

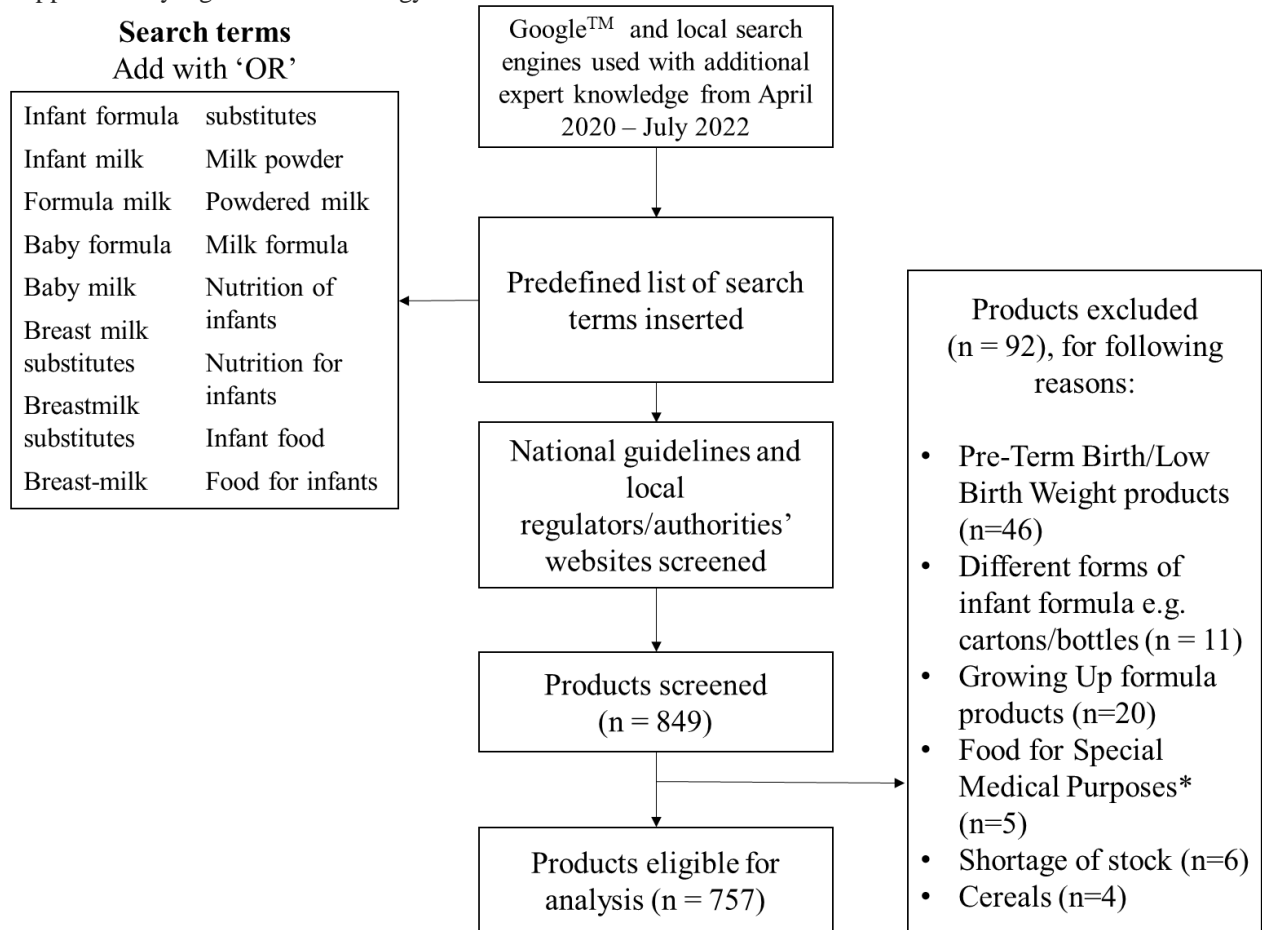
# International Survey of Infant Formula Health and Nutrition Claims

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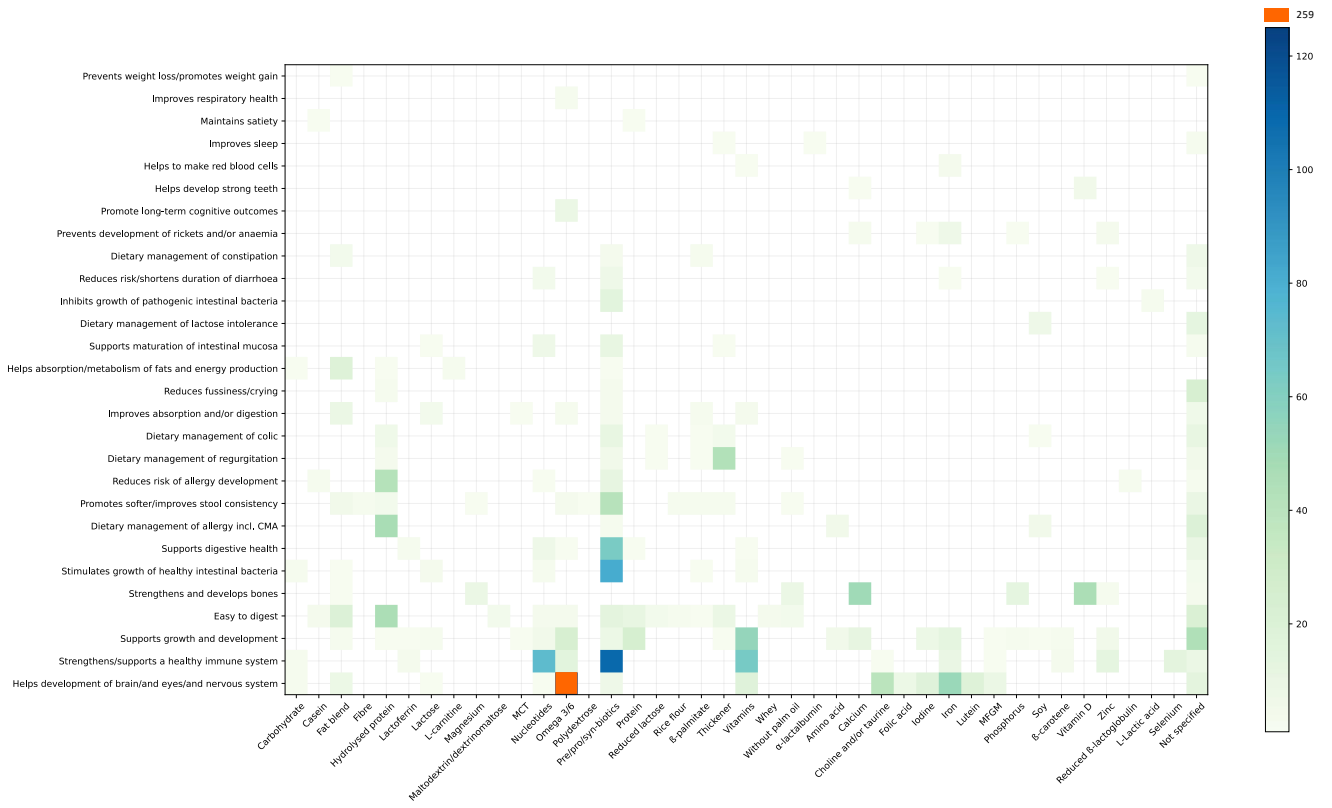
## Supplementary Figures

Supplementary Figure 1. Methodology Flowchart

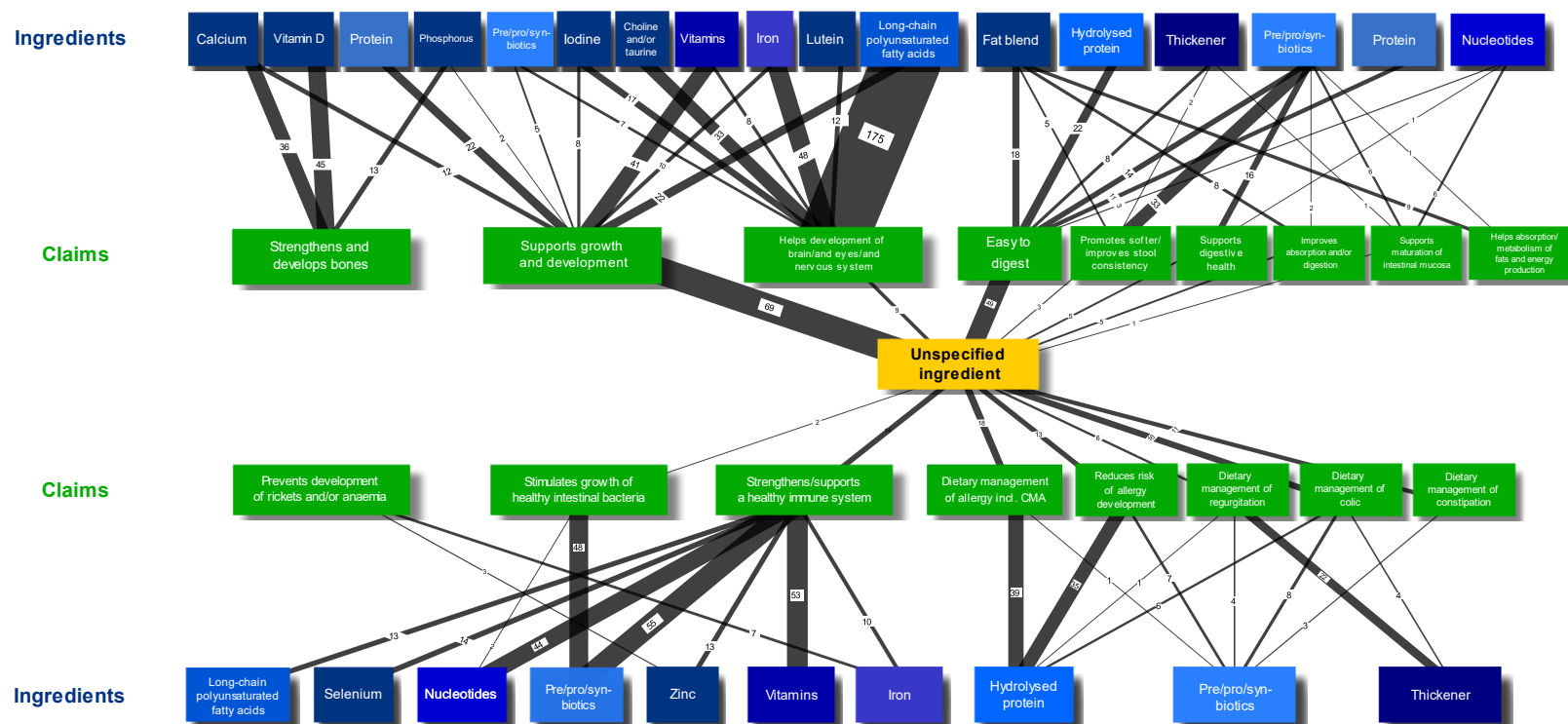


\*Food for Special Medical Purposes including formulas for inborn errors of metabolism, such as galactosemia; residual lactose formula; fructose-based formula; MCT-enhanced formula; low calcium formula.

Supplementary Figure 2. Heat map illustrating ingredients linked to health and nutrition claim for all countries

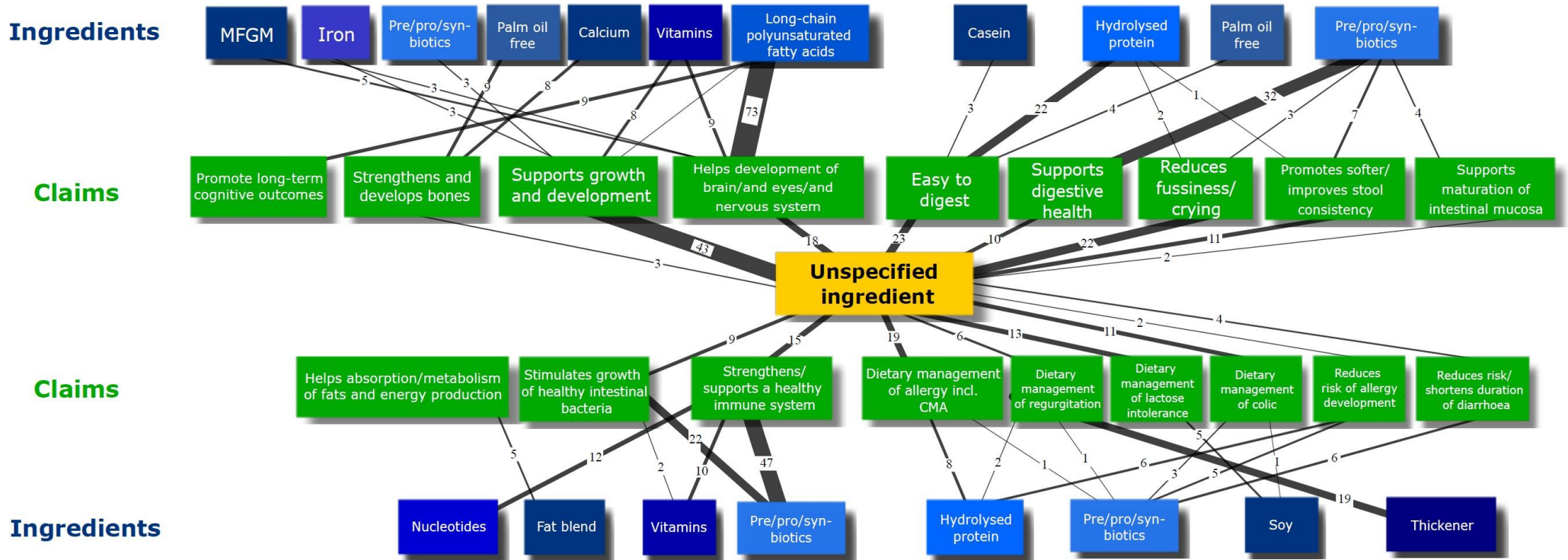


Supplementary Figure 3. Network plot of claims associated with ingredients in infant formula marketed in those countries surveyed in 2020



Network plot of claims associated with ingredients, with a frequency of ten or more, from Australia, Canada, Germany, India, Italy, Japan, Norway, Pakistan, Russia, Spain and the United Kingdom. The yellow midpoint represents health claims associated with a non-specified ingredient. Blue labels represent the type of ingredient; green labels represent health and nutrition claims. The thickness of the lines represents the frequency of health claims being associated with an ingredient.

Supplementary Figure 4. Network plot of claims associated with ingredients in infant formula marketed in those countries surveyed in 2022



Network plot of claims associated with ingredients, with a frequency of three or more, from Saudi Arabia, Nigeria, South Africa and USA. The yellow midpoint represents health claims associated with a non-specified ingredient. Blue labels represent the type of ingredient; green labels represent health and nutrition claims. The thickness of the lines represents the frequency of health claims being associated with an ingredient.

## Supplementary Tables

Supplementary Table 1. Health and nutrition claim type for all countries surveyed

Country	Number of health and nutrition claims/Number of infant formula products (Ratio)	Products with $\geq 1$ health or nutrition claim (%)	Growth and development effect	Functional process or outcome effect	Effect on a disease, disorder or condition	Physiological process or outcome effect	WHO code compliance score (/100)	Ever breastfed percentage (UNICEF 2018 report)	Human Development Index (UNDP 2020)
USA	340/76 (4.5)	76 (100%)	123 (36%)	115 (34%)	24 (7%)	78 (23%)	No legal measures	74%	0.926
Russia	367/103 (3.6)	98 (95%)	148 (40%)	68 (19%)	65 (18%)	86 (23%)	18	92%	0.824
Saudi Arabia	226/70 (3.2)	63 (90%)	65 (29%)	55 (24%)	54 (24%)	52 (23%)	77	Not reported	0.854
Norway	102/32 (3.2)	23 (72%)	52 (51%)	11 (11%)	19 (19%)	20 (20%)	39	95%	0.957
UK	159/60 (2.7)	52 (87%)	69 (43%)	29 (18%)	28 (18%)	33 (21%)	39	81%	0.932
India	157/60 (2.6)	46 (77%)	75 (48%)	24 (15%)	16 (10%)	42 (27%)	78	96%	0.645
Pakistan	106/43 (2.5)	33 (77%)	55 (52%)	12 (11%)	13 (12%)	26 (25%)	73	94%	0.557
Canada	99/49 (2.0)	43 (88%)	47 (48%)	27 (27%)	13 (13%)	12 (12%)	No legal measures	89%	0.929
South Africa	87/51 (1.7)	42 (82%)	5 (6%)	20 (23%)	45 (52%)	17 (19%)	87	Not reported	0.709
Japan	33/21 (1.6)	17 (81%)	16 (49%)	8 (24%)	7 (21%)	2 (6%)	No legal measures	Not reported	0.919
Nigeria	31/19 (1.6)	14 (74%)	19 (61%)	7 (23%)	3 (10%)	2 (6%)	84	95%	0.539
Germany	56/43 (1.3)	30 (70%)	31 (55%)	4 (7%)	13 (23%)	8 (14%)	39	82%	0.947
Spain	29/19 (1.5)	12 (63%)	13 (45%)	3 (10%)	5 (17%)	8 (28%)	39	77%	0.904

Country	Number of health and nutrition claims/Number of infant formula products (Ratio)	Products with $\geq 1$ health or nutrition claim (%)	Growth and development effect	Functional process or outcome effect	Effect on a disease, disorder or condition	Physiological process or outcome effect	WHO code compliance score (/100)	Ever breastfed percentage (UNICEF 2018 report)	Human Development Index (UNDP 2020)
Italy	69/82 (0.8)	43 (52%)	8 (12%)	11 (16%)	44 (64%)	6 (9%)	39	86%	0.892
Australia	23/29 (0.8)	16 (55%)	5 (22%)	2 (9%)	15 (65%)	1 (4%)	No legal measures	92%	0.944
<b>Total</b>	<b>1884/757 (Median = 2)</b>	<b>608/757 (80%, Median = 23)</b>	<b>728/1884 (39%)</b>	<b>393/1884(21%)</b>	<b>364/1884 (19%)</b>	<b>393/1884 (21%)</b>			

Data shown are claim rates for each country surveyed, claim type, World Health Organization (WHO) breast feeding code compliance score (Marketing of Breast-milk substitutes: Status report 2020)(1), Ever breastfed percentage (UNICEF 2018 report)(2), Human Development Index (UNDP 2020)(3). Claims were classified here into four different categories, based on the approach of Berry 2017 (4): (i) Growth and development effect (ii) Functional process or outcome effect (iii) Effect on a disease, disorder or condition (iv) Physiological process or outcome effect.

Supplementary Table 2. Most common claims made for infant formula marketed in those countries surveyed in 2020

<b>Claim</b>	<b>Number (%) of products with relevant claim (Total of 413 products with ≥1 claim)</b>	<b>Number of claims with an ingredient cited</b>	<b>Example claim</b>	<b>Number (%) of 0-6/0-12 months formula (infant) products with ≥1 claim (Total 137 infant products)</b>	<b>Number (%) of 6–12 month formula (Follow-On) products with ≥1 claim (Total of 78 Follow-On products)</b>	<b>Number (%) of FSMP products with ≥1 claim (Total of 198 FSMP products)</b>
Helps/supports development of brain and/or eyes and/or nervous system	210 (51%)	47	<i>"Contains a clinically proven level of DHA, an important building block of your baby's developing brain."</i>	74 (54%)	54 (69%)	75 (38%)
Helps/supports growth and development	161 (40%)	61	<i>"Arachidonic acid: Components contained in breast milk helps growth and development."</i>	58 (42%)	35 (45%)	49 (25%)
Strengthens/supports a healthy immune system	148 (36%)	44	<i>"Studies have shown positive effects of nucleotides for the infants' immune function and in periods with rapid growth like in the newborn period."</i>	63 (46%)	46 (60%)	39 (20%)
Easy to digest	123 (30%)	42	<i>"Amino acids means that this will be easily digestible, and is good for infants with stomach - and digestive - conditions."</i>	46 (34%)	14 (18%)	61 (31%)
Dietary management of allergy incl. cow's milk allergy (CMA)	68 (16%)	25	<i>"It helps babies in consuming milk and get the protein without an allergic response."</i>	0 (0%)	0 (0%)	51 (26%)
Stimulates growth of healthy intestinal bacteria	56 (14%)	13	<i>"Whey proteins, lactose and nucleotides to support the growth of useful gut bacteria."</i>	22 (16%)	12 (15%)	22 (11%)
Strengthens and develops bones	52 (13%)	21	<i>"Supports the normal development of bones and</i>	17 (12%)	28 (36%)	7 (4%)



			<i>teeth with vitamin D (according to the law)."</i>			
Promotes softer/improves stool consistency	50 (12%)	22	<i>"Contains a blend of 2 dietary fibres, GOS and polydextrose, shown to soften stools."</i>	20 (15%)	8 (10%)	22 (11%)
Reduces risk of allergy development	49 (12%)	18	<i>"It is clinically demonstrated to help reduce future allergy challenges at 3 years."</i>	13 (9%)	3 (4%)	26 (13%)
Dietary management of colic	40 (10%)	17	<i>"It is formulated to aid digestive malabsorption with an enriched level of sn-2 palmitate to help ease constipation (soften stools) and a reduced level of lactose to help ease colic."</i>	5 (4%)	3 (4%)	25 (13%)
Dietary management of regurgitation	32 (8%)	17	<i>"Contains rice starch that becomes thicker in your baby's stomach is clinically proven to reduce frequent spit up."</i>	0 (0%)	0 (0%)	20 (10%)
Improves absorption and/or digestion	24 (6%)	14	<i>"Improved absorption and digestion due to the presence of: An easy to digest fat blend including MCT/LCT"</i>	7 (5%)	5 (6%)	12 (6%)
Dietary management of constipation	10 (2%)	6	<i>"NAN Sensilac is an infant formula based on cow's milk, especially developed for children with sensitive stomachs and those with a tendency to constipation."</i>	4 (3%)	1 (1%)	4 (2%)

Number of products with relevant claim  $\geq 10$  made for different categories of infant formula: from birth (0-6/0-12 months); follow on (6-12 months); food for special medical purposes (FSMP), from Australia, Canada, Germany, India, Italy, Japan, Norway, Pakistan, Russia, Spain and the United Kingdom, 2020

Supplementary Table 3. Most common claims made for infant formula marketed in those countries surveyed in 2022

Claim	Number (%) of products with relevant claim (Total 195 with ≥1 claim)	Number of claims with an ingredient cited	Example claim	Number (%) of 0-6/0-12 months formula (infant) products with ≥1 claim (Total of 85 infant products)	Number (%) of 6-12-month formula (Follow-On) products with ≥1 claim (Total of 17 Follow-On products)	Number (%) of FSMP products with ≥1 claim (Total of 93 FSMP products)
Helps/supports development of brain and/or eyes and/or nervous system	113 (58%)	125	<i>"Omega-3 DHA like that found in Enfamil has been clinically shown to: improve attention span, problem solving, and visual development."</i>	63 (74%)	8 (47%)	41 (44%)
Strengthens/supports a healthy immune system	91 (47%)	99	<i>"2'FL-HMO is a prebiotic similar to that found in breast milk, shown to help support digestive and immune health."</i>	25 (29%)	7 (41%)	31 (33%)
Helps/supports growth and development	63 (32%)	27	<i>"Clinically shown to support the growth of exclusively formula-fed infants."</i>	24 (28%)	5 (30%)	26 (28%)
Easy to digest	59 (30%)	40	<i>"Easy-to-digest 60:40 whey-to-casein ratio prior to partial hydrolyzation, patterned after mature breast milk."</i>	29 (34%)	2 (12%)	28 (34%)
Stimulates growth of healthy intestinal bacteria	35 (18%)	37	<i>"The prebiotic blend in Enfamil Reguline has been clinically proven through multiple published studies to promote beneficial bacteria in the digestive tract and to soften stools."</i>	18 (21%)	3 (18%)	14 (15%)
Dietary management of allergy incl. cow's milk allergy (CMA)	28 (14%)	10	<i>"Helps more babies overcome cow's milk allergy and return to consuming regular milk proteins in as fast as 6 months of feeding."</i>	1 (1%)	0 (0%)	20 (22%)

Claim	Number (%) of products with relevant claim (Total 195 with ≥1 claim)	Number of claims with an ingredient cited	Example claim	Number (%) of 0-6/0-12 months formula (infant) products with ≥1 claim (Total of 85 infant products)	Number (%) of 6–12-month formula (Follow-On) products with ≥1 claim (Total of 17 Follow-On products)	Number (%) of FSMP products with ≥1 claim (Total of 93 FSMP products)
Dietary management of regurgitation	22 (11%)	24	<i>"A thickened milk-based infant formula design to reduce frequent spit-up that also has brain- building DHA as recommended by experts."</i>	0 (0%)	0 (0%)	18 (19%)
Strengthens and develops bones	25 (13%)	24	<i>"Promotes Strong Bones: Has no palm oil to promote excellent calcium absorption for strong bones."</i>	16 (19%)	2 (12%)	7 (8%)
Promotes softer/improves stool consistency	21 (11%)	14	<i>"Promotes soft stools similar to those reported for breastfed infants."</i>	13 (15%)	2 (12%)	6 (6%)
Dietary management of colic	15 (8%)	4	<i>"Fast relief from severe crying/colic."</i>	1 (1%)	0 (0%)	12 (13%)
Reduces risk of allergy development	14 (7%)	12	<i>"It is clinically demonstrated to help reduce future allergy challenges at 3 years."</i>	4 (5%)	2 (12%)	8 (9%)
Dietary management of constipation	10 (5%)	2	<i>"Helps significantly relieve the symptoms of mild constipation, such as slow passage of the stools, acting along the baby's digestive system."</i>	1 (1%)	0 (0%)	7 (8%)
Improves absorption and/or digestion	11 (6%)	6	<i>"The Gerber formula also has a fat blend with MCT oil to help facilitate fat absorption."</i>	4 (5%)	0 (0%)	7 (8%)

Number of products with relevant claim ≥ 10 made for different categories of infant formula: from birth (0-6/0-12 months); follow on (6-12 months); food for special medical purposes (FSMP), from Nigeria, South Africa, Saudi Arabia and USA

Supplementary Table 4. Most common ingredients cited in claims for infant formula marketed in those countries surveyed in 2020

<b>Ingredient</b>	<b>Number (%) of products with relevant ingredient/Total of 413 products with ≥1 claim (%)</b>	<b>Number of separate claims cited for relevant ingredient</b>	<b>Example claim</b>	<b>Number (%) of 0-6/0-12 months formula (infant) products with ≥1 claim related to relevant ingredient (Total of 137 infant products)</b>	<b>Number (%) of 6-12 month formula (Follow-On) products with ≥1 claim related to relevant ingredient (Total of 78 Follow-On products)</b>	<b>Number of FSMP products with ≥1 claim related to relevant ingredient (Total of 198 FSMP products)</b>
Not specified	185 (45%)	266	-	65 (47%)	20 (26%)	98 (49%)
Pre/pro/syn-biotics	129 (31%)	216	<i>“This specific blend prebiotics has been shown to encourage the growth and activity of beneficial bacteria in the infant gut, as well as improve stool frequency and consistency.”</i>	56 (41%)	25 (32%)	47 (24%)
Long-chain polyunsaturated fatty acids	186 (45%)	213	<i>“With the addition of long chain omega 3 and omega 6 fatty acids, the proteins have been replaced with amino acids, assisting with the healthy brain and eye development of children.”</i>	67 (49%)	48 (62%)	71 (36%)
Vitamins	86 (21%)	156	<i>“Vitamins A, C &amp; D to help support the normal function of baby’s immune system...”</i>	29 (21%)	34 (44%)	24 (12%)
Hydrolysed protein	83 (20%)	108	<i>“...contains a unique combination of starch and 100% whey, partially hydrolysed protein for the dietary management of reflux and regurgitation.”</i>	9 (7%)	2 (3%)	72 (36%)

Number of separate claims cited for ≥ 20 ingredients in different categories of infant formula: from birth (0-6/0-12 months); follow on (6-12 months); food for special medical purposes (FSMP), from Australia, Canada, Germany, India, Italy, Japan, Norway, Pakistan, Russia, Spain and the United Kingdom, 2020

Supplementary Table 5. Most common ingredients cited in claims for infant formula marketed in countries surveyed in 2022

Ingredient	Number (%) of products with relevant ingredient/ (Total of 195 products with $\geq 1$ claim)	Number of separate claims cited for relevant ingredient	Example claim	Number (%) of 0-6/0-12 months formula (infant) products with $\geq 1$ claim related to relevant ingredient (Total of 85 infant products)	Number (%) of 6-12 month formula (Follow-On) products with $\geq 1$ claim related to relevant ingredient (Total of 17 Follow-On products)	Number (%) of FSMP products with $\geq 1$ claim related to relevant ingredient (Total of 93 FSMP products)
Not specified	122 (63%)	207	-	15 (18%)	2 (12%)	30 (32%)
Pre/pro/syn-biotics	96 (49%)	173	<i>“Prebiotics and vitamins to help support digestive and immune health.”</i>	28 (33%)	3 (17%)	15 (16%)
Long-chain polyunsaturated fatty acids	92 (47%)	109	<i>“DHA has been demonstrated in clinical studies to: Support cognitive and visual development. Promote long-term cognitive outcomes through 5 years of age.”</i>	9 (11%)	1 (6%)	7 (8%)
Hydrolysed protein	37 (19%)	44	<i>“Partially hydrolyzed protein for easy digestion.”</i>	3 (4%)	0 (0%)	3 (3%)
Vitamins	30 (15%)	37	<i>“Features our exclusive blend of DHA, lutein, and vitamin E, ingredients found in breast milk that are important for helping to support baby’s brain and eye development.”</i>	4 (5%)	2 (12%)	2 (2%)

Number of separate claims cited for  $\geq 20$  ingredients in different categories of infant formula: from birth (0-6/0-12 months); follow on (6-12 months); food for special medical purposes (FSMP), from Nigeria, South Africa, Saudi Arabia and USA

Supplementary Table 6. Scientific substantiation of 10 most common infant formula health and nutrition claims across all countries surveyed

Type of claim	Total number of claims citing references	Number (%) of claims citing registered clinical trials	Number (%) of claims citing unregistered clinical trials	Number (%) of claims citing review articles	Number (%) of claims citing meta/pooled analyses/systematic reviews	Number (%) of claims citing other peer-reviewed citation*	Number (%) of claims citing reports/guidelines/regulations	Number (%) of claims with non-peer reviewed citation cited
All claims	560	107 (32 trials)	209 (96 trials)	103 (52 articles)	28 (8 articles)	56 (38 articles)	19 (10 articles)	38 (24 articles)
Helps/supports development of brain and/or eyes and/or nervous system	136	13 (12%)	63 (30%)	19 (18%)	16 (57%)	8 (14%)	11 (58%)	6 (16%)
Strengthens/supports a healthy immune system	94	21 (20%)	19 (9%)	32 (31%)	1 (4%)	12 (20%)	1 (5%)	8 (21%)
Stimulates growth of healthy intestinal bacteria	56	14 (13%)	13 (6%)	21 (20%)	0 (0%)	5 (9%)	0 (0%)	3 (8%)
Dietary management of allergy incl. cow's milk allergy (CMA)	49	8 (7%)	25 (12%)	6 (6%)	0 (0%)	4 (7%)	3 (16%)	3 (8%)
Helps/supports growth and development	36	10 (9%)	13 (6%)	2 (2%)	3 (11%)	5 (9%)	1 (5%)	2 (5%)
Reduces risk of allergy development	36	7 (7%)	8 (4%)	12 (12%)	2 (7%)	4 (7%)	0 (0%)	3 (8%)
Easy to digest	27	4 (4%)	8 (4%)	2 (2%)	5 (18%)	5 (9%)	0 (0%)	3 (8%)
Promotes softer/improves stool consistency	24	5 (5%)	11 (5%)	3 (3%)	0 (0%)	3 (5%)	0 (0%)	2 (5%)
Dietary management of colic	15	1 (1%)	11 (5%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)	2 (5%)
Strengthens and develops bones	7	0 (0%)	2 (1%)	2 (2%)	0 (0%)	0 (0%)	0 (0%)	3 (8%)

\*Including cohort studies; experimental studies; animal studies; cross-sectional studies; textbook chapters.

Supplementary Table 7. Risk of bias assessments of registered clinical trials

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT00298337(5)	Similac Gold (Russia)	Decrease in eczema (as result of oligosaccharides of breastmilk)	No. Non randomised comparison from the placebo group of an RCT	Same population - but trial outcome is only regarding infants born by C-section	Both claim and trial relate to oligosaccharides. But claim is regarding Similac Gold and trial outcome was not related to same product	Consistent with claim	Decrease in eczema in high risk infants born by C-section at 2 years, but not at 5 years, using logistical regression models	-	Not relevant	Funded by Nestlé Author(s) affiliated to Nestlé
NCT00338689(6)	SMA Pro First Infant (UK)	Contains closer amino acid profile to that of breastmilk which is thought to help support appropriate growth	No. Breastmilk group not randomised	Same	Both claim and study relate to low protein formula. However in trial, both infant and follow on formula is used, with differing protein contents.	Claim implies breastmilk. Trial used high protein formula	Branched chain amino acids in plasma of infants and their breakdown products. Nothing about growth or comparing AA profile of formula milk to BM.	-	Not relevant	Independent funding and authorship with no relevant conflict of interests declared
NCT01148667(7)	Nutramigen with LGG (UK)	Faster resolution of CMA symptoms vs Nutramigen without LGG	Yes	Claim implies all infants with CMA, trial looked at infants with atopic dermatitis	Same - LGG	Consistent with claim	Atopic dermatitis after 3 months, using SCORAD but authors state no differences between the two groups	-	Not relevant	Part-funded by Mead Johnson Author(s) not affiliated to formula industry
NCT01285830(8)	Neocate Syneo (UK)	Gut microbiota dysbiosis in early infancy may delay oral tolerance, which can play an important role in the development of immune related conditions such as food allergy and atopic dermatitis	No. Trial is an RCT but this is an observational study looking at infants with and without IgE eczema	Infants with and without eczema	Both looked at probiotics, but different probiotics used in claim and in trial	Consistent with claim	Lower diversity of total gut microbiota in infants with eczema at age 1 month and 12 months	-	Not relevant	Part-funded by Biogaia Author(s) not affiliated to probiotic industry

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT00655720(9)	Nutramigen 2 DHA hypoallergen (Norway)	Nutramigen is documented to promote healthy growth and development of children with cow-milk allergy	No. Comparator was non randomised CDC growth chart	Claim regarding children with CMA. Study looks at healthy infants fully formula fed at age 14 days	Same - LGG	Claim implies CDC growth chart. Trial uses formula without LGG	Mean weight for all participants fell between the 25th - 75th centiles on the CDC weight-for-age growth chart	-	Not relevant	Funded by Mead-Johnson Author(s) affiliated to Mead-Johnson
NCT01634490(10)	Nutramigen with LGG (UK)	Clinical evidence demonstrates that the combination of Nutramigen with LGG® accelerates the return to milk† and reduces the incidence of other allergic manifestations‡ in infants with cow's milk allergy (CMA)	No. Open non randomised trial	Same	Same - EHCF with LGG	Consistent with claim	The rate of children acquiring oral tolerance to CMP in intervention group after 12 months was significantly higher (P <0.05)	-	Not relevant	No funder stated Authors declare no conflict of interest
NCT01808105(11)	SMA pro (UK)	Research suggests that infants fed a formula supplemented with structurally identical HMO 2'FL had immune markers closer to breast-fed infants	No. Comparison is with observational breastfed group.	Same - but in trial all subjects were exclusively formula fed by day 5, which is not common	Same - 2'FL. Though not clear in trial which 2-FL formula is being referred to.	Consistent with claim	Similar cytokine profile with breastmilk. Though no equivalence analysis shown.	-	Not relevant	Funded by Abbott Author(s) affiliated to Abbott
NCT01808105(11)	Similac Alimentum (South Africa)	Contains 2'-FL* for immune support in the gut and beyond	Yes	Same - but in trial all subjects were exclusively formula fed by day 5, which is not common	Same - 2'FL. Though not clear in trial which 2-FL formula is being referred to.	Consistent with claim	Multiple immune changes reported, although their relationship to infant health is not clear. Stool IgA assessments undertaken but not yet reported.	High	>60% of randomised subjects not included in analysis. Outcomes not mentioned in clinical trial registration record.	Funded by Abbott Author(s) affiliated to Abbott



Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT01808105(11)	Enfamil Neuro Pro Infant Gentlease, Similac Pro-Advance 20, Similac Pro Sensitive and Similac Pro Total Comfort 20 (USA)	2'-FL HMO: Shown to support a baby's immune health	Yes	Same - but in trial all subjects were exclusively formula fed by day 5, which is not common	Same - 2'FL. Though not clear in trial which 2-FL formula is being referred to.	Consistent with claim	Multiple immune changes reported, although their relationship to infant health is not clear.	High	>60% of randomised subjects not included in analysis. Outcomes not mentioned in clinical trial registration record.	Funded by Abbott Author(s) affiliated to Abbott
NCT00712608 (12)	Enfamil Reguline (USA)	Exclusive NaturalDefense Dual Prebiotic blend clinically proven to promote beneficial bacteria in the gut	Yes	Same – but in trial all subjects were exclusively formula fed by day 16	Same – PDX and GOS	Enfamil LIPIL used in trial, which is not hydrolysed. Enfamil Reguline is partially hydrolysed	No relevant outcome presented	High	10-20% of randomised participants appear to be inappropriately excluded from analysis	Funded by Mead Johnson Author(s) affiliated to Mead Johnson
NCT00712608 (12)	Enfamil Reguline (USA)	Exclusive NaturalDefense Dual Prebiotic blend clinically proven to... help support gut health	Yes	Same – but in trial all subjects were exclusively formula fed by day 16	Same – PDX and GOS	Enfamil LIPIL used in trial, which is not hydrolysed. Enfamil Reguline is partially hydrolysed	Significant increase in stool frequency reported at 1 of 4 timepoints; and significantly looser stools reported at 2 of 4 timepoints. No differences reported in growth, gassiness, fussiness or formula intake between groups	High	10-20% of randomised participants appear to be inappropriately excluded from analysis	Funded by Mead Johnson Author(s) affiliated to Mead Johnson

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT00941564(13,14)	Similac Advance (South Africa)	No palm oil foreasy digestion	Yes	Same	Same	Nestle Nan Pro which contained palm olein, palm kernel, canola oils and higher levels of calcium and phosphorus	Trial reports differences in calcium absorption and in stool consistency	Some concerns		Funded by Abbott Author(s) affiliated to Abbott
NCT01119170 (15,16)	Nan SpecialPro Lactose Free (South Africa)	Contains L. reuteri (10 <sup>6</sup> cfu/g) which promotes healthy gut microbiota	Yes	Same – but in trial almost all subjects appear to have been exclusively formula fed from less than 72 hours age, which is not common	Same	Formula used in trial not stated, and no mention of formula being lactose free	Bifidobacteria and Lactobacilli reported	High	≥34% of missing outcome data relevant outcomes, for unclear reasons, with asymmetric losses between treatment groups	Funded by Nestlé Author(s) affiliated to Nestlé
NCT00893711 (17)	Nan SpecialPro Sensitive (South Africa)	Active Limosilactobacillus reuteri cultures have a proven anti-colic effect and improve gut comfort	Yes	Same	Trial intervention was an unspecified dose of L. reuteri in oil administered as drops 30 minutes before a feed	Sunflower oil and medium-chain triglyceride oil	Crying time reported in manuscript	High	No prospective trial registration and incomplete reporting of crying time outcomes	Funded by BioGaia AB Author(s) not affiliated to formula industry

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT00893711(17)	Nan Lactogen 1 (South Africa)	Limosilactobacillus reuteri (13 <sup>6</sup> cfu/100 ml) is the only proven lactic acid producing culture to reduce crying time in colicky babies	Yes	Same	Trial intervention was an unspecified dose of L. reuteri in oil administered as drops 30 minutes before a feed	Sunflower oil and medium-chain triglyceride oil	Crying time reported in manuscript	High	No prospective trial registration and incomplete reporting of crying time outcomes	Funded by BioGaia AB Author(s) not affiliated to formula industry
NCT00893711(17)	Nan Lactogen 1 (South Africa)	Limosilactobacillus reuteri (13 <sup>6</sup> cfu/100 ml) is the only proven lactic acid producing culture to reduce crying time in colicky babies	Yes	Same	Trial intervention was an unspecified dose of L. reuteri in oil administered as drops 30 minutes before a feed	Sunflower oil and medium-chain triglyceride oil	No description of colonising the digestive tract in publication	High	No prospective trial registration and incomplete outcome reporting	Funded by BioGaia AB Author(s) not affiliated to formula industry
NCT02456831 (18)	Similac Isomil soy (Saudi Arabia)	Clinically shown to reduce fussiness, gas in infants experiencing general intolerance on cow's milk formula	Yes	Same	Trial intervention was similac isomil soy formula with iron	Trial comparators were 5% and 10% hydrolysed soya formula products	Trial reports non-significant differences between groups in fussiness and gas in favour of Similac Isomil soy	High	No prospective trial registration. Over 30% of randomised participants missing from analysis, at least some of which appears to be related to the outcomes and not intention to treat analysis..	Funded by Abbott Author(s) affiliated to Abbott

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT00503789(19)	Enfamil AR and Enfamil Reguline (USA)	Prebiotic blend... to promote soft stools; help support gut health and promote soft, comfortable stools in 1 week	Yes	Same	Same	Enfamil LIPIL used in trial, which is not hydrolysed or thickened. Enfamil Reguline is partially hydrolysed and Enfamil AR includes starch thickener	Stool characteristics and bifidobacterial/lactobacilli reported in manuscripts	High	Significant number of participants appear to have been inappropriately excluded from analysis	Funded by Mead Johnson Author(s) affiliated to Mead Johnson
NCT00503789(19,20)	Enfamil Neuro Pro Infant, Enfamil Enspire Infant, Enfamil Infant, Enfamil AR and Enfamil Reguline (USA)	Prebiotic blend... support immune health by promoting the growth of beneficial bacteria (bifidobacteria and lactobacilli)	Yes	Same	Same	Enfamil LIPIL used in trial, which is not hydrolysed or thickened. Enfamil Reguline is partially hydrolysed and Enfamil AR includes starch thickener	Stool bifidobacteria and lactobacilli reported in manuscripts. Immune outcomes not reported.	High	Significant number of participants appear to have been inappropriately excluded from analysis	Funded by Mead Johnson Author(s) affiliated to Mead Johnson

<b>Trial registration</b>	<b>Product in claim</b>	<b>Claims cited to trial reference</b>	<b>Claim related to randomised comparison?</b>	<b>Relevance of trial population</b>	<b>Relevance of trial intervention</b>	<b>Relevance of trial comparator</b>	<b>Relevance of trial outcome</b>	<b>ROB</b>	<b>Key ROB issues</b>	<b>Trial conflict of interest</b>
NTR2726(21)	Aptamil Premium (South Africa)	Supports the natural development of a healthy microbiota	Yes	Same	Same	Aptamil premium is a partially hydrolysed, lactose-reduced formula with prebiotic. Trial intervention was a prebiotic supplemented, non-hydrolysed, lactose-based formula	Stool bifidobacteria and other genera reported in manuscript	High	Per protocol analysis on less than half of randomised participants	Funded by Danone Nutricia Author(s) affiliated to Danone Nutricia
NTR2838(22)	Aptamil Prosyneo (South Africa)	Restores balance of challenged gut microbiota	Yes	Same	Same	Same	Stool bifidobacteria count	Some concerns		Funded by Danone Nutricia Author(s) affiliated to Danone Nutricia
ACTRN12608000047392(23)	Nanny (Russia)	The formation of healthy digestion and normal microbiocenosis (the role of food components)	Yes	Same	Same - goats milk	Consistent with claim	Lachnospiraceae compositions of the faeces of babies fed goat-milk were more similar to those of breast milk-fed infants than were those of cow milk-fed babies	High	70% of randomised subjects not included in analysis. No imputation or selection process described.	Funded by Dairy Goat Cooperative Author(s) affiliated to Dairy Goat Cooperative

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT01891916(24)	Enfamil Nutramigen with Enflora LGG (USA)	Nutramigen with Probiotic LGG is the only formula with two published studies showing the reduction in the incidence of allergic manifestations like asthma and eczema	Yes	Same	Same - LGG	Consistent with claim	Reduced absolute risk difference for the occurrence of at least 1 allergic manifestation over 36 months	High	28% missing data from total randomised subjects, 18% due to exclusion at diagnostic DBPCFC. Post-randomisation exclusion of participants based on DBPCFC is not mentioned in trial registration or protocol.	Independently funded, formula supplied by Mead Johnson  Author conflict of interest related to formula industry
ACTRN12610000566033(25)	Enfamil Nutramigen with Enflora LGG (USA)	Nutramigen with Probiotic LGG is the only formula with two published studies showing the reduction in the incidence of allergic manifestations like asthma and eczema	Yes	Same	Same - LGG	Consistent with claim	Allergic manifestations like asthma and eczema are not reported in the cited publication	High	31% of subjects missing from analysis. Participants were excluded after randomisation based on the outcome of a DBPCFC. It is not clear whether this was a justified exclusion of non-eligible participants. In the manuscript and the retrospective clinical trial registry, the relevant inclusion criterion is 'suspected CMA'.	Part-funded by Mead Johnson  Author(s) not affiliated to formula industry
ACTRN12610000566033(25)	Enfamil Nutramigen with Enflora LGG (USA)	Fast return to milk protein. Helps infants consume milk protein without an allergic reaction in as little as 6 months of feeding	Yes	Same	Same - LGG	Consistent with claim	Higher probability of acquiring tolerance to CMP at 6 and 12 months in intervention group	High	31% of subjects missing from analysis. Participants were excluded after randomisation based on the outcome of a DBPCFC. It is not clear whether this was a justified exclusion of non-eligible participants. In the	Part-funded by Mead Johnson  Author(s) not affiliated to formula industry

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
ACTRN12610000566033(25)	Nutramigen with LGG (UK)	8 out of 10 infants get back to milk after 12 months of use	Yes	Same	Same - LGG	Consistent with claim	Higher probability of acquiring tolerance to CMP at 6 and 12 months in intervention group	High	manuscript and the retrospective clinical trial registry, the relevant inclusion criterion is 'suspected CMA'.  31% of subjects missing from analysis. Participants were excluded after randomisation based on the outcome of a DBPCFC. It is not clear whether this was a justified exclusion of non-eligible participants. In the manuscript and the retrospective clinical trial registry, the relevant inclusion criterion is 'suspected CMA'.	Part-funded by Mead Johnson  Author(s) not affiliated to formula industry
NCT00338689(26)	SMA Advanced Infant formula (UK)	Available evidence from The Childhood Obesity Project Study, a large independent Randomised Controlled Trial (RCT), suggests that higher protein intakes increase plasma and tissue levels of insulin-releasing amino acids and of insulin and insulin-like growth factor 1 (IGF-1), and thereby increase weight gain and adipogenic activity	Yes	Same	Both claim and study relate to low protein formula. However in trial, both infant and follow on formula is used, with differing protein contents. Unclear which product used in trial	Consistent with claim	z-score for estimated difference of BMI between formula groups was 0.23 at 24 months (CI 0.089-0.36)	High	44% missing data at 24 months. At least 15% excluded inappropriately.	Independent funding and authorship with no relevant conflict of interests declared  Danone were a partner in the project and provided formula

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT00338689(27)	SMA Advanced First infant milk and SMA Pro First infant milk (UK)	Available evidence from The Childhood Obesity Project Study, a large independent Randomised Controlled Trial (RCT), suggests that higher protein intakes increase plasma and tissue levels of insulin-releasing amino acids and of insulin and insulin-like growth factor I (IGF-I), and thereby increase weight gain and adipogenic activity	Yes	Same	Same - low protein formula. However in trial, both infant and follow on formula is used, with differing protein contents.	Consistent with claim	Reduced BMI z scores at 6 years	High	52% missing data at 6 years. At least 16% excluded inappropriately.	Independent funding and authorship with no declared author conflict of interests  Danone were a partner in the project and provided formula
NCT00624689(28)	Enfamil Enspire Infant Gentlease (USA)	Milk fat globule membrane (MFGM) provides brain-building benefits and is shown to support cognitive outcomes at 12 months	Yes	Same	Same - MFGM.	Consistent with claim	Improved cognitive development at 12 months of age, using the Bayley Scales of Infant and Toddler Development (p=0.008).	High	12% of randomised subjects excluded from analysis, unclear reasons. Not clear if outcome assessors blinded to intervention at the 12 month outcome.	Part-funded by Semper AB  Author(s) not affiliated to formula industry
NCT00624689(28)	Semper Baby Nutra defence (Russia)	Clinically proven: the use of milk formula with MFGM & Milk fat ... significantly increases the cognitive development of infants compared with infants who received the milk formula without MFGM	Yes	Same	Same - MFGM.	Consistent with claim	Improved cognitive development at 12 months of age, using the Bayley Scales of Infant and Toddler Development (p=0.008).	High	12% of randomised subjects excluded from analysis, unclear reasons. Not clear if outcome assessors blinded to intervention at the 12 month outcome.	Part-funded by Semper AB  Author(s) not affiliated to formula industry



Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT00624689(29)	Semper Baby Nutra defence (Russia)	Clinically proven: the use of milk formula with MFGM & Milk fat reduces the frequency of infections ... of infants compared with infants who received the milk formula without MFGM	Yes	Same	Same - MFGM.	Consistent with claim	Lower incidence of acute otitis media up to age 6 months (p=0.034).	High	High risk of bias in selecting results. Of the 6 infections looked at, only AOM had a favourable result - and this was only at 6 months. At 12 months there were no favourable results which support the claim	Part-funded by Semper AB Author(s) not affiliated to formula industry
NCT00664768(30)	Neocate Syneo (USA)	Clinically shown to: Support growth and development	Yes	Same	Same - probiotics	Consistent with claim	Week 16 growth measurements with 90% confidence intervals were similar to the control group	High	Growth data appear to be selectively reported, without presenting the per protocol analysis which would be usual for a growth equivalence study	Funded by Danone Nutricia Author(s) affiliated to Danone Nutricia
NCT00664768(30)	Neocate Syneo (USA)	Clinically shown to: Effectively resolve food allergy symptoms	Yes	Same	Same - probiotics	Consistent with claim	Study formulas were well accepted. Severity of allergy symptoms decreased with time and no significant differences were observed between groups.	High	No data presented and these outcomes were not stated in the trial registration record.	Funded by Danone Nutricia Author(s) affiliated to Danone Nutricia
NCT00664768(30)	Neocate Syneo (UK)	Influences the diversity and abundance of gut microbiota	Yes	Same	Same - probiotics	Consistent with claim	Increased bifidobacteria as mean % of total bacteria in intervention group at 16 weeks (p<0.001)	High	Inappropriate ITT analysis - 34% of subjects excluded. Unclear reasons for all exclusions. At least 9% were inappropriately excluded for ITT analysis	Funded by Danone Nutricia Author(s) affiliated to Danone Nutricia

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT00716105(31)	SMA Pro Follow-on (UK)	Specially designed to help support appropriate growth	Yes	Same	Same - low protein formula	Consistent with claim	Weight gain (g/day) from 3 to 6 months was similar in the intervention and control groups (EXPL-CTRL -0.84 g/day; 95% confidence interval - 2.25 to 0.57)	High	Analyses are all undertaken on the ITT dataset, without a PP analysis, which is unusual for a non-inferiority trial and suggests selection of the result on the basis of the findings.	Funded by Nestlé Author(s) affiliated to Nestlé
NCT00753818(32)	Pregestimil Lipil (UK)	clinically proven to support brain and eye development	Yes	Same	Same - DHA	Consistent with claim	Visual evoked potential (VEP) visual acuity at 12 months better in intervention group (p < 0.001)	High	Per protocol analysis used in study instead of ITT. 30% of data missing	Funded by Mead-Johnson Author(s) affiliated to Mead-Johnson
NCT00753818(33)	Enfamil Infant and other Enfamil products (USA)	Support cognitive and visual development	Yes	Same	Same - DHA	Consistent with claim	Improved cognitive development in intervention group - assessed by rule-learning and inhibition tasks and the Peabody Picture Vocabulary Test at 5 years	High	Not an appropriate ITT analysis. Over 40% of subjects excluded inappropriately. 9 different cognitive assessment scales used at 1-4 timepoints. No difference was seen for most assessments and at second study site. Primary assessment and timepoint of interest not specified.	Funded by Mead-Johnson Author(s) affiliated to Mead-Johnson

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT00753818(33)	Enfamil Infant and other Enfamil products (USA)	Promote long-term cognitive outcomes through 5 years of age	Yes	Same	Same - DHA	Consistent with claim	Improved cognitive development in intervention group - assessed by rule-learning and inhibition tasks and the Peabody Picture Vocabulary Test at 5 years	High	Not an appropriate ITT analysis. Over 40% of subjects excluded inappropriately. 9 different cognitive assessment scales used at 1-4 timepoints. No difference was seen for most assessments and at second study site. Primary assessment and timepoint of interest not specified.	Funded by Mead-Johnson Author(s) affiliated to Mead-Johnson
NCT00753818(33)	Pregestamil Lipil (UK)	clinically proven to support brain and eye development	Yes	Same	Same - DHA	Consistent with claim	Improved cognitive development in intervention group - assessed by rule-learning and inhibition tasks and the Peabody Picture Vocabulary Test at 5 years	High	Not an appropriate ITT analysis. Over 40% of subjects excluded inappropriately. 9 different cognitive assessment scales used at 1-4 timepoints. No difference was seen for most assessments and at second study site. Primary assessment and timepoint of interest not specified.	Funded by Mead-Johnson Author(s) affiliated to Mead-Johnson
NCT00820833(34)	SMA pro (UK)	Specially designed to help support appropriate growth	Yes	Study evaluated infants of overweight mothers. Product in claim aimed at all infants	Same - low protein formula	Consistent with claim	Unclear what is meant by 'appropriate growth'. Trial shows reduced weight gain between 3-6 months of age as desired outcome of intervention (p = 0.024)	High	No mention of allocation sequence concealment. 17% missing data from randomised subjects. Study retrospectively registered.	Funded by Nestlé Author(s) affiliated to Nestlé

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT01215656(35)	Hipp Combiotic (Russia)	Inspired by breast milk, breast milk probiotics, for the immune system, for brain development. The effectiveness of the combination of L. fermentum hereditum and GOS are clinically confirmed	Yes	Same	Same - L. fermentum. Unclear which brand used in trial though "standard powdered follow-on"	Consistent with claim	Reduced incidence in GI infections (p=0.032) and URTIs (p=0.026) between age 6-12 months	High	Inappropriate ITT analysis - 13% subjects excluded.	Funded by Puleva Food Author(s) affiliated to Puleva Food
NCT01346644(36)	Hipp Combiotic (Russia)	Inspired by breast milk, breast milk probiotics, for the immune system, for brain development. The effectiveness of the combination of L. fermentum hereditum and GOS are clinically confirmed	Yes	Same	Same - L. fermentum. Unclear which brand used in trial	Consistent with claim	The incidence rate of gastrointestinal infections in infants of the control group was 3 times higher than in the probiotic group (p = 0.018) at 6 months of age	High	End point recorded in registry as 36 months, but paper only showed results to 6 months. Another associated paper which did follow up to 36 months showed unfavourable results.	Funded by Puleva Food and HiPP Author(s) affiliated to Puleva Food and HiPP
NCT01569776(37)	SMA Alfamino (UK)	Severe symptom management (in context of allergy)	Yes	Same	Same - amino acid formula	Consistent with claim	Hypoallergenicity measured by 2 x DBPCFCs two weeks apart (crossover trial)	High	10.8% missing data due to non-adherence. Only simple per protocol analysis used	Funded by Nestlé Author(s) affiliated to Nestlé
NCT01583673(38)	Alfamino Infant (USA)	Clinically demonstrated in healthy infants to promote adequate growth.	Yes	Same	Unclear if same brand in trial as in claim	Consistent with claim	Mean WHO weight-for-age z-scores were negative (<0) up to 4 months of age, however weight gain was equivalent between intervention and control	High	48% missing data. Poor adherence to intervention with no analysis to estimate the effect of adhering to intervention	Funded by Nestlé Author(s) affiliated to Nestlé
NCT01583673(38)	SMA Alfamino (UK)	SMA Alfamino® is nutritionally complete* and is designed to support growth, tolerance and absorption in the most	Yes	Claim implies product is aimed for children with allergies but trial uses healthy infants	Unclear if same brand in trial as in claim	Consistent with claim	Mean WHO weight-for-age z-scores were negative (<0) up to 4 months of age, however weight gain was equivalent	High	48% missing data. Poor adherence to intervention with no analysis to estimate the effect of adhering to intervention	Funded by Nestlé Author(s) affiliated to Nestlé

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT01715246(39)	NAN Supreme 1 (South Africa)	challenging allergy conditions.  2'-FL and LNnT may help reduce the risk of diarrhoea	Yes	Same	Same - 2'Fl and LNnT. Unclear which brand used in trial	Consistent with claim	between intervention and control  No significant difference between groups in proportion of stools in each consistency category, or in stool frequency. At 1 timepoint a single continuous measure of stool softness was significantly lower in the intervention group than the control group.	High	17% of randomised participants excluded from analysis and only simple per protocol analysis used	Funded by Nestlé  Author(s) affiliated to Nestlé
NCT01715246(39)	Signature ProCare with Dual HMO's, Non-GMO Infant Formula (US)	Human Milk Oligosaccharides (HMOs, not from human milk) are prebiotics that support baby's immunity ... by encouraging growth of beneficial bacteria in the gut. ProCare boosted 2'-FL HMO to a level that aligns with mother's milk and added LNnT, another HMO naturally occurring in breast milk. We chose them because studies show that these two abundant HMOs work better together to support baby's ... developing immune system	Yes	Same	Same - 2'Fl and LNnT. Unclear which brand used in trial	Consistent with claim	Statistically significant differences between groups in favour of the intervention in the specific outcomes bronchitis and lower respiratory tract infection, which were not specified in the trial registration	High	17% of randomised participants excluded from analysis and only simple per protocol analysis used	Funded by Nestlé  Author(s) affiliated to Nestlé

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT01715246(39)	Signature ProCare with Dual HMO's, Non-GMO Infant Formula (US)	Human Milk Oligosaccharides (HMOs, not from human milk) are prebiotics that support baby's ... digestive health by encouraging growth of beneficial bacteria in the gut. ProCare boosted 2'-FLHMO to a level that aligns with mother's milk and added LNnT, another HMO naturally occurring in breast milk. We chose them because studies show that these two abundant HMOs work better together to support baby's digestive comfort	Yes	Same	Same - 2'Fl and LNnT. Unclear which brand used in trial	Consistent with claim	In a subgroup analysis the outcome colic was significantly less frequent at one timepoint in the intervention group. Colic was not specified as an outcome in the trial registration.	High	17% of randomised participants excluded from analysis and only simple per protocol analysis used	Funded by Nestlé Author(s) affiliated to Nestlé
NCT01715246(39)	SMA Advanced First Infant Milk (UK)	Shown to be safe, well tolerated, and support a ge-appropriate growth	Yes	Same	Same - 2'Fl and LNnT. Unclear which brand used in trial	Consistent with claim	z scores for BMI and weight for age/length for age/HC for age did not differ significantly between the groups at any study visit and tracked closely with the WHO growth standards.	High	17% of randomised participants excluded from analysis and only simple per protocol analysis used	Funded by Nestlé Author(s) affiliated to Nestlé
NCT01808105(11,40)	Similac Alimentum (UK)	Help support the immune needs of infants with CMA in the gut and beyond.	Yes	Same	Same - 2'FL. Unclear which brand used in trial	Consistent with claim	Similar cytokine profile with breastmilk. Though no equivalence analysis done and unclear how this 'helps support the immune needs of infants'	High	63% of randomised subjects excluded from analysis.	Funded by Abbott Author(s) affiliated to Abbott

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT01808105(11,40)	Similac Gold (Russia)	The effectiveness is clinically proved: Similac Gold is the first in Russia infant formula with oligosaccharides of breast milk 2'-FL which is the unique ingredient, providing the immune system strengthening, previously found only in breast milk.	Yes	Same	Same - 2'FL. Unclear which brand used in trial	Consistent with claim	Similar cytokine profile to breastmilk up to 4 months of age - unclear how this provides "immune strengthening"	High	63% of randomised subjects excluded from analysis.	Funded by Abbott Author(s) affiliated to Abbott
NCT01861600(41)	SMA Comfort (UK)	SN-2-enriched fat blend to help promote softer stools	Yes	Same	Both claim and trial evaluate SN-2, but trial uses S-26 Gold according to trial registry, and claim is for SMA Comfort	Consistent with claim	Softer stools at week 8. (20% more mushy soft stools, P= 0.026; 50% fewer formed stools, P=0.003).	High	Trial registered 4 years after study start date. No mention of primary outcome (stool softness) in registry, so high risk of selecting results based on findings.	Funded by Nestlé Author(s) affiliated to Nestlé
NCT01891916(24)	Nutramigen with LGG (UK)	~50% reduction in the incidence of ≥1 other allergic manifestation compared to Nutramigen alone during a period of 3 year	Yes	Same	Yes - LGG	Consistent with claim	Reduced absolute risk difference for the occurrence of at least 1 allergic manifestation over 36 months	High	28% missing data from total randomised subjects, 18% due to exclusion at diagnostic DBPCFC. Post-randomisation exclusion of participants based on DBPCFC is not mentioned in trial registration or protocol.	Independently funded, formula supplied by Mead Johnson Author conflict of interest related to formula industry
NTR2521(42)	Cow&Gate Hungry first infant (UK)	Prebiotic oligosaccharides (scGOS/lcFOS* in a 9:1 ratio). This specific prebiotic blend encourages the growth and activity of beneficial bacteria in the infant gut, and improves stool frequency and consistency	Yes	Same	Same - prebiotics (FOS/GOS). unclear which brand used in trial - "commercially available" formula	Consistent with claim	Softer stools at 17 weeks. Nothing on stool frequency	High	Number included in analysis unclear, but potentially 37% missing from randomised subjects. Some are inappropriate exclusions (adverse effects).	Funded by Nutricia Research Author(s) affiliated to Nutricia Research

Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
									Unclear how missing data were handled	
NTR3979(43)	Neocate Syneo (UK)	Typical gut microbiota of cow's milk allergic infants: lower levels of infant-like Bifidobacteria species	Unclear	Same	Same - synbiotics (FOS + bifidobacterium)	Consistent with claim	Unclear outcome - we have assessed bifidobacteria as % of total bacteria at week 8 (p<0.001)	High	10% dropout from randomised subjects. Outcome only reported as % of bacteria in stool samples. The absolute counts of bifidobacteria using FISH, which is specified in the trial registry as the primary outcome, was not reported.	Funded by Danone Nutricia Author(s) affiliated to Danone Nutricia
NCT01956682(44)	SMA Anti-reflux (UK)	Unique combination of easily digestible starch and 100% whey, partially hydrolysed protein, to help manage reflux and regurgitation	Yes	Same	Product in claim is SMA anti-reflux, and has no probiotics. Brand in trial is Nan AR and contains probiotics	Consistent with claim	Reduced mean number of daily regurgitation episodes over 4 weeks (p< 0.0001)	Some concerns		Independently funded Author conflict of interest related to formula industry



Trial registration	Product in claim	Claims cited to trial reference	Claim related to randomised comparison?	Relevance of trial population	Relevance of trial intervention	Relevance of trial comparator	Relevance of trial outcome	ROB	Key ROB issues	Trial conflict of interest
NCT01956682(44)	NAN Specialpro Anti regurgitation (South Africa)	Contains a combination of ingredients: OPTIPRO®, Limosilactobacillus reuteri (lactic acid producing culture), corn starch and potato starch, scientifically proven for the management of regurgitation.	Yes	Same	Product in claim is not hydrolysed. Trial intervention was partially hydrolysed whey formula	Consistent with claim	Reduced mean number of daily regurgitation episodes over 4 weeks (p< 0.0001)	Some concerns		Independently funded Author conflict of interest related to formula industry
NCT01956682(44)	NAN Specialpro Anti regurgitation (South Africa)	Active Lactobacillus reuteri cultures which have a proven anti-regurgitation effect and promote gut maturation.	Yes	Same	Claim relates to Lactobacillus reuteri only. Trial intervention was multifaceted, combining partially hydrolysed whey formula, starch thickener and Lactobacillus reuteri.	Consistent with claim	Reduced mean number of daily regurgitation episodes over 4 weeks (p< 0.0001)	Some concerns		Independently funded Author conflict of interest related to formula industry

AA, amino acid based infant formula; BM, breast milk; BMI, body mass index; CI, confidence interval; CDC, Centers for Disease Control and Prevention; CMA, cow's milk allergy; CMP, cow's milk protein; DBPCFC, double-blind placebo-controlled food challenge; DHA, docosahexaenoic acid; FOS, fructo-oligosaccharides; GOS, galacto-oligosaccharides; HC, head circumference; IgE, immunoglobulin E; ITT, intention to treat analysis; LGG, L. Rhamnosus GG; MFGM, milk fat globule membrane; NCT, national clinical trial number; PP, per protocol analysis; RCT, randomised controlled trial; SCORAD, SCORing Atopic Dermatitis scale; UK, United Kingdom; URTI, upper respiratory tract infection.

Supplementary Table 8. Risk of bias assessments of systematic reviews (ROBIS)

AA, arachidonic acid.; DHA, docosahexaenoic acid; IF, infant formula; LCPUFA, long-chain polyunsaturated fatty acid; ROBIS, Risk of Bias In Systematic Reviews; WHO, World Health Organization

Study	Claims cited to study reference	Product/ingredient within scope of systematic review?	Does the study address claim?	ROBIS risk of bias	Key ROBIS issues	Was the study funded by a company that could benefit from the outcome?	Were one or more of the authors affiliated with a company that could benefit from the outcome?
Lasekan 2017 (45)	No palm oil for easy digestion.	Yes	Unclear. The authors report results of a meta-analysis suggesting that NoPALM-based formulas may be associated with a softer stools compared with PALM-based. This is not necessarily indicative of being 'easy to digest'.	High	No study protocol or risk of bias assessment, and these weaknesses were not taken into account in interpretation of findings.	Yes	Yes
Birch 2010(46)	Shown to improve respiratory health through the first 3 years of life when infants were fed through 12 months	Yes	Yes	High	No study protocol or risk of bias assessment, purposive sampling.	Yes	Yes
Birch 2010 (46)	DHA is: Clinically proven† to support mental, visual and immune system development	Partially	Unclear. Authors assessed Blinded study nurses reviewed medical charts for upper respiratory infection (URI), wheezing, asthma, bronchiolitis, bronchitis, allergic rhinitis, allergic conjunctivitis, otitis media, sinusitis., atopic dermatitis (AD), and urticaria. Whether this can be considered an "immune system development" is unclear. However, the original study used on sweep visual evoked potential acuity, an objective measure of visual cortex maturity as primary outcomes.	High	No study protocol or risk of bias assessment, purposive sampling.	Yes	Yes
Drover 2009 (47)	Omega-3 DHA like that found in Enfamil has been	Yes	Yes. Children who have previously received supplemented infant formula had more intentional solutions	High	No predefined study protocol for pooled analysis	No (but donated IF)	No

	clinically shown to: 9-12 months improve attention span, problem solving, and visual development		(successful task completions) and higher intention scores (goal-directed behaviors) than controls.			and risk of bias assessment, purposive sampling.		
Alexander et al. 2016 (48)	Specially designed to help support appropriate growth / A lower protein content formula has been shown to provide growth rates more like a breastfed baby.	Partially. SMA Advanced is partially hydrolysed, which appears to be outside the scope of the reference	Yes. Evaluates whether whey-predominant infant formula with the stated protein content supports growth according to WHO growth standards.	High	No study protocol or risk of bias assessment.	Yes	Yes	
Alexander 2010 (49)	Reduces risk for atopic eczema by 55 %	Yes	Yes. Evaluates effect of partially hydrolysed whey protein on the development of atopic dermatitis.	High	No pre-specified protocol or risk of bias assessment. Search strategy likely to be inadequate.	Yes	Yes	
Czerkies 2018 (50)	Easy-to-digest	Yes	Not clear. Reports a pooled analysis suggesting that PHF-W feeding may lead to softer stools compared with CMF. This is not necessarily indicative of being 'easy to digest'.	High	No study protocol, search strategy or risk of bias assessment.	Yes	Yes	
Morale 2005 (51)	Contains 0.3% DHA of total fatty acids, the level approved by the EFSA for normal visual development until 12 months (with an intake of 100 mg DHA per day)	Partially. Ingredient is relevant, but trial products were standard formula, and claim is made for amino acid formula.	Yes. Data pooled from four trials evaluating LCPUFA and visual acuity.	High	No study protocol, search strategy or risk of bias assessment.	No (but donated IF in trials)	Yes	
Brenna 2007 (52)	DHA is an ingredient that supports brain development	No. Systematic review assesses breastmilk fatty acid concentrations; product is an infant formula with added fatty acids; there is no direct link between the claim and the referenced systematic review.	No. This descriptive meta-analysis evaluates DHA and AA in breast-milk world-wide. Thus, it is not an appropriate reference to substantiate the claim that an IF would help development of brain/eye/nervous system.	Not relevant				



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