the abundance of administered *Bifidobacterium* or *Lactobacillus* strains and was associated with reductions in some Enterobacteriaceae, particularly during the first weeks of life.

These findings indicate that specific components of the infant microbiome can be modified through probiotic supplementation. However, successful colonization by an administered strain does not necessarily imply clinical benefit. A probiotic may increase *Bifidobacterium* abundance without reducing allergy, respiratory disease, obesity, or gastrointestinal symptoms.

Clinical trials should therefore distinguish between:

- microbial colonization;
- microbial community structure;
- microbial function;
- immune outcomes;
- and clinically relevant health outcomes.

A 2022 systematic review by Martín-Peláez et al. similarly found that maternal probiotic, prebiotic, or synbiotic interventions could influence the microbiota of children born by cesarean section, particularly by promoting *Bifidobacterium* colonization. However, substantial heterogeneity in strains, doses, timing, and intervention duration prevented identification of a universally effective protocol.

3.10. Prebiotics

Prebiotics provide substrates that are selectively utilized by beneficial microorganisms.

Human milk provides a physiological example through HMOs. This concept has inspired the development of infant formulas containing prebiotic oligosaccharides.

Prebiotic supplementation may be particularly attractive because it supports ecological growth rather than introducing microorganisms directly. However, responses depend on the microorganisms already present in the infant gut.

In the systematic review by Carpay et al. (2022), studies of prebiotics showed less consistent results than studies of probiotics or synbiotics. Some studies reported increased bifidobacterial abundance, whereas others demonstrated changes in potentially less desirable taxa.

This variability illustrates the ecological principle that the same substrate can produce different effects depending on the microbial community in which it is introduced.

3.11. Synbiotics

Synbiotics combine live microorganisms with substrates intended to support their growth or activity.

The rationale is straightforward: probiotic organisms may have limited persistence if the intestinal environment does not provide suitable substrates. Providing a compatible prebiotic may support their persistence or activity within the intestinal ecosystem.

Evidence in cesarean-born infants is promising but remains heterogeneous, with some studies reporting favorable changes in microbial composition. Several trials have reported increases in the abundance of selected bacterial groups, including supplemented bifidobacteria. Nevertheless, there is insufficient evidence to recommend a single synbiotic formulation universally (Carpay et al., 2022).

Future trials should compare standardized strains and formulations and should follow infants for sufficiently long periods to determine whether microbial effects persist after supplementation ends.

3.12. Vaginal Seeding

Vaginal seeding involves exposing a cesarean-born infant to maternal vaginal microorganisms after birth, usually by transferring vaginal fluid to the newborn's mouth, skin, or other sites. The rationale is based on the observation that vaginally delivered infants acquire microorganisms from the maternal vaginal and perineal microbiota. Vaginal seeding therefore attempts to reproduce part of this microbial exposure after cesarean delivery.

Earlier studies suggested that vaginal seeding might partially modify the microbial communities of cesarean-born infants. However, subsequent evidence indicates that vaginal seeding does not fully reproduce the microbial exposure associated with vaginal birth.

A 2024 systematic review identified eight studies involving 558 cesarean-born infants, including 274 exposed to vaginal seeding. The review found that vaginal seeding may selectively influence the abundance of bacterial genera, including *Bacteroides* and *Lactobacillus*, while findings regarding overall microbial diversity were inconsistent (Wang et al., 2024).

These findings are important because they challenge the assumption that transfer of a small amount of maternal vaginal fluid can reproduce the complex microbial exposure associated with vaginal birth. Vaginal birth involves exposure to microorganisms from multiple maternal and environmental sources, whereas vaginal seeding provides a limited and artificial route of microbial transfer. Consequently, vaginal seeding cannot reproduce all of the microbial exposures and perinatal conditions associated with vaginal delivery (Wang et al., 2024).

Safety remains a major concern regarding the routine clinical implementation of vaginal seeding. Maternal vaginal secretions can contain microorganisms that are asymptomatic or harmless in the mother but potentially pathogenic in a newborn. Of particular concern are pathogens capable of vertical transmission, including group B *Streptococcus* and herpes simplex virus. For this reason, the American College of Obstetricians and Gynecologists does not recommend or encourage vaginal seeding outside the context of an institutional review board-approved research protocol until adequate data regarding its safety and clinical benefit become available (American College of Obstetricians and Gynecologists, 2017).

3.13. Maternal Microbial Transfer

Maternal microbial transfer is broader than vaginal seeding and includes strategies intended to facilitate transfer of maternal microorganisms from different body sites. The rationale is that the infant naturally acquires microorganisms from multiple maternal sources during the perinatal and early postnatal period. Reproducing only vaginal exposure may therefore be insufficient to replicate the complexity of maternal microbial transmission.

A 2026 systematic review by Jurgiel et al. evaluated maternal microbial transfer after cesarean delivery and included 10 studies involving approximately 1,450 participants. The review concluded that maternal microbial transfer has potential to modify neonatal microbiota but, its efficacy in producing sustained microbiota changes and improving clinical outcomes remains uncertain (Jurgiel et al., 2026).

This broader approach reflects a shift from focusing exclusively on the replacement of potentially absent vaginal microorganisms toward consideration of the infant gut microbiota as a developing ecological system. Rather than attempting to reproduce a single microbial exposure, maternal microbial transfer seeks to influence the composition and development of the infant microbiota through selected maternal microbial sources.

Nevertheless, maternal microbial transfer presents important safety and standardization challenges. The maternal microbiota contains both microorganisms that may contribute to normal microbial development and microorganisms that may be potentially pathogenic under specific circumstances. Any therapeutic application would therefore require careful selection of the microorganisms or biological material transferred, together with appropriate assessment of maternal and neonatal safety.

At present, the clinical efficacy of maternal microbial transfer remains uncertain. The 2026 systematic review by Jurgiel et al. found inconsistent effects on microbial diversity and limited evidence regarding clinically relevant health outcomes. Further randomized controlled trials with standardized intervention protocols and long-term follow-up are needed before maternal microbial transfer can be considered an established clinical strategy (Jurgiel et al., 2026).

4. Discussion

The evidence reviewed in this article supports an association between cesarean delivery and altered early-life gut microbiota development. The most consistent evidence concerns altered acquisition and transmission of selected maternal-associated microorganisms, particularly *Bacteroides* and *Bifidobacterium*, as well as differences in microbial succession during the first weeks and months of life (Podlesny & Fricke, 2021).

However, the interpretation of these findings requires a shift away from a simplistic “vaginal versus cesarean microbiome” model.

The first important point is that cesarean delivery is a complex exposure. It changes the infant's route of microbial acquisition, but it is also associated with antibiotic exposure, differences in labor, maternal characteristics, breastfeeding practices, hospitalization, and clinical indications. These factors may independently influence the development of the infant gut microbiota and may therefore contribute to differences attributed to delivery mode (Shao et al., 2019; Mueller et al., 2015).

The second point is that microbial differences do not automatically represent disease. Microbiota composition varies substantially between individuals, and differences between infants born by cesarean and vaginal delivery should therefore not automatically be interpreted as evidence of an abnormal microbial state. The concept of dysbiosis should be applied cautiously, particularly when microbiological differences are identified without evidence of functional impairment or adverse clinical outcomes (Mueller et al., 2015).

The third point is that early microbial alterations may be relevant even when they are transient. The infant gut microbiota undergoes substantial developmental changes during the first months and years of life, and the persistence of a microbial difference should therefore be considered when evaluating its potential biological or clinical significance. Findings that differ between early infancy and later developmental stages may reflect the dynamic nature of microbiome maturation rather than a permanent effect of delivery mode (Rutayisire et al., 2016; Shao et al., 2019).

4.1. The “Bacterial Baptism” Hypothesis Revisited

The bacterial baptism hypothesis proposes that vaginal birth provides an important microbial inoculum that shapes subsequent microbiota development. There is substantial evidence supporting the existence of delivery-mode-associated microbial differences (Shao et al., 2019; Podlesny & Fricke, 2021). Nevertheless, the hypothesis is incomplete.

Maternal and environmental factors contribute to infant microbial exposure, while the maternal microbiota itself varies considerably between individuals. The critical review by Stinson et al. (2018) emphasized that cesarean-associated microbiome differences should not be attributed solely to absence of exposure to the vaginal microbiota.

The evidence from Shao et al. (2019) further supports a multifactorial model. The microbiome of cesarean-born infants was characterized not only by reduced maternal strain transmission but also by increased representation of microorganisms associated with the hospital environment.

Thus, the microbiological differences associated with cesarean delivery may reflect a combination of:

- reduced exposure to maternal microorganisms;
- altered timing of microbial exposure;
- exposure to healthcare-associated microorganisms;
- antibiotic-mediated ecological perturbation;
- differences in breastfeeding;
- and differences in labor and perinatal circumstances.

4.2. Is Cesarean-Associated Microbiota Really “Dysbiosis”?

4.2. Is Cesarean-Associated Microbiota Really “Dysbiosis”?

The term “dysbiosis” is frequently used in microbiome research, but its meaning is not always consistent across studies. A difference in microbiota composition from that observed in another population does not necessarily indicate a pathological microbial state.

For cesarean-born infants, evidence of altered microbial composition is relatively consistent. However, evidence regarding functional consequences is more variable, and evidence that cesarean-associated microbiota alterations directly contribute to later disease remains limited. Microbial composition and microbial function should therefore be considered separately when interpreting microbiome findings.

Accordingly, this review favors the term “cesarean-associated microbiota alterations” unless a specific study provides evidence supporting the presence of a clinically or biologically relevant dysbiotic state (Mueller et al., 2015).

This distinction is also important for clinical communication. Cesarean delivery should not automatically be interpreted as producing a pathological gut microbiome, because current evidence demonstrates microbiological differences more consistently than it demonstrates functional impairment or adverse clinical consequences directly attributable to these differences.

4.3. Temporal Dynamics

The microbiome is highly dynamic during infancy. Some differences associated with cesarean delivery appear to diminish as infants age (Rutayisire et al., 2016; Shao et al., 2019).

Microbial communities undergo substantial changes during infancy as dietary exposures, environmental microbial exposure, and gastrointestinal maturation progress. Consequently, differences observed at one developmental stage may not necessarily persist into later childhood.

Nevertheless, the transient nature of some microbiota differences does not necessarily mean that they are biologically irrelevant. Early infancy represents a period of substantial microbial and host development, and the timing of microbial exposure may therefore be relevant to subsequent physiological processes.

It is possible that microbial signals during this developmental period may interact with the maturation of host immune and metabolic pathways. However, whether transient cesarean-associated microbiota alterations have lasting effects on these processes remains uncertain. The available evidence does not currently establish that temporary differences in microbial composition lead to persistent functional or clinical consequences.

This question requires longitudinal studies integrating repeated microbiome measurements with functional, immune, and clinical outcomes. Such studies could help determine whether early microbiota differences represent temporary variations in microbial succession or whether their timing is associated with measurable long-term effects.

4.4. Microbiome Function Versus Microbial Taxonomy

4.4. Microbiome Function Versus Microbial Taxonomy

One limitation of many microbiome studies is the emphasis on taxonomic composition. The presence or abundance of a particular bacterial genus does not necessarily indicate the functional activity of the microbial community. Studies of the infant gut microbiome have demonstrated that taxonomic and functional analyses provide complementary information and that taxonomic composition alone may not fully explain microbial functionality (Lugli et al., 2023).

Functional metagenomic and metatranscriptomic approaches can provide additional information that cannot be inferred from taxonomic composition alone. In a large-scale analysis of infant gut microbiomes, Lugli et al. (2023) combined shotgun metagenomic and metatranscriptomic data to characterize both microbial composition and patterns of microbial gene expression. The comparison demonstrated that metatranscriptomic analyses can provide information about enzymatic activity and metabolic processes that is not directly apparent from taxonomic classification.

Two microbial communities may therefore differ in their taxonomic composition while retaining similar functional capacities, whereas communities with apparently similar taxonomic profiles may differ in their metabolic activity. This distinction is particularly relevant when interpreting cesarean-associated microbiota

alterations, because changes in the abundance of *Bifidobacterium*, *Bacteroides*, or other bacterial groups should not automatically be interpreted as evidence of altered host physiology.

The importance of functional characterization is also illustrated by studies examining strain-level microbiome properties. Wampach et al. (2018) demonstrated that birth mode was associated not only with differences in microbial composition but also with differences in strain-conferred gut microbiome functions and immunostimulatory potential. These findings further support the concept that microbial strain characteristics and functional potential may provide information that cannot be captured by taxonomic abundance alone.

Consequently, future research on cesarean-associated microbiota should incorporate functional measurements alongside taxonomic analyses. Integrating metagenomic, metatranscriptomic, and, where appropriate, metabolomic data with clinical outcomes may help determine whether microbiological differences associated with cesarean delivery have measurable biological consequences (Lugli et al., 2023; Wampach et al., 2018).

4.5. Clinical Implications

The current evidence does not justify recommending cesarean-born infants for routine microbiome testing. At present microbiome composition varies considerably during infancy, and clinically validated reference ranges defining a universally „normal” infant gut microbiome have not been sufficiently established.

Commercial microbiome tests marketed directly to consumers should therefore be interpreted with caution. Although such tests may provide information about microbial composition, the clinical significance of many reported differences remains uncertain, particularly in infants whose microbiome is undergoing rapid developmental changes. Results from microbiome testing should not be used as a basis for dietary or therapeutic interventions in the absence of established clinical indications.

Similarly, routine probiotic administration solely because an infant was born by cesarean delivery cannot currently be universally recommended on the basis of microbiome restoration alone. Evidence from randomized controlled trials indicates that probiotics and synbiotics can modify selected components of the infant gut microbiota, but the observed effects vary according to the strain, formulation, dose, timing, and population studied (Carpay et al., 2022). Furthermore, changes in microbial composition do not necessarily translate into clinically meaningful health benefits.

From a clinical perspective, emphasis should therefore remain on established aspects of infant care, including support for breastfeeding when possible and appropriate, avoidance of unnecessary antibiotic exposure, and developmentally appropriate complementary feeding. These measures may also influence microbiome development, but their clinical importance extends beyond microbiota modulation alone.

4.6. Social and Public Health Context

Cesarean delivery has implications that extend beyond its effects on the infant microbiota, including maternal and neonatal care and broader population health.

Any discussion of microbiome consequences must therefore avoid implying that cesarean delivery should be avoided regardless of clinical circumstances. Cesarean delivery is an essential medical intervention when indicated.

The relevant public health question is not whether cesarean delivery should be eliminated, but whether unnecessary cesarean procedures can be reduced while preserving maternal and neonatal safety and whether safe strategies can mitigate potentially modifiable consequences.

This distinction is particularly important in health communication. Microbiome research should not be used to generate fear around medically necessary cesarean delivery.

4.7. Evaluation of Microbiota-Modulating Interventions

Current intervention studies indicate that the infant microbiome is modifiable.

Probiotics, prebiotics, and synbiotics can alter bacterial abundance. However, the central unanswered question is whether these changes produce meaningful health benefits.

From a clinical microbiome perspective, an effective microbiota intervention should ideally demonstrate:

1. reproducible microbial modification;
2. persistence of the modification;
3. functional improvement;
4. favorable immune or metabolic effects;
5. and clinically meaningful health benefits.

Many existing studies have primarily demonstrated changes in microbial composition, while providing less evidence regarding persistence, functional consequences, and clinically meaningful health outcomes.

The systematic review by Carpay et al. (2022) is particularly informative because it found consistent microbial effects across several interventions, while also highlighting substantial heterogeneity between products and protocols. The authors concluded that the available evidence was insufficient to support clinical recommendations for specific products.

Similarly, the systematic review by Martín-Peláez et al. (2022) identified effects of maternal probiotic, prebiotic, and synbiotic interventions on the intestinal microbiota of children born by cesarean section, while emphasizing the need for more standardized studies.

4.8. Vaginal Seeding: Promise and Limitations

Vaginal seeding is a scientifically interesting intervention because it directly addresses the hypothesis that the absence of maternal vaginal exposure contributes to delivery-mode-associated microbiome differences (Stinson et al., 2018; Wang et al., 2024).

However, the current evidence does not demonstrate that vaginal seeding prevents allergic disease, asthma, obesity, gastrointestinal disorders, or other long-term outcomes (Wang et al., 2024; Jurgiel et al., 2026).

The 2024 systematic review by Wang et al. demonstrated that microbial changes can occur, but effects on diversity and overall microbiome composition were inconsistent.

The 2026 systematic review of maternal microbial transfer further emphasizes uncertainty regarding clinical outcomes (Jurgiel et al., 2026).

Therefore, vaginal seeding should not currently be presented to parents as an established preventive therapy (Wang et al., 2024; Jurgiel et al., 2026; American College of Obstetricians and Gynecologists, 2017).

4.9. Toward Precision Microbiome Modulation

The future of microbiome intervention may increasingly involve greater personalization, reflecting the substantial heterogeneity of developing infant microbiome (Lugli et al., 2023).

Instead of attempting to reproduce a generic “vaginal microbiome,” future approaches may focus on identifying specific microbial functions or ecological characteristics that could be modified in individual infants (Stinson et al., 2018; Lugli et al., 2023).

For example, individual infants may differ in the abundance of particular bacterial groups or in the functional potential of their microbial communities (Lugli et al., 2023). Interventions could then be designed to target these specific ecological characteristics.

Such an approach would represent a transition from microbiome replacement toward more targeted microbiome modulation.

5. Limitations and Future Perspectives

The evidence base has several important limitations.

First, much of the literature is observational. This makes causal inference difficult because cesarean delivery is associated with numerous maternal and perinatal characteristics (Stinson et al., 2018; Shao et al., 2019).

Second, microbiome methodologies are heterogeneous. Studies differ in sample collection, sequencing methods, bioinformatic approaches, and taxonomic classification (Rutayisire et al., 2016; Carpay et al., 2022).

Third, the timing of stool collection varies substantially. A microbiome sample obtained on day three cannot be directly compared with a sample obtained at six months (Rutayisire et al., 2016; Shao et al., 2019).

Fourth, breastfeeding is often incompletely characterized. Differences in breastfeeding status, duration, and feeding practices may complicate interpretation of microbiome findings (Shao et al., 2019).

Fifth, antibiotic exposure is not always characterized in sufficient detail, which may complicate the interpretation of microbiome differences associated with cesarean delivery (Dierikx et al., 2022).

Sixth, relatively few studies combine microbiome measurements with long-term clinical follow-up (Jurgiel et al., 2026).

Seventh, most research focuses on bacterial communities. Future studies should also consider other components of the microbiome, including viruses, fungi, archaea, and bacteriophages, where appropriate.

Future research should therefore use standardized longitudinal designs beginning during pregnancy and continuing through infancy and childhood.

Ideally, studies should collect:

- maternal gut, vaginal, oral, and skin microbiota;
- neonatal microbiota;
- detailed antibiotic exposure;
- labor and delivery characteristics;
- gestational age;
- breastfeeding and formula feeding;
- introduction of complementary foods;
- maternal metabolic and immune characteristics;
- environmental exposures;
- immune biomarkers;
- microbial metabolites;
- and clinically relevant outcomes.

Multi-omics approaches combining metagenomics, transcriptomics, metabolomics, proteomics, and immune profiling may provide a more complete understanding of microbial function (Lugli et al., 2023).

Randomized controlled trials should also move beyond microbial endpoints. The primary outcomes should include clinically meaningful measures such as infection rates, allergic disease, respiratory disease, gastrointestinal symptoms, growth, metabolic health, and neurodevelopment.

Safety should receive particular attention in interventions involving direct maternal microbial transfer (Jurgiel et al., 2026, American College of Obstetricians and Gynecologists, 2017).

Another important priority is standardization. Future trials should clearly define probiotic strains, doses, administration schedules, prebiotic substrates, intervention duration, and follow-up periods (Carpay et al., 2022).

Long-term follow-up is essential. An intervention that modifies the microbiota for four weeks may have limited clinical relevance if the effect disappears after supplementation ends (Carpay et al., 2022).

6. Conclusions

Cesarean delivery is consistently associated with differences in the development of the infant gut microbiota, particularly during the first weeks and months of life. These differences commonly include delayed or reduced acquisition of maternal-associated microorganisms such as *Bacteroides* and *Bifidobacterium*, differences in the abundance of *Bifidobacterium*, altered microbial succession, and increased representation of microorganisms associated with healthcare environments (Shao et al., 2019; Rutayisire et al., 2016; Podlesny&Fricke, 2021).

However, cesarean delivery should not be considered an isolated cause of infant microbiota alteration. Perinatal antibiotics, breastfeeding, gestational age, maternal characteristics, indication for cesarean delivery, labor exposure, and environmental factors may also influence microbial development (Stinson et al., 2018; Shao et al., 2019; Podlesny&Fricke, 2021).

Current evidence also suggests that cesarean-associated microbiota differences are dynamic and may partially diminish as the microbiome matures. Consequently, the presence of an altered microbial profile in early infancy does not necessarily indicate a persistent adverse microbial state or future disease. (Rutayisire et al., 2016; Shao et al., 2019).

Associations between cesarean delivery and several childhood health outcomes, including allergic diseases, have been observed in epidemiological studies. However, the evidence does not establish that microbiota alterations mediate these relationships. Confounding and other pathways remain important considerations (Liu et al., 2024; Stinson et al., 2018).

Breastfeeding represents an important postnatal factor supporting infant gut microbiota development after cesarean delivery (Shao et al., 2019). Probiotics, prebiotics, and synbiotics can modify aspects of microbial composition, including the abundance of selected bacterial groups, but evidence for long-term clinical benefits remains insufficient to support a universal intervention (Carpay et al., 2022; Martín-Peláez et al., 2022).

Vaginal seeding and maternal microbial transfer represent experimental strategies currently under investigation. Current research demonstrates that these approaches can modify aspects of the neonatal microbiota, but their ability to reproduce the microbiome of vaginally delivered infants and improve long-term

health outcomes remains uncertain. Safety concerns further limit their clinical application (Wang et al., 2024; Jurgiel et al., 2026; American College of Obstetricians and Gynecologists, 2017).

The future of this field should therefore focus not on simply reproducing a “vaginal microbiome,” but on understanding the functional requirements of a healthy developing microbial ecosystem. Longitudinal, standardized, multi-omics studies and adequately powered randomized controlled trials are needed to determine whether targeted microbiota modulation can translate into clinically meaningful benefits.

Cesarean delivery is an essential medical procedure when clinically indicated, and microbiome research should not undermine its appropriate use. Instead, understanding the microbial consequences of different birth circumstances may contribute to more individualized postnatal care and to the development of interventions that can safely support healthy infant development.

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