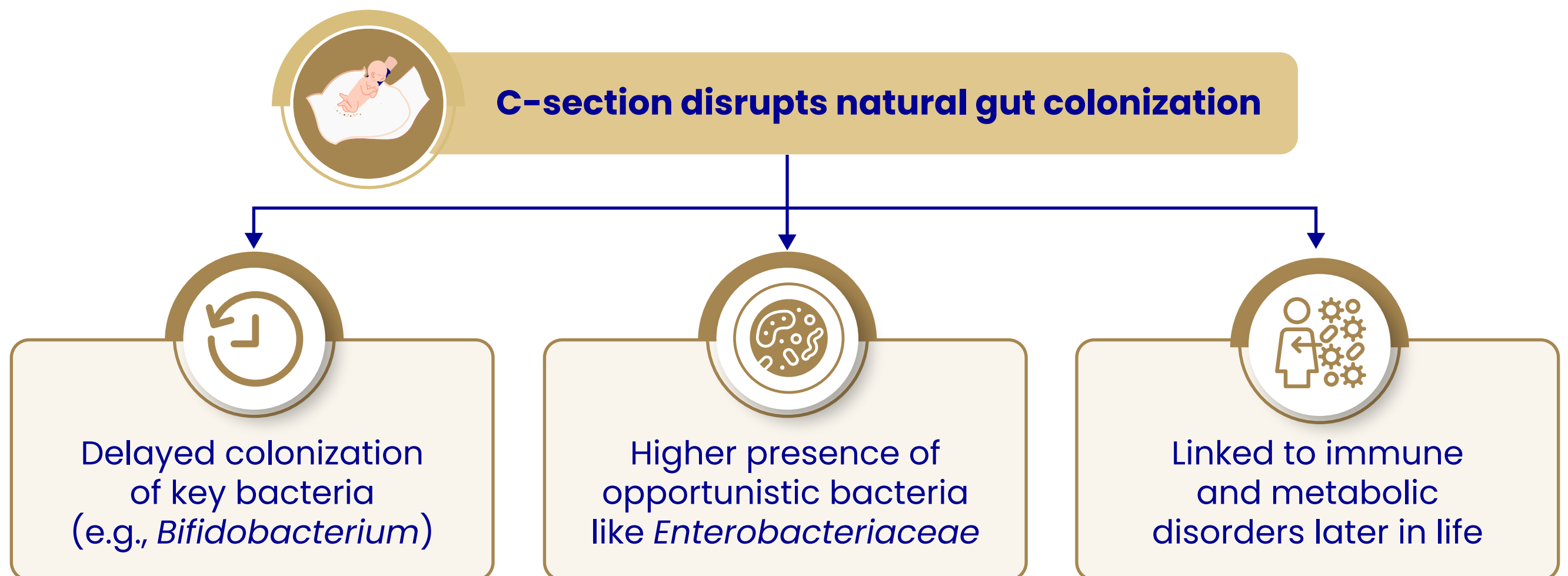


Modulating Infant Gut Microbiota Through Synbiotics: Evidence from Early-Life Supplementation



Gut Health Support for Cesarean-Born Infants

Studies suggest cesarean sections may impact immune and metabolic health through epigenetic and microbial imprinting.



The disruption of gut microbiota, particularly the lack of *Bifidobacteria*, can affect immune development.



Study Overview



Objective

To evaluate the impact of scGOS/lcFOS (9:1) and *Bifidobacterium breve* M-16V on the gut microbiota of infants born via cesarean section.



Methodology and Study Design

This was an exploratory, randomized, double-blind, controlled study conducted in Singapore and Thailand.





Study Design



A total of 153 healthy term infants delivered by C-section and were randomly assigned to:

Control group (n=50) with no synbiotics

Synbiotic group (n=52) scGOS/lcFOS (9:1) with *Bifidobacterium breve* M-16V



Reference (n=30)

Non-randomized infants born vaginally

- ▶ The study formulas were given from birth (within the first 1–3 days) and continued until the infants reached 16 weeks of age.
- ▶ Stool samples were collected at multiple time points: days 3 and 5, and weeks 2, 4, 8, 12, 16, and 22.

The composition of the gut microbiota was assessed using fluorescent in situ hybridization and quantitative real-time polymerase chain reaction (qRT-PCR).

Primary Outcome:

*Total fecal *Bifidobacteria*

Secondary Outcome:

- ▶ **Safety:** Growth metrics, GI tolerance, and adverse events
- ▶ **Gut microbiota diversity:** Shifts in diversity and key bacterial taxa
- ▶ **Strain-specific detection:** *B. breve* M-16V and other *Bifidobacterium* species

- ▶ **Enterobacteriaceae reduction:** Decrease in *Enterobacteriaceae* abundance
- ▶ **Gut environment markers:** Fecal pH and acetate levels
- ▶ **Metabolite profiling:** SCFAs (acetate, propionate, butyrate) and lactate

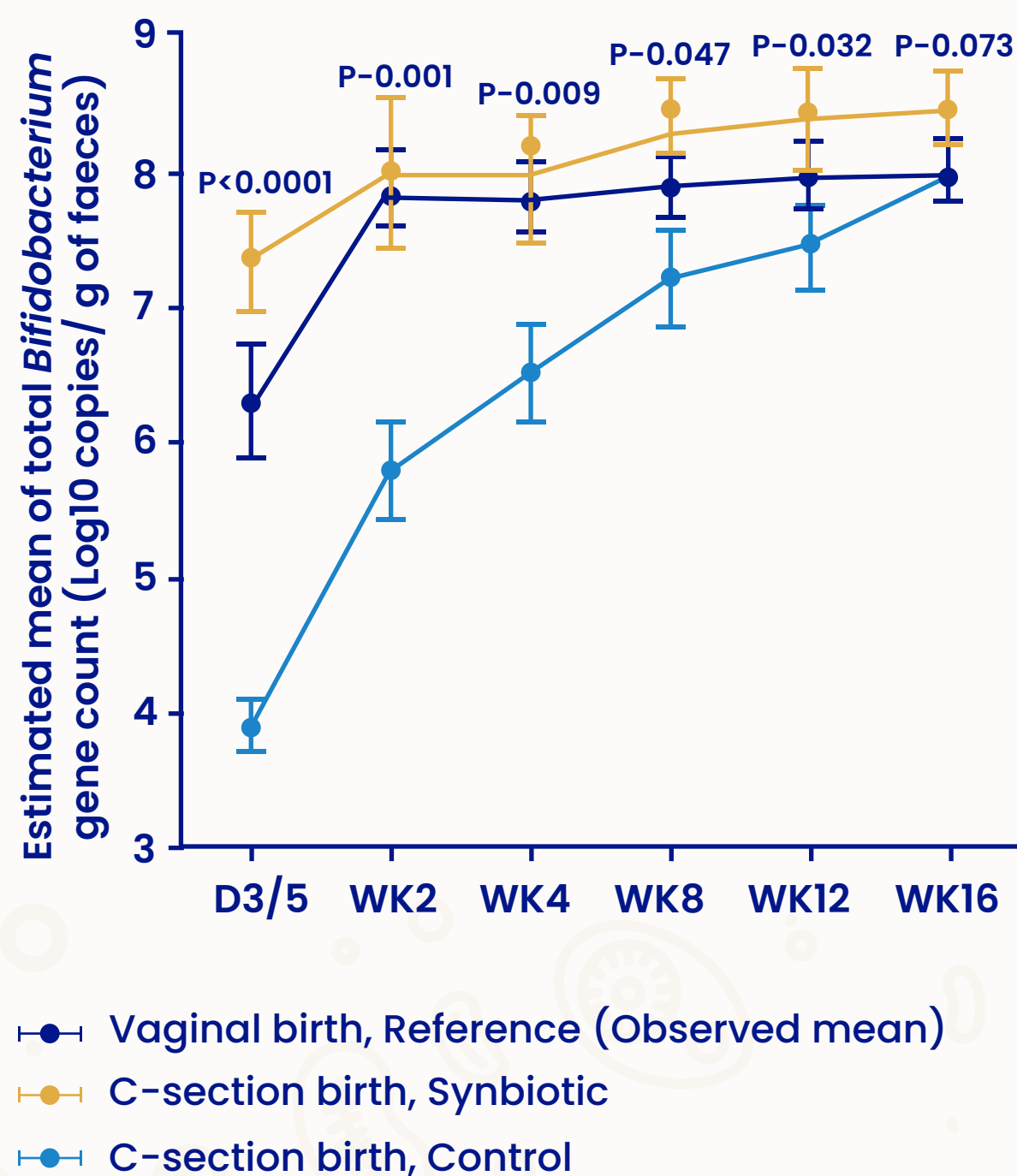


Key Microbial Outcomes



1 Total *Bifidobacterium* Load

- Synbiotic group showed **significantly higher total *Bifidobacterium* counts** from Day 3/5 ($P < 0.0001$).
- Consistent *Bifidobacterium* colonization sustained until Week 16.



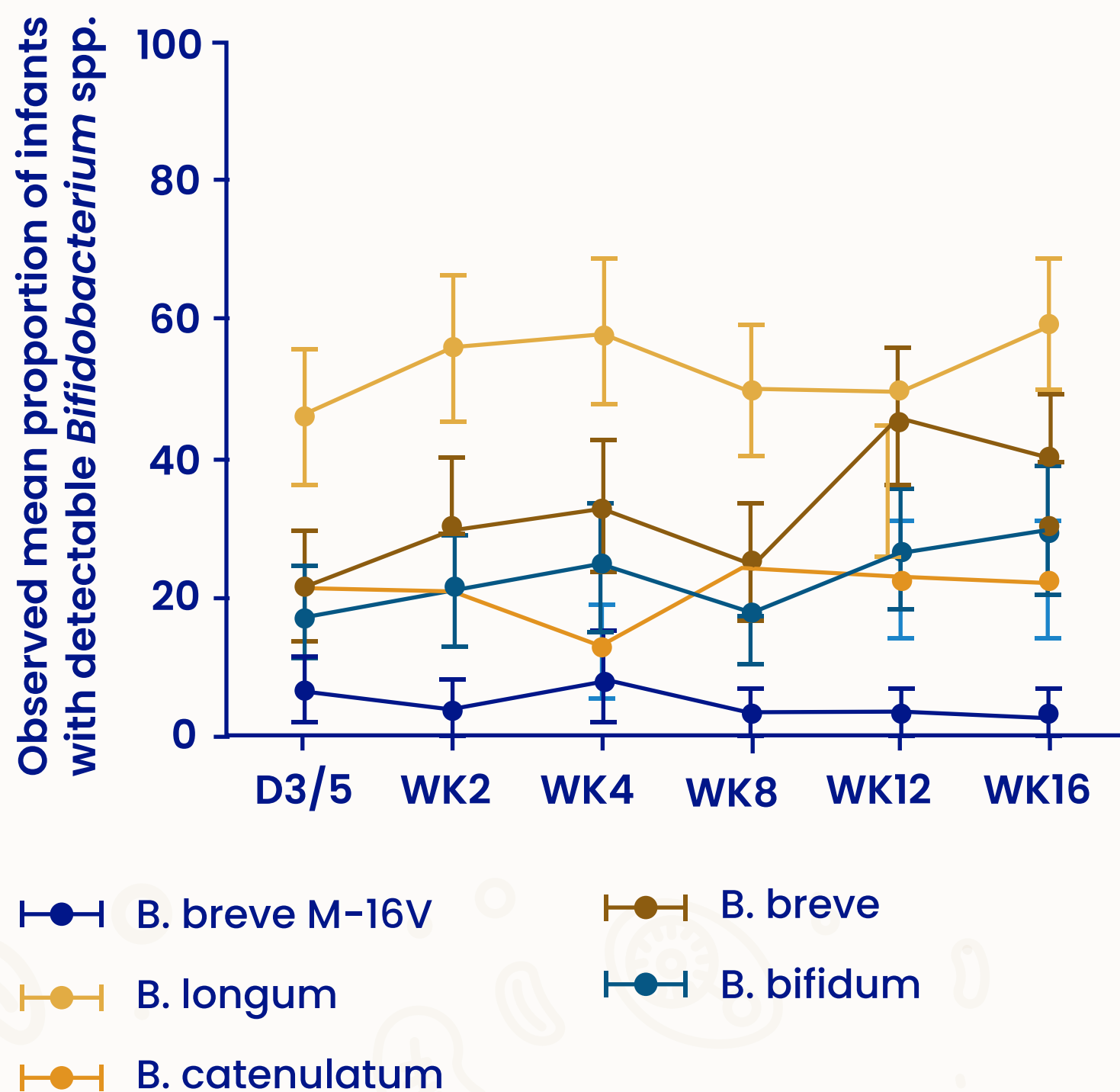


Key Microbial Outcomes (cont.)



2 Reduction in Enterobacteriaceae

- Enterobacteriaceae—a marker of dysbiosis—was **significantly reduced** in the synbiotic group from Day 3/5 ($P = 0.002$).



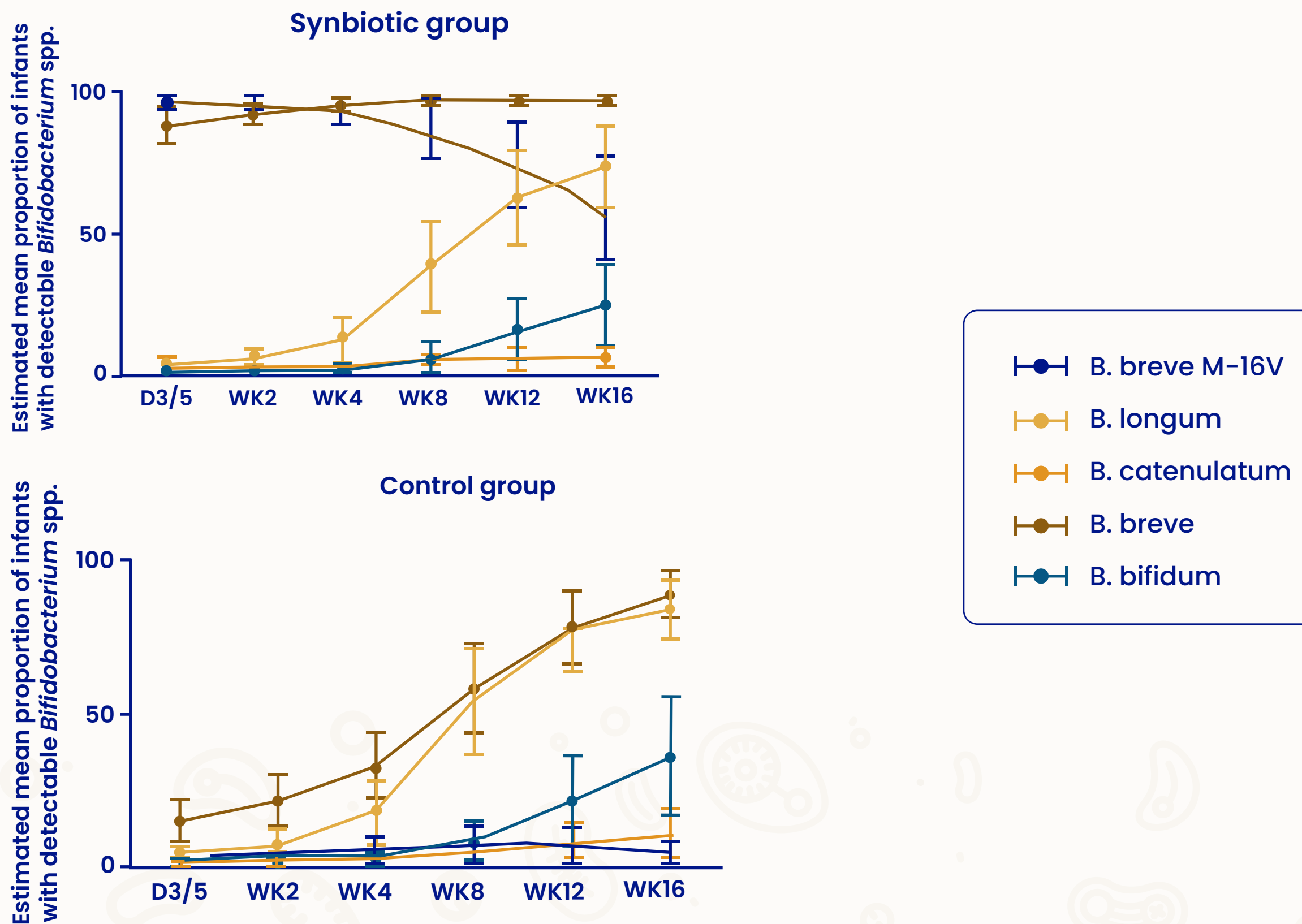


Key Microbial Outcomes (cont.)



3 Colonization by beneficial species

- ▶ *B. breve* M-16V detected in nearly all synbiotic-fed infants by Day 3/5.
- ▶ 39% retained colonization even 6 weeks post-intervention.



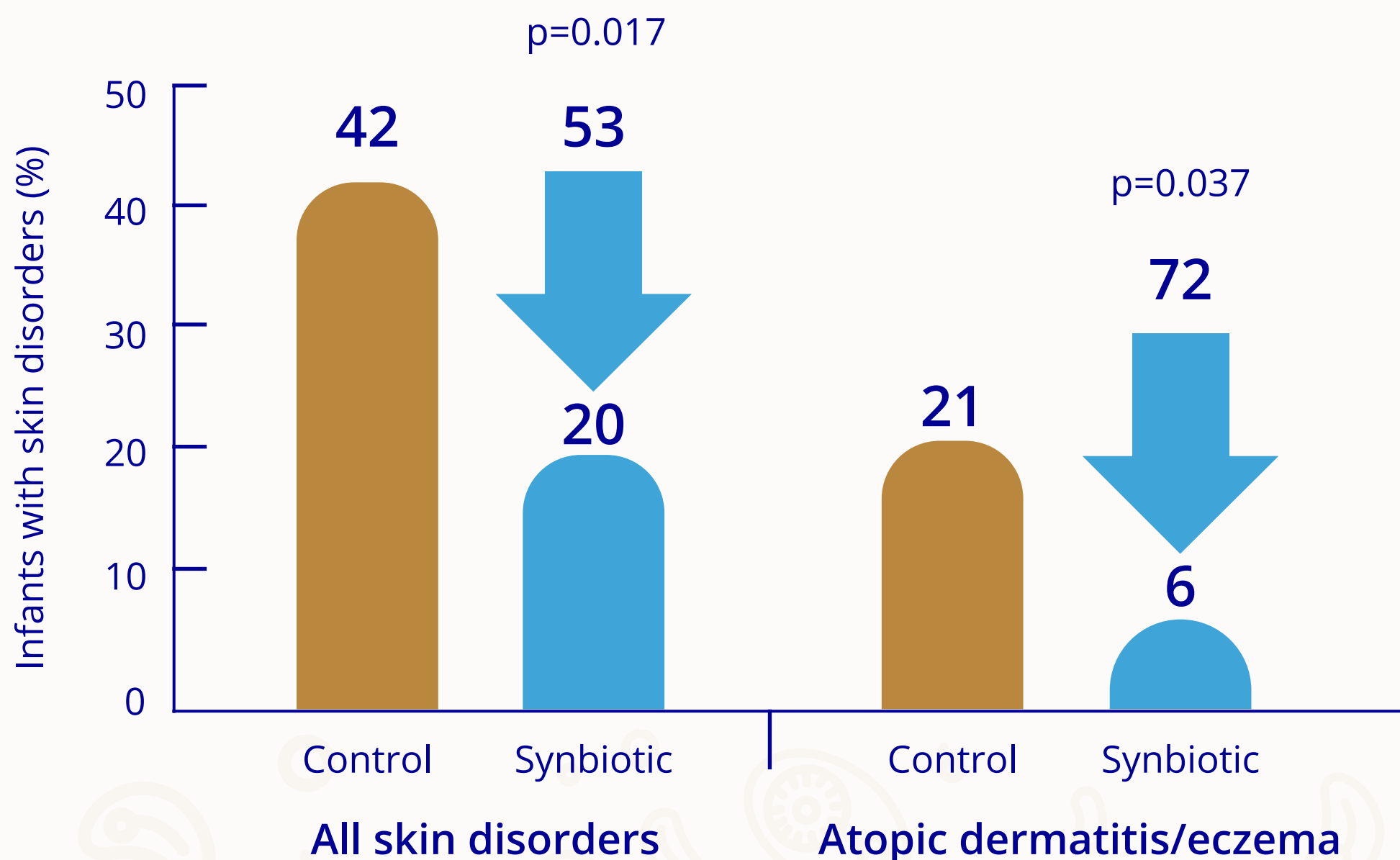


Key Microbial Outcomes (cont.)



4 Skin-Related Adverse Events (Post Hoc Analysis)

- **53% reduction in overall skin disorders** among infants receiving synbiotic supplementation compared to the control group
- **72% reduction in atopic dermatitis/eczema** with synbiotic use versus control group





Synbiotic Impact: Microbial Balance and Clinical Tolerance

Synbiotic supplementation with scGOS/lcFOS (9:1) and *Bifidobacterium breve* M-16V may help restore gut health in cesarean-born infants within 3 days.



Healthier Gut Environment & supports immunity

- ▶ Acetate (main SCFA) by Day 3/5 ($P < 0.0001$)
- ▶ Fecal pH from Day 3/5 to Week 4 ($P < 0.001$)
- ▶ This Favors beneficial microbes, mimics vaginally delivered gut profile



Good Tolerability & Safety

- ▶ Well tolerated across all groups
- ▶ Eczema incidence was reduced by 72% in the synbiotic group compared to the control group (20% vs 42%, $P = 0.017$)

Key Takeaways



- » Synbiotic supplementation (scGOS/lcFOS (9:1) and *Bifidobacterium breve* M-16V) restores early *Bifidobacterium* colonization in C-section-delivered infants within 3 days.
- » Synbiotics increase acetate production and lowers fecal pH, creating a gut environment similar to that of vaginally born infants.
- » This modulation supports immune development and may reduce the risk of immune-mediated disorders later in life.
- » Synbiotics offer a safe, clinically validated alternative to unregulated approaches like vaginal seeding.

Abbreviations

lcFOS: Long-chain fructooligosaccharide; **scGOS:** Short-chain galacto-oligosaccharide.

Reference

Chua MC, et al. J Pediatr Gastroenterol Nutr. 2017 Jul;65(1):102-106.

Disclaimer

The World Health Organization (WHO)* has recommended that pregnant women and new mothers be informed of the benefits and superiority of breast-feeding, in particular, the fact that it provides the best nutrition and protection from illness for babies. Mothers should be given guidance on the preparation for and maintenance of lactation, with special emphasis on the importance of the well-balanced diet both during pregnancy and after delivery. Unnecessary introduction of partial bottle feeding or other foods and drinks should be discouraged since it will have a negative effect on breast-feeding. Similarly, mothers should be warned of the difficulty of reversing a decision not to breastfeed. Before advising a mother to use an infant formula, she should be advised of the social and financial implications of her decision. For example, if a baby is exclusively bottle-fed, more than one can (500g) per week will be needed, so the family circumstances and cost should be kept in mind. Mother should be reminded that breast milk is not only the best but also the most economical food for babies. If a decision to use infant formula is taken, it is important to give instruction on correct preparation methods, emphasizing that unboiled water, unsterilized bottles or incorrect dilution can lead to illness.

*See: International Code of Marketing of Breast Milk Substitutes, adopted by the World Health Assembly in Resolution WHA 34.22, May 1981.

Importance of Breastfeeding: (i) Immediately after delivery, breast milk is yellowish and sticky. This milk is called colostrum, which is secreted during the first week of delivery. Colostrum is more nutritious than mature milk because it contains more protein, more anti-infective properties which are of great importance for the infant's defense against dangerous neonatal infections. It also contains higher levels of, Vitamin 'A', (ii) breast milk- (A) is, a complete and balanced food and provides all the nutrients needed by the infant [for the first six months of life] (B) has anti-infective properties that protect the infants from infection in the early months (C) is always available; (D) needs no utensils or water (which might, carry germs) or fuel for its preparation, (iii) breastfeeding is much cheaper than feeding infant milk substitutes as the cost of the extra food needed by the mother is negligible compared to the cost of feeding infant milk substitutes, (iv) mothers who breast-feed usually have longer periods of infertility after child birth than non-lactators; (b) details of management of breast feeding, as under:- (i) breast-feeding- (A) immediately after delivery enables the contraction of the womb and helps the mother to regain her figure quickly; (B) is successful when the infant suckles frequently and the mother wanting to breast-feed is confident in her ability to do so (ii) in order to promote and support breast-feeding the mother's natural desire to breast feed should always be encouraged by giving, where needed, practical advice and making sure that she has the support of her relatives. (iii) adequate care for the breast and nipples should be taken during pregnancy. (iv) it is also necessary to put the infant to the breast as soon as possible after delivery, (v) let the mother and the infant stay together after the delivery, the mother and her infant should be allowed to stay together (in hospital, this is called "rooming-in"); (vi) give the infant colostrum as it is rich in many nutrients and anti-infective factors protecting the infants from infections during the few days of its birth; (vii) the practice of discarding colostrum and giving sugar water, honey water, butter or other concoctions instead of colostrum should be very strongly discouraged; (viii) let the infants suckle on demand; (ix) every effort should be made to breast-feed the infants whenever they cry; (x) mother should keep her body and clothes and that of the infant always neat and clean.

IMPORTANT NOTICE: MOTHER'S MILK IS BEST FOR YOUR BABY

Breast milk is best for babies. At Danone, we support breast feeding and believe that breast milk is the best food for babies as the sole source of nutrition for the first 6 months of life and is recommended to be continued until 2 years with the introduction of appropriate complementary foods after 6 months of age.

IMPORTANT NOTICE: Breastfeeding is the best for babies and a healthy diet / maternal nutrition is important when breastfeeding. A decision not to breastfeed can be difficult to reverse. Infant formula is suitable from birth when babies are not breastfed. It is recommended that all formula milks be used on the advice of a doctor, midwife, health visitor, public health nurse, dietitian, pharmacist, or other professional responsible for maternal and child-care and the financial implications should be considered. All preparation and feeding instructions should be followed carefully as inappropriate preparation could lead to health hazards.