

WHAT HMOs ARE AND WHAT THEY DO FOR BABIES

Human milk oligosaccharides (HMOs) have a high profile in infant feeding at the moment, but what exactly are they, and what do they do?

At 10–15g per litre human milk oligosaccharides (HMOs) are, after lactose and fats, the third most common solid component of breast milk.^{1,2} For a while scientists were puzzled why a mother would devote so much effort to making HMOs because the benefits to a baby are not obvious.

Although HMOs are carbohydrates, they do not act like a food nutrient.

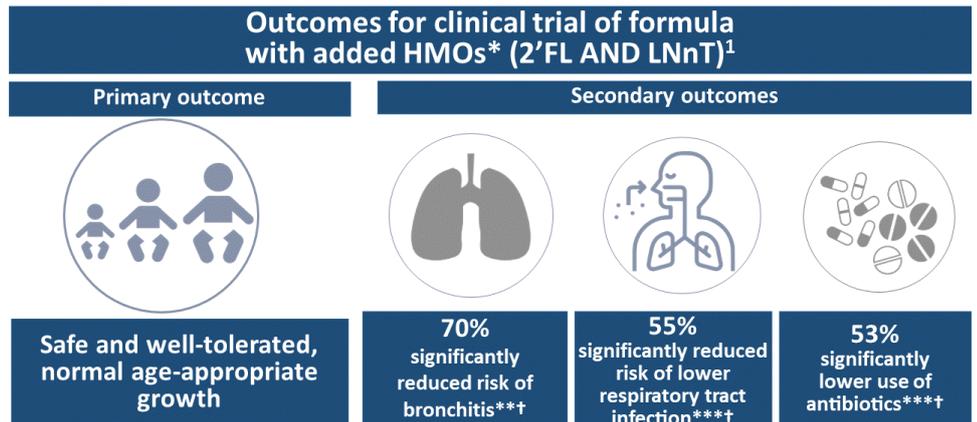
The 1% mystery

Only about 1% of the HMOs that a baby ingests with breast milk is digested and absorbed from the gut.¹ So if HMOs are not directly providing nutrition to a baby, what are they doing?

Trying to work that out has seen HMOs become one of the hot topics of infant feeding research, with hundreds of research studies published in the last few years.

HMOs are formed from the building blocks of 5 simple carbohydrates (monosaccharides). Compared with the oligosaccharides FOS and GOS (added to some formulas but not found in breast milk), they are complex molecules with multiple effects.^{1–3}

Research over the past decade or so has generated substantial evidence that HMOs are crucial to the health benefits of breastfeeding (and provides yet another reason



HMOs: structurally identical Human Milk Oligosaccharides, not sourced from breast milk
 † Parent-reported, reviewed and verified by study physicians, versus formula without HMOs
 ** p<0.01; *** p<0.05

1. Puccio G, et al *JPGN* 2017;64: 624–631.

to believe breast milk is the best form of infant nutrition).^{1,2}

Population of microbes

One key role they play is in influencing the populations of microbes in the gut, the gut microbiota. It has been known for more than 100 years that the bacteria in breast-fed and formula-fed infants are quite different.² HMOs are now believed to be a key driver in establishing a healthy community of gut bacteria in the newborn (HMOs are found in particularly high levels in colostrum).^{1,2}

Healthy gut community

HMOs act as a food source for microbes and drive the growth of a healthy community of gut bacteria. But the effect is targeted. Particular bacteria thrive on specific HMOs in breast milk.⁴

But HMOs are more than just food for bacteria and their effects go well beyond those of GOS and FOS

(the oligosaccharides added to some formulas).

For example, HMOs reduce infections by combining with disease-causing bacteria. These harmful bacteria need to attach to the gut and multiply to cause disease. When they combine with HMOs they pass through the gut harmlessly.²

‘Good’ bacteria thrive

In laboratory studies, potentially disease-causing bacteria grow poorly or not at all in the presence of HMOs, while ‘good’ bacteria like Bifidobacteria thrive.^{6,7}

In the presence of GOS and FOS, a wide range of bacteria, including beneficial bacteria are able to grow.⁷ This may explain why reviews of the evidence conclude that GOS and FOS have no clinically meaningful effect on rates of infection.⁸

There is evidence too that HMOs help rebalance the im-



↻ -mune system after birth. Babies who keep some features of the immature foetal immune system run the risk of an excessive inflammatory response to challenges from environmental allergens. This may result in atopic

conditions like eczema and asthma.^{2,5}

Distinct immune system effects
Elsewhere HMOs boost the levels of immune system cells both in the gut but also in the rest of the

body. By comparison the effects of GOS/FOS on immune system cells are limited.⁸

It is these effects and their complex, varied structures, that make HMOs distinct from GOS and FOS.

Growth similar to WHO growth standards with promising respiratory infection effects

The research described above has paved the way for a number of clinical randomised controlled trials (RCT) on HMOs. These have assessed HMOs* in formula-fed babies, by comparing an HMO* supplemented formula with a control formula (identical except lacking the HMOs*).

The RCT is the gold standard for comparing two treatments, and to show the statistical significance of any differences.

In one study a formula with 2 HMOs* added (2'FL and LNnT) showed that growth over 12 months was similar in infants fed the formula with HMOs* and the control formula. Growth curves were similar to WHO growth standards.¹⁰

The two HMOs* in the study, 2'FL and LNnT, are among the most abundant HMOs in breast milk and have been extensively studied.^{11,12,13} The study also found statistically significant

differences between the groups for secondary outcomes (see figure on page 1).

These were reported by parents and reviewed and verified by clinicians. For infants fed the HMO*-added formula, compared to those fed control formula there was:¹⁰

- 55% lower risk of lower respiratory tract infections
- 70% lower risk of bronchitis
- >50% lower use of antibiotics or antipyretics

These findings are promising and consistent with the known effects of HMOs derived from research on breast milk.^{1,2,14}

They will need to be confirmed in further research to establish cause and effect.

*HMOs: structurally identical Human Milk Oligosaccharides, not sourced from breast milk.

References:

1. Bode L. The functional biology of human milk oligosaccharides *Early Human Development* 2015;91:619–622. 2. Bode L. Human milk oligosaccharides: Every baby needs a sugar mama *Glycobiology* 2012;9:1147–1162. 3. Jantscher-Krenn E and Bode L. Human milk oligosaccharides and their potential benefits for the breast-fed neonate *Minerva Pediatr* 2012;64:83-99. 4. Borewicz K et al. Correlating Infant Fecal Microbiota Composition and Human Milk Oligosaccharide consumption by Microbiota of 1-Month-Old Breastfed Infants *Mol. Nutr. Food Res.* 2019, 1801214. 5. Berger A. Th1 and Th2 responses: what are they? *BMJ* 2000;321:424. 6. Yu ZT et al. Utilization of major fucosylated and sialylated human milk oligosaccharides by isolated human gut microbes, *Glycobiology* 2013;23:1281–1292. 7. Hoeflinger JL et al. In Vitro Impact of Human Milk Oligosaccharides on Enterobacteriaceae *Growth J. Agric. Food Chem.* 2015;63:3295–3302. 8. EFSA Panel on Dietetic Products, Nutrition and Allergies *EFSA Journal* 2010;8(2):1430. 9. Puccio G et al. Effects of Infant Formula With Human Milk Oligosaccharides on Growth and Morbidity: A Randomized Multicenter Trial *JPGN* 2017;64:624–631. 10. Smilowitz JT et al. Breast Milk Oligosaccharides: Structure-Function Relationships in the Neonate *Annu Rev Nutr.* 2014;34:143–169. 11. Austin S et al. Temporal Change of the Content of Oligosaccharides in the Milk of Chinese Urban Mothers *Nutrients* 2016;8:346. 12. Bode L et al. Structure-Function Relationships of Human Milk Oligosaccharides *Adv Nutr* 2012;3:383S–391S. 13. Goehring KC et al. Similar to Those Who Are Breastfed, Infants Fed a Formula Containing 2'-Fucosyllactose Have Lower Inflammatory Cytokines in a Randomized Controlled Trial *J Nutr.* 2016;146:2559–2566.

IMPORTANT NOTICE: The World Health Organisation (WHO) has recommended that pregnant women and new mothers be informed on the benefits and superiority of breastfeeding – 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 a 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 breastfeeding. 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 (400 g) per week will be needed, so the family circumstances and costs should be kept in mind. Mothers should be reminded that breast milk is not only the best, but also the most economical food for babies. If a decision to use an infant formula is taken, it is important to give instructions on correct preparation methods, emphasising that unboiled water, unsterilised bottles or incorrect dilution can all lead to illness.

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