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ANALYSIS

Health and nutrition claims for infant formula are poorly substantiated and potentially harmful

Marketing claims for infant formula should be banned, argue **Daniel Munblit and colleagues**

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Despite improvements in infant formula over its 150 year history, it is still associated with health risks for mother and infant compared with breastfeeding. Manufacturers try to limit these risks through changes to formula composition, which are often accompanied by health or nutrition claims that aid product differentiation or increase market value. Academics and regulators have raised concerns, however, that these claims are often unfounded and may undermine efforts to support breastfeeding.[1-6] The current regulatory environment allows claims to be made for food products with low levels of evidence, but the potential harms associated with claims are higher for infant formula than for other foods. How can we prevent the harms associated with infant formula claims while ensuring formula fed infants can benefit from improvements in formula composition?

Potential harms of health and nutrition claims

Health and nutrition claims are commonly made for a wide variety of food products, and the level of evidence supporting such claims is variable. However, special consideration is needed for claims related to infant formula products, which we define as breastmilk substitutes for use in the first year of life, including follow-on formula and foods for special medical purposes. Infant formula is consumed by a substantial proportion of the world's infants, often in large volumes in relation to their body weight—typically 150-200 mL/kg/day for a young infant fed solely on formula milk, the equivalent of 11-14 L/day for a 70 kg adult. The developmental status of infants means that any potential harms associated with infant formula claims may have a high cumulative impact over their life.[7]

Mothers are also vulnerable during the period when they make infant feeding choices, with up to 20% experiencing a mental illness during pregnancy or the first year of their infant's life.[8]

Aggressive promotion of infant formula can influence decisions to use formula milk in place of breast milk,[9] and health and nutrition claims are likely to contribute to this process by narrowing the perceived benefits of breast milk over formula.

Box 1 lists some of the established risks of using infant formula in place of breast milk for infant and mother. The potential for an adverse effect on breastfeeding means that claims for infant formula can cause more harm than those for most other food products. Even if the claims are scientifically well substantiated, there is a problem of inequity. Given the unique role of early nutritional influences on health and development, limiting access to improved infant formula products to those who pay a premium is difficult to justify. Any compositional changes that are supported by good evidence should be included in all relevant products. Poorly substantiated claims may also cause inappropriate price inflation for consumers or healthcare providers. If these claims imply effective treatment of problems such as colic, gastro-oesophageal reflux, cow's milk allergy, or poor weight gain, they may cause harm by delaying appropriate investigations or treatments for underlying medical problems.

Box 1: Some known risks of using infant formula in place of breast milk

- Increased gastrointestinal diseases, including necrotising enterocolitis[10 11]
- Increased infectious diseases, including respiratory tract infection[4]
- Altered adiposity and intellectual development[4]
- Increased maternal breast cancer through reduced duration of breastfeeding[4]
- Adverse effects related to formula contamination or reconstitution problems—eg, bacterial infection or burn injury
- Increased cost of purchasing milk

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Scientific evidence behind claims

Several groups have suggested that the scientific basis of claims made to consumers and healthcare professionals for infant formula is weak.[1-6] Concerns include the risk of bias in scientific evidence underlying such claims and selective use of data to support claims. Evidence used to support claims often includes conference abstracts rather than peer reviewed papers, and post hoc analyses or selective data rather than prespecified analyses or comprehensive evidence syntheses.[2] Table 1 gives some examples of poorly substantiated claims as illustration. Our first example is partially hydrolysed whey protein dominant formula, which has carried claims of reduced eczema or milk allergy in many regions for many years based on selected data from individual trials and two industry funded systematic reviews in 2010.[19 20] However, two rigorous and independent systematic reviews subsequently found no evidence to support this claim, and in 2016 the UK Food Standards Agency's committee on toxicity concluded there is "no evidence that hydrolysed formula prevents eczema or milk allergy."[13]

One of the most common claims made in the United States is that polyunsaturated fatty acids in infant formula improve cognitive development. This claim is based on evaluation of a subset of outcome measures in fewer than 150 participants in one trial. In contrast a 2017 Cochrane review that found a lack of clear or consistent benefit included 11 trials with more than 1000 participants.[17 21]

Claims to reduce crying, colic, or other signs of infant distress are made for many products in different regions, often without citing specific scientific evidence. Limited evidence from individual trials supports dietary interventions to treat colic, but as summarised in a 2018 Cochrane review the evidence is sparse and has a high risk of bias, leaving the Cochrane authors "unable to recommend any intervention."[18]

Regulation of infant formula claims

Health and nutrition claims for infant formula are regulated in a similar way to other food products, with some additional information requirements.[22-25] The regulatory framework for claims on foods is less demanding than for medicines, and premarket approval by regulators is often not required for health and nutrition claims. The issues of clinical trial transparency and publication of complete study reports or datasets, which are beginning to gain traction in drug development, have not yet been fully addressed for food claims.[26] This lack of regulatory oversight explains the widespread presence of poorly substantiated claims for infant formula.

WHO recommendations

The World Health Organization International Code of Marketing of Breastmilk Substitutes and subsequent World Health Assembly resolutions recommend against promoting infant formula to the public and state that information for healthcare professionals should be "scientific and factual" (box 2). This is not legally binding, and few countries have fully enacted its recommendations into law. Promotion of infant formula to the public, including use of health and nutrition claims, is still permitted in most countries.[6]

Box 2: WHO code on marketing of breastmilk substitutes

- Informational and educational materials intended to reach pregnant women and mothers of infants and young children should not use any pictures or text which may idealise the use of breastmilk substitutes
- Information provided by manufacturers and distributors to health professionals should be restricted to scientific and factual matters, and not imply or create a belief that bottle feeding is equivalent or superior to breastfeeding
- Neither the container nor the label should have pictures of infants; nor should they have other pictures or text which may idealise the use of infant formula
- There should be no advertising or other form of promotion to the general public of products within the scope of the code
- Nutrition and health claims should not be permitted for breastmilk substitutes, except where specifically provided for in national legislation

Codex food standards

Codex Alimentarius is a set of food standards established under the United Nations Food and Agriculture Organization and WHO. These influence national and regional regulations but are not legally binding. Codex provides a list of compositional requirements for infant formula.[27] It allows optional ingredients such as DHA to be added to infant formula if they are ordinarily present in human milk and have adequate safety testing. Codex does not recommend premarket approval of health and nutrition claims associated with these optional ingredients.

National and regional regulations

Most regions allow some claims about infant formula without regulatory review of the evidence and allow promotion of formula to the public and healthcare professionals. In the US most labels on food for infants carry at least one claim about the function of an ingredient (table 2).[21] These do not need premarket authorisation or need to meet the "significant scientific standard" and are protected by the First Amendment right to free speech, provided that they are truthful and not misleading.[28] However, the Food and Drug Administration may investigate claims to ensure they are not misleading.[24]

The European Union banned health and nutrition claims for infant formula from 22 February 2020 (table 3),[22] but there are several exceptions. These include "contains DHA," "reduced lactose," and potentially protein hydrolysates for preventing cow's milk allergy), and the prohibition does not apply to follow-on formula. Foods for special medical purposes are regulated separately—they carry statements such as "for the dietary management of colic and constipation" and branding as "comfort milks," which some consumers may view as health claims but do not require premarket authorisation and are sometimes poorly substantiated.[18 29] This failure of regulation and associated potential for harm suggests the need for a new approach.

New approach to regulating claims

Current regulations do not effectively prevent potentially misleading claims that may carry health risks for a vulnerable population.[30] Even when the claims for infant formula have strong scientific support, their use may be inappropriate since they still risk undermining breastfeeding and limit access to improvements in these important nutritional products to those able to pay a premium price.

We propose that any changes to the composition of infant formula should require premarket approval, and the bar for scientific substantiation needs to be significantly higher than that currently used by manufacturers to justify their claims.[31]

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When a change in infant formula composition has been shown to have a beneficial health effect, that change should be added to Codex standards so that all formula fed infants can benefit. Moreover, using the new ingredient as a health claim before assessment and inclusion in the mandatory Codex standards should be banned. This will avoid misleading consumers and undermining breastfeeding.

Restrictions on use of health and nutrition claims for infant formula should be balanced by adequate incentives for manufacturers to develop new or improved products. For example, if a new ingredient or formulation became part of the Codex compositional requirements, manufacturers could license the new technology, knowhow, or product to other manufacturers rather than limit its use to their own products. This would require a change in culture across the industry, with a focus on scientifically validated improvements in formula composition rather than on generating data which meet a bare minimum standard of evidence in order to support a poorly substantiated claim to aid product differentiation or pricing.

Infants and their carers are not being adequately protected from adverse consequences of claims about infant formula. The current regulatory environment is permissive and associated with poorly substantiated and potentially harmful claims. Global action is needed to break the current cycle of weak scientific evidence and unreliable claims and move to a new era where carers of infants are given accurate information about infant formula products in a manner that does not undermine breastfeeding.

Key messages

- Infant formula health and nutrition claims are regulated in a similar way to other food claims
- Infant formula claims carry a higher risk of harm than most other food claims because of the developmental vulnerability of infants and the potential to undermine breastfeeding
- Infant formula claims are poorly substantiated, suggesting that current legal protections for infants and their carers are inadequate
- Health and nutrition claims should not be permitted on infant formula
- Any scientifically proved compositional improvements in infant formula should be made mandatory for all relevant products

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Tables

Table 1| Examples of recent poorly substantiated health or nutrition claims for infant formula

Claim and intervention	Specific claim	Evidence cited in claim	Recent independent scientific opinion	Evidence cited in independent opinion
Prevention of eczema and milk allergy Partially hydrolysed whey protein (pHF)	*UK marketing** To parents: "To reduce the risk of developing allergy to cow's milk proteins." To healthcare professionals: "Clinically proven to reduce the risk of developing eczema by over 50%"	*GINI trial*—Adjusted relative risk of atopic dermatitis in the first year of life 0.54 (95% CI 0.34 to 0.87) in a per protocol analysis of 47% of randomised participants from one trial[12]	*UK Food Standards Agency*[13]—"No evidence that the use of pHF in place of standard formula influences the risk of eczema in children" "No difference seen in food allergy to cow's milk"	*UK Food Standards Agency*[13] *Eczema at age 0-4*—12 trials of pHF, odds ratio 0.84 (95% CI 0.67 to 1.07); 7 trials of Nestlé pHF, OR 0.94 (0.75 to 1.17) *Cow's milk sensitization*—7 trials, OR 1.30 (0.65 to 2.60)
			Cochranereview[14]—"Prolonged feeding with a pHF versus a standard cow's milk formula was not associated with any differences in infant or childhood allergic disease, asthma, eczema or rhinitis; or infant food allergy or cow's milk allergy"	*Cochrane review*[14]—7 trials reported eczema at age 0-2 years. Risk ratio 0.96 (0.80 to 1.14). No trial was considered at low risk of bias, and authors cited concerns about risk of reporting or publication bias. One trial reported cow's milk allergy at age 0-2 years. RR 2.31 (0.24 to 21.97)
Cognitive development Long chain polyunsaturated fatty acids: docosahexaenoic acid (DHA) and arachidonic acid (ARA)	*US marketing* "Enfamil Infant has DHA shown to foster learning ability through age 5"†	*DIAMOND trial*—Secondary outcomes from 46-77% of 159 randomised infants at one site of the trial: no effect of DHA/ARA on one measure of attention; increased "sustained attention" in infants fed formula with ARA plus 0.32% DHA (P=0.035) or 0.64% DHA (P=0.005) but not 0.96% DHA compared with control formula without DHA or ARA.[15] DHA/ARA was associated with higher Peabody picture vocabulary test scores at 5 years (P=0.003), higher Weschler primary preschool test of intelligence at age 6 years using one tailed test (P=0.029), and higher Stroop scores at 3-5 years (P=0.039), but no difference for six other assessments.[15] Evaluation of outcomes in 55% of 181 randomised participants from the other trial site showed no difference between groups in a measure of school readiness and a measure of receptive vocabulary at 2.5-3.5 years, and worse performance in the DHA groups in receptive vocabulary at 2 years (P=0.002)[16]	*Cochrane review*[17]—Most of the included randomised trials reported no benefits or harms of long chain polyunsaturated fatty acid (LCPUFA) supplementation on neurodevelopmental outcomes. "Routine supplementation of full-term infant milk formula with LCPUFA cannot be recommended at this time"	*Cochrane review*[17]—11 trials of DHA±ARA evaluated neurodevelopmental outcomes in the first 2 years of life, 9 of which used the Bayley scales of infant development. Meta-analysis of 4 trials (661 participants) of DHA and AHA supplementation versus no supplementation in fully formula fed term infants found a mean difference at 18 months of 0.06 points (−2.01 to 2.14) on the Bayley mental development index and mean difference of 0.69 points (−0.78 to 2.16) on the Bayley psychomotor development index. There was a lack of clear or consistent benefit shown in other evaluations or at other time points from the 11 trials reporting relevant data
Infant crying or distress Comfort milks with hydrolysed protein, prebiotic, or low lactose	*UK and Russian marketing*‡ UK: "Aptamil Comfort is proven to help soothe the symptoms of colic and constipation" Russia: "Improves colic and constipation"	Specific scientific studies are not cited	*Cochrane review*[18]—"Evidence of the effectiveness of dietary modifications for the treatment of infantile colic is sparse and at significant risk of bias . . . Even if some results look positive (eg for hydrolysed protein formulas), it is possible that the advantages mentioned could simply be due to bias or chance. Based on the evidence presented, we cannot recommend hydrolysed protein formulas or other dietary modifications"	*Cochrane review*[18]—5 trials evaluated extensively hydrolysed formula and 1 trial evaluated partially hydrolysed formula with prebiotics and low lactose. All evidence was rated as very low certainty due to a high risk of bias in almost all included trials, imprecision because of small study sizes, and concerns about selective reporting. Meta-analysis was not possible because of heterogeneity of populations, interventions, and outcome measures[8]

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Table 1 (continued)

Claim and intervention	Specific claim	Evidence cited in claim	Recent independent scientific opinion	Evidence cited in independent opinion

‡ Aptaclub and Nutriclub websites, accessed 6 August 2019. https://web.archive.org/web/20190806101402/https://www.aptaclub.co.uk/products/aptamil/specialty-milks/aptamil-comfort.html. This claim has since been removed and on 7 April 2020 the website said Aptamil Comfort is "specially tailored for the dietary management of colic and constipation (https://www.aptaclub.co.uk/products/aptamil/specialty-milks/aptamil-comfort.html)
https://web.archive.org/web/20190806101851/http://www.colic.nutriclub.ru/nutrilon_comfort/colic/.

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Table 2| US approach to classifying health and nutrition claims for foods

Type of claim	Example	FDA authorisation required?	Level of evidence
Nutrient content	Excellent source of vitamin D	No, but must adhere to FDA regulations	If a nutrient content claim is not defined in the regulations, its use is prohibited
Structure-function*	DHA supports your infant's brain development	No	Manufacturer must have substantiation for the claim but is not required to supply data to FDA†
Qualified health claim	"Little scientific evidence suggests that, for healthy infants who are not exclusively breastfed and who have a family history of allergy, feeding a 100% whey protein partially hydrolyzed infant formula from birth up to 4 months of age instead of a formula containing intact cow's milk proteins may reduce the risk of developing atopic dermatitis throughout the 1st year of life."	No, but FDA reviews before marketing and decides whether to exercise enforcement discretion	Significant scientific agreement standard not met‡
Health claim	"Healthful diets with adequate folate may reduce a woman's risk of having a child with a brain or spinal cord defect."	Yes	Significant scientific agreement standard met‡

* Structure-function claims should derive from the product's character as a food to avoid regulation as a drug. †It is a statutory requirement that claims in food labelling must be truthful and not misleading (section 403(a), Federal Food, Drug and Cosmetic Act (21 U.S.C. 343(a)). ‡Significant scientific agreement standard: "there is agreement among experts that the totality and quality of the scientific evidence available is sufficient to substantiate the relationship which a health claim refers to."

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Table 3| EU approach to classifying health and nutrition claims for foods

Type of claim	Example	EFSA authorisation required?	Level of evidence
Nutrition	Source of calcium	No*	Generally accepted scientific evidence†
Health claims other than those referring to the reduction of disease risk and to children's development and health	Iron contributes to the normal function of immune system	Yes	Generally accepted scientific evidence†
Reduction of disease risk and claims referring to children's development and health‡	DHA intake contributes to the normal visual development of infants up to 12 months of age	Yes	Generally accepted scientific evidence†

EFSA European Food Standards Agency. *Nutrition claims must adhere to the list of permitted nutrition claims https://ec.europa.eu/food/safety/labelling_nutrition/claims/nutrition_claims_en. †Comparable with the US significant scientific agreement standard. ‡The presentation or advertising must also include a statement indicating that the disease to which the claim is referring has multiple risk factors and that altering one of these risk factors may or may not have a beneficial effect.

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