Danone Nutricia Campus

Nutrition Essentials: C-Section Delivery

Strategies to rebalance the gut microbiome

The role of the gut microbiome in infant development

A balanced gut microbiota is essential for proper immune, metabolic and cognitive development in infants and children.[1]

The gut microbiome plays an important role in regulating host processes such as:[1]

Immune function[1]

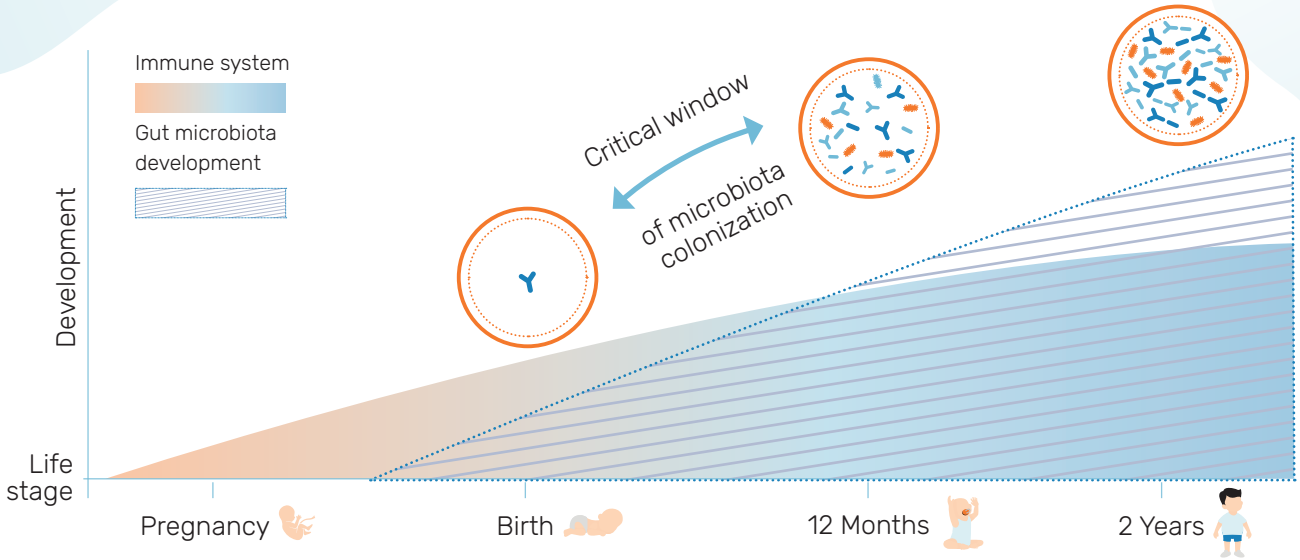
Stress responses[1]

Neuroplasticity[2]

Energy metabolism[3]

Gene expression[3]

Factors influencing the development of the gut microbiome in early life



Neonatal factors[4]:

Maternal microbiota
Mode of delivery
Gestational age

Postnatal factors[4]:

Feeding type (breastfeeding vs formula feeding)
Antibiotic use
Environment (for example, family lifestyle)

How does mode of delivery affect microbiome colonization in the gut?

- Mode of delivery is generally accepted as a major factor that influences initial gut microbiota colonization.[4]
- Babies delivered by vaginal birth have a different gut microbiome than babies delivered by Caesarean-section (C-section).[5]
- Vaginally delivered infants are exposed to maternal vaginal and fecal microbes which then colonize the gut.[4]
- Babies delivered by C-section do not come into direct contact with maternal vaginal and fecal microbes and are more likely to be colonized by maternal skin and environmental microbes.[4]

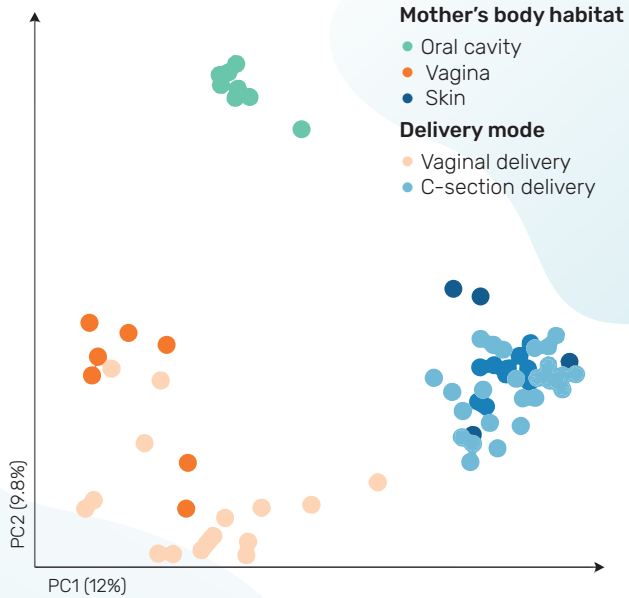
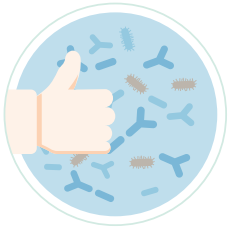


Figure adapted from Dominguez-Bello et al. PNAS 2020;107:11971–11975.

Differences in gut microbiota composition between infants delivered vaginally and through C-section

Infants born by C-section have delayed gut microbiota colonization as well as lower levels of important 'keystone colonizers' such as *Bifidobacterium* and *Bacteroides*.[5,6]

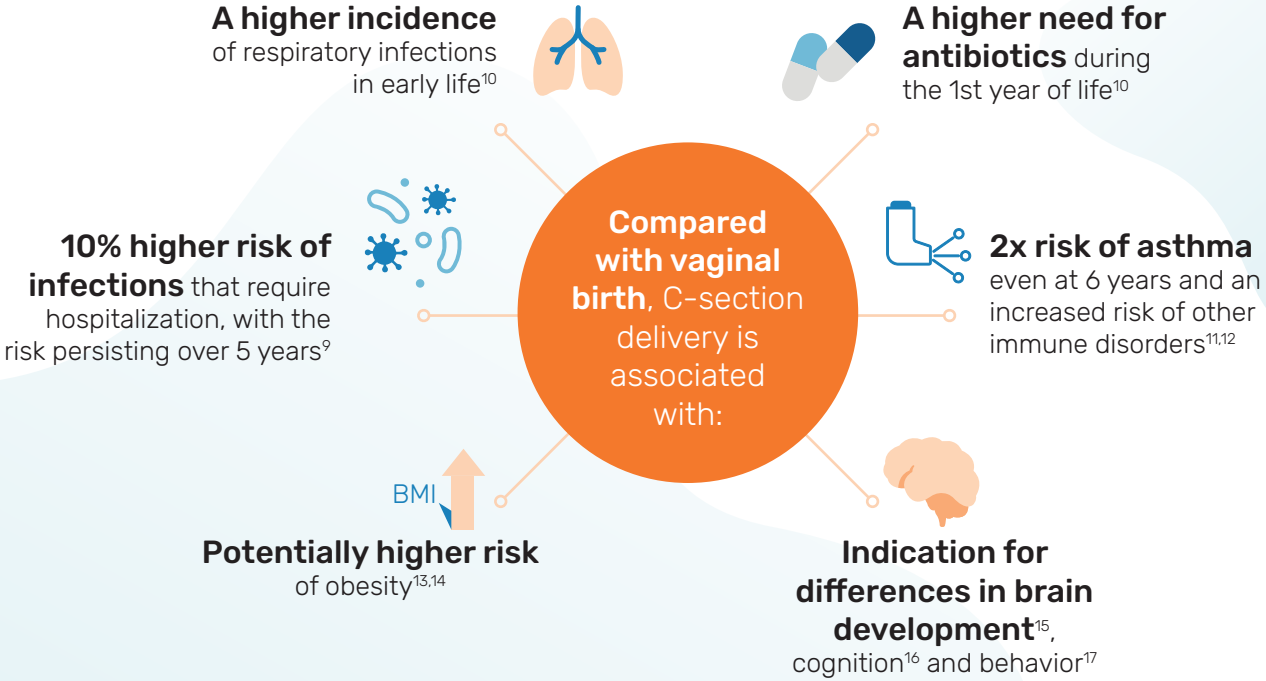


Vaginally delivered infants show a greater diversity of gut microbiota compared with C-section delivered infants.[4]

These differences in infant gut microbiome are present at 1 year and beyond.[7,8] This can have long-term effects on immunological and metabolic development of infants.[7]

The gut microbiota of C-section infants differs significantly from that of vaginally delivered infants, which may have serious consequences on the long-term health of C-section infants.

Long term impact of C-section delivery



Increasing C-section rates across the world are a cause for concern

- C-section can be a medically necessary intervention to prevent maternal and newborn mortality.[18]
- However, C-section delivery is associated with short- and long-term risks.[18]
- The World Health Organization (WHO) has stated that C-section use should not exceed 10%–15% of all births.[18]

In 2015, an estimated

29.7 million

babies were born through C-section, almost twice as many as in 2000.[19]

It is projected that by 2030,

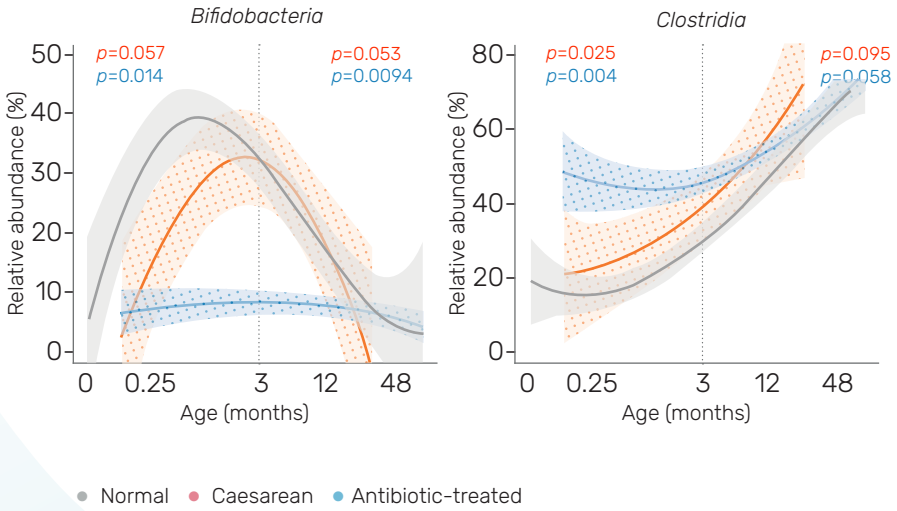
28.5%

of pregnant women worldwide will deliver by C-section.[20]

The impact of C-section delivery on infant health is thus becoming an increasing concern.

Does early life antibiotic exposure impact gut microbiome development?

- Antibiotic use in infants reduces gut microbiota diversity and impacts abundance of *bifidobacteria* as important early life colonizers.[58]
- Infants treated with antibiotics showed reduced infant-type *bifidobacteria* while adult-type *clostridia* increased in abundance.[58]



Impact of antibiotic use in early life

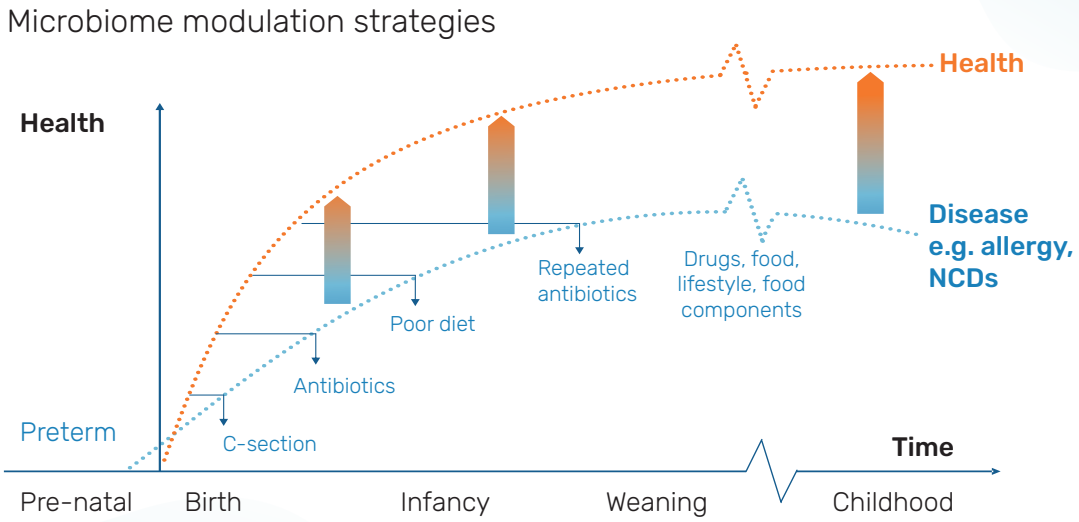
Early life antibiotic use is associated with an increase in immune-related disorders and impacts metabolism. There is also some evidence that it can affect cognitive development.

Impact of antibiotic use on:

- Higher likelihood of *Clostridioides difficile* infection[21]
- Higher risk of developing allergies and asthma[22-25]
- Higher susceptibility to develop auto-immune disease and non-communicable disorders[25]
- Metabolism[26]
- Increased susceptibility to obesity[27,28]
- Cognitive development[64]

Nutritional strategies offer a good opportunity to rebalance the compromised microbiota in early life[65]

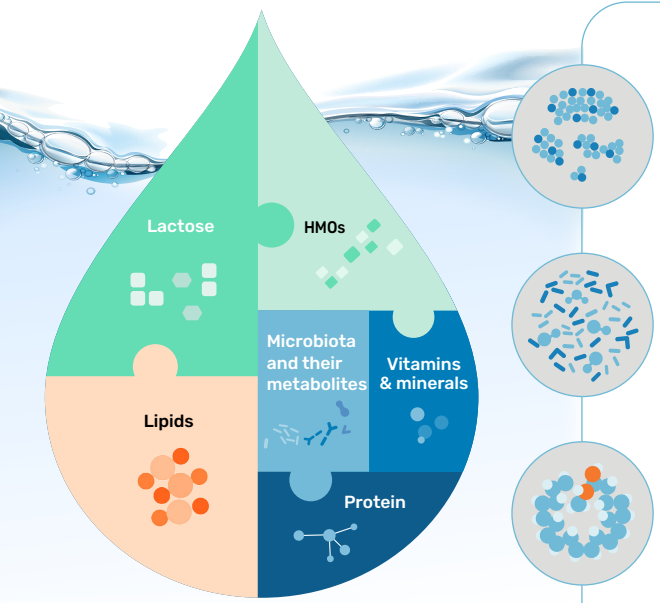
To support infant development, a nutritionally complete diet is important to ensure adequate intake of nutrients such as iron and vitamin D.[30]



NCD, non-communicable diseases

Breast milk is the gold standard in infant nutrition

Breast milk contains nutritional and bioactive compounds that support development of a healthy gut microbiota and immune system[31-45]



*88% water

Immune cells and other immune modulatory components
Conferring active and passive immunity

>200 identified Human Milk Oligosaccharide (HMOs)
Prebiotic effect, direct effect on immune cells and blocking the entry of pathogens to reduce infections

Bacteria and bacterial metabolites
To support the development and functioning of a healthy gut and immune system

Unique lipids profile with essential fatty acids and complex lipid structures
To support brain development

Nucleotides, vitamins, minerals, micronutrients
Essential for growth and development

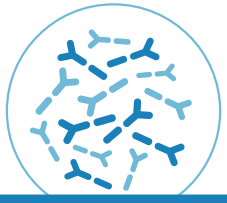
Carbohydrates (including lactose) and lipids
Most important sources of energy

Proteins
Essential for growth and development

The role of prebiotic, probiotic and synbiotics in gut microbiota colonization

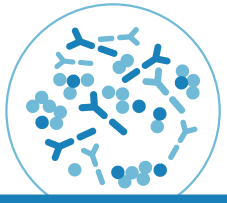
Prebiotics

Substrates that are selectively utilized by host micro-organisms, conferring a health benefit.[47]



Probiotics

Live micro-organisms which when administered in adequate amounts confer a health benefit on the host.[66]



Synbiotics

A mixture of pre- and probiotics that improve the survival of live microbial dietary supplements in the gastrointestinal tract by selectively stimulating the growth of health-promoting bacteria.[67]

Biotics-containing formula: A valid nutritional alternative

When exclusive breastfeeding is not possible, biotics-containing formula could be considered as a valid nutritional alternative.

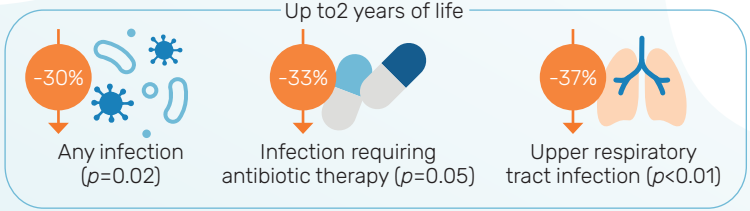
Several biotics are available in the market, but only a few have been proven to provide health benefit to infants.

Prebiotics with proven benefits: scGOS/lcFOS (9:1) and 2'-FL

- Short-chain galacto-oligosaccharide (scGOS)/long-chain fructo-oligosaccharides (lcFOS) (9:1) is a unique blend of scGOS and lcFOS which has demonstrated positive effects on infant microbiota and health in over 40 studies.[49-51]
- 2'-fucosyllactose (2'-FL) is the most abundant HMO found in breast milk.[52]

scGOS/lcFOS (9:1) in infant formula:

- Increased beneficial bacteria[53,54,57]
- Reduced infections[55-57,68]



- Suppressed the growth of harmful bacteria[51,53,57,59]

Adding 2'-FL to scGOS/lcFOS enhances immune and microbiota benefits.

- Improved influenza vaccination response[60,61]
- More favorable microbial ecosystem[60]

Bifidobacterium breve **M-16V is a probiotic with proven health benefits**

- *Bifidobacterium* are a family of beneficial bacteria naturally found in the gut of breastfed infants.[62]
- *B. breve* M-16V is a species originally isolated from a healthy infant gut.[63]
- *B. breve* M-16V has been extensively studied, with well-established clinical data on its safety and efficacy in infants.[63]

B. breve **M-16V dietary supplementation:**

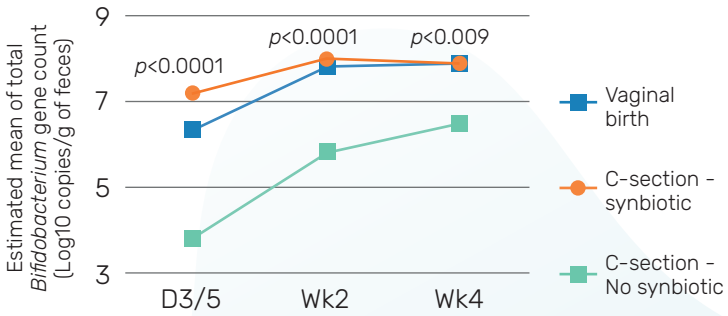
Promotes early gut microbial colonization

Regulates immune response to prevent allergic disorders

Infant formula with *B. breve* M-16V and scGOS/lcFOS (9:1) corrects delayed gut colonization in babies born by C-section

JULIUS study: Randomized, double-blind multicentre study[29]

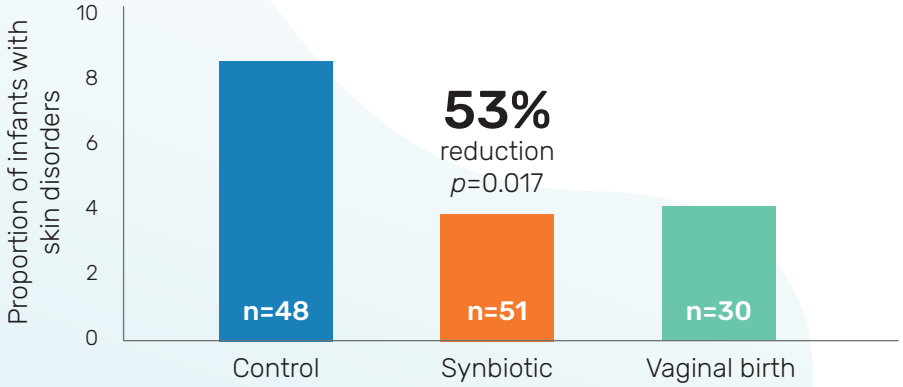
- **153 infants delivered by C-section** randomized to receive synbiotic (n=52), prebiotic (n=51), or control formula (n=50)
- From day 3/5 to week 4, the **proportion of *bifidobacteria* in the synbiotic group was significantly higher than the control group**.[29]
- The delayed colonization of *bifidobacteria* in infants born by C-section was restored with synbiotic treatment resembled the vaginally born reference.[29]



Reduced incidence of skin disorders with infant formula containing *B. breve* M-16V and scGOS/lcFOS (9:1)

Compared with the control group, significantly fewer infants in the synbiotic group reported skin disorder-related adverse events.[29]

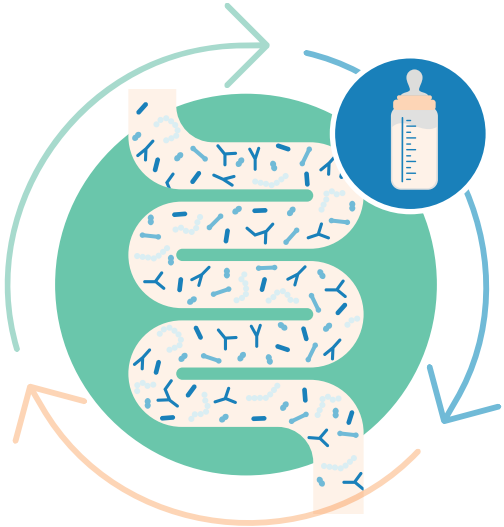
Incidence of skin disorders during 16 weeks of intervention (reported AEs)



Summary

The gut microbiota plays a key role in immunoregulation and normal development.

The gut microbiome colonization is influenced by various factors such as mode of delivery at birth and feeding type during infancy.



Where breastfeeding is not possible, including babies delivered by C-section, choosing an evidence-based synbiotic infant formula can support the development of a healthy gut microbiome.

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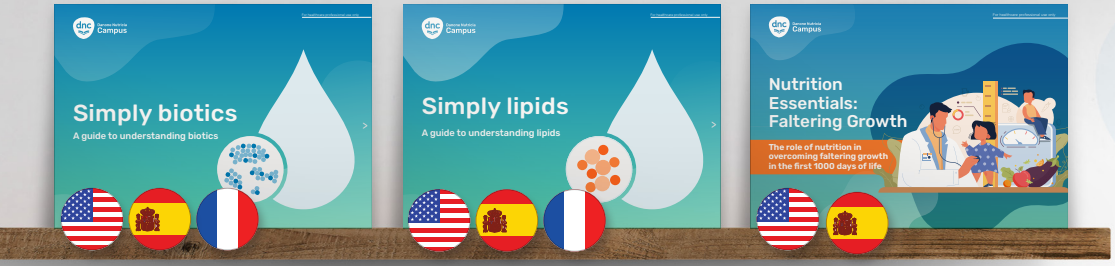

Early Life Nutrition

- Simply Biotics
- Simply Lipids
- Nutrition Essentials: Faltering Growth
- Nutrition Essentials: Iron Deficiency
- Nutrition Essentials: C-section Delivery

Adult Nutrition

- Nutrition Essentials: Frailty
- Nutrition Essentials: Oncology
- Nutrition Essentials: Stroke