Table 1 Characteristics of the study population according to the type of formula consumed at 2 months, Elfe study (n=8,389) [a]

	No LCPUFA enrichment	DHA/ARA only enrichment	DHA/ARA/EPA enrichment
n	**5,255**	**2,207**	**927**
Maternal age at delivery, years	30.9 ± 5.0	31.1 ± 4.8	31.0 ± 4.9
Maternal pre-pregnancy BMI, kg/m^2	23.7 ± 5.1	23.5 ± 4.9	23.6 ± 4.7
Mothers living in urban area, % (n)	75.9% (3,990)	77.1% (1,701)	80.6% (747)
Mothers with at least a Master's degree, % (n)	17.1% (901)	20.6% (455)	22.4% (208)
Employed mothers, % (n)	73.7% (3,873)	78.4% (1,731)	75.8% (703)
Monthly household income, euros	1610 ± 918	1738 ± 959	1783 ± 1272
Maternal smoking, % (n)			
Never smoker	53.7% (2,824)	54.5% (1,202)	56.9% (527)
Smoker only before pregnancy	24.3% (1,275)	25.7% (568)	25.1% (233)
Smoker only in early pregnancy	4.0% (212)	4.3% (96)	3.8% (35)
Smoker throughout pregnancy	18.0% (944)	15.5% (341)	14.2% (132)
n-3 fatty acids supplementation during pregnancy, % (n)	11.0% (579)	13.4% (296)	11.1% (103)
Maternal diet quality during pregnancy (PANDiet)	54.8 ± 9.0	55.0 ± 9.0	54.9 ± 9.1
Caesarean section, % (n)	19.4% (1,022)	19.2% (423)	20.6% (191)
Gestational age, wk	39.2 ± 1.5	39.2 ± 1.5	39.2 ± 1.5
Boys	51.8% (2721)	50.1% (1105)	49.2% (456)
Birth weight, % (n)			
Small weight for gestational age	10.0% (523)	10.1% (223)	10.6% (98)
Adequate weight for gestational age	79.9% (4,200)	80.4% (1,774)	80.6% (747)
Large weight for gestational age	10.1% (532)	9.5% (210)	8.8% (82)
First born, % (n)	46.2% (2,426)	47.9% (1,057)	45.7% (424)
Exclusively formula-fed infants at 2 months, % (n)	77.1% (4,052)	71.9% (1,587)	66.0% (612)
First physician consulted after hospital discharge, % (n)			
Paediatrician	34.5% (1,814)	40.1% (885)	38.8% (360)
Other child doctor	13.2% (696)	12.4% (273)	14.0% (130)
General practitioner	46.9% (2,463)	41.9% (924)	43.0% (398)
None/Other	5.4% (282)	5.6% (125)	4.2% (39)
Family history of allergic diseases, % (n)	54.1% (2,844)	55.9% (1,234)	56.7% (526)
Ever infection from 2 months to 5.5 years, % (n) [b]			
Gastrointestinal infection	13.2% (694)	13.5% (299)	13.9% (129)
Lower respiratory tract infection	37.7% (1,981)	39.1% (863)	35.4% (328)
Upper respiratory tract infection	31.6% (1,661)	34.9% (771)	30.6% (284)
Ever allergy or allergic symptoms from 2 months to 5.5 years, % (n)			
Wheezing	41.7% (2,190)	44.9% (992)	40.3% (374)
Itchy rash	45.7% (2,403)	45.9% (1,012)	46.8% (434)
Food allergy	6.2% (327)	6.9% (153)	4.9% (45)
Asthma medication [c]	41.2% (2,165)	44.1% (974)	38% (352)

ARA arachidonic acid; *BMI* Body mass index; *CU* Consumption unit; *DHA* docosahexaenoic acid; *EPA* Eicosapentaenoic acid; *LCPUFA* Long chain polyunsaturated fatty acids; *PANDiet* Probability of Adequate Nutrient Intake Dietary score

[a] Values are percentages (numbers) or means ± standard deviation as appropriate.

[b] Infections that required emergency consultation or hospitalization.

[c] From 0 to 3.5 years; data were not available at the 5.5-year follow-up.

Table 2 Adjusted associations between consumption of LCPUFA-enriched formula at 2 months and risk of infections in the overall sample and among exclusively formula-fed infants, Elfe study [a]

		Gastrointestinal infection		Lower respiratory tract infection		Upper respiratory tract infection	
	N	OR [95% CI]	NC	OR [95% CI]	NC	OR [95% CI]	NC
Overall sample (n=8,389)							
LCPUFA enrichment							
DHA-ARA							
Not enriched		1.00 [Ref]	694	1.00 [Ref]	1981	1.00 [Ref]	1661
Enriched	3134	1.06 [0.93; 1.21]	428	1.02 [0.93; 1.12]	1191	1.07 [0.97; 1.18]	1055
DHA-ARA-EPA							
Not enriched		1.00 [Ref]	993	1.00 [Ref]	2844	1.00 [Ref]	2432
Enriched	927	1.07 [0.88; 1.31]	129	0.89 [0.77; 1.03]	328	0.90 [0.78; 1.05]	284
LCPUFA content [b]							
DHA							
Not enriched		1.00 [Ref]	694	1.00 [Ref]	1981	1.00 [Ref]	1661
DHA <10 mg/100 kcal	1433	1.06 [0.89; 1.26]	199	**1.15 [1.02; 1.30]**	587	1.13 [1.00; 1.28]	495
DHA ≥10 mg/100 kcal	1024	0.92 [0.75; 1.13]	122	0.88 [0.76; 1.02]	355	0.99 [0.86; 1.15]	333
Enriched but DHA content unknown	677	1.27 [1.01; 1.60]	107	0.97 [0.82; 1.15]	249	1.05 [0.88; 1.25]	227
EPA							
Not enriched		1.00 [Ref]	993	1.00 [Ref]	2844	1.00 [Ref]	2432
EPA <3.2 mg/100 kcal	295	1.21 [0.87; 1.67]	46	0.94 [0.74; 1.21]	108	0.90 [0.70; 1.17]	86
EPA ≥3.2 mg/100 kcal	560	0.94 [0.72; 1.22]	69	**0.82 [0.68; 0.99]**	188	0.86 [0.71; 1.04]	170
Enriched but EPA content unknown	72	1.61 [0.88; 2.94]	14	1.24 [0.77; 1.99]	32	1.28 [0.79; 2.07]	28
Exclusively formula-fed infants (n=6,251)							
LCPUFA enrichment							
DHA-ARA							
Not enriched		1.00 [Ref]	533	1.00 [Ref]	1515	1.00 [Ref]	1258
Enriched	2199	1.01 [0.86; 1.18]	288	1.01 [0.91; 1.13]	823	1.10 [0.98; 1.23]	733
DHA-ARA-EPA							
Not enriched		1.00 [Ref]	730	1.00 [Ref]	2124	1.00 [Ref]	1822
Enriched	612	1.17 [0.92; 1.49]	91	0.89 [0.74; 1.06]	214	**0.80 [0.67; 0.97]**	169
LCPUFA content [b]							
DHA							
Not enriched		1.00 [Ref]	533	1.00 [Ref]	1515	1.00 [Ref]	1258
DHA <10 mg/100 kcal	1139	1.03 [0.85; 1.26]	154	1.14 [0.99; 1.31]	459	**1.17 [1.02; 1.35]**	396
DHA ≥10 mg/100 kcal	635	0.83 [0.63; 1.09]	70	0.87 [0.73; 1.04]	217	0.94 [0.78; 1.13]	191
Enriched but DHA content unknown	425	1.22 [0.91; 1.62]	64	0.90 [0.73; 1.12]	147	1.16 [0.93; 1.44]	146
EPA							
Not enriched		1.00 [Ref]	730	1.00 [Ref]	2124	1.00 [Ref]	1822
EPA <3.2 mg/100 kcal	231	**1.45 [1.02; 2.07]**	41	0.98 [0.74; 1.29]	86	0.80 [0.59; 1.08]	62
EPA ≥3.2 mg/100 kcal	317	0.85 [0.59; 1.23]	36	**0.77 [0.60; 0.98]**	100	**0.74 [0.57; 0.97]**	84
Enriched but EPA content unknown	64	1.91 [1.03; 3.53]	14	1.22 [0.73; 2.02]	28	1.16 [0.69; 1.95]	23

DHA docosahexaenoic acid; *EPA* eicosapentaenoic acid; *LCPUFA* polyunsaturated fatty acids; *NC* number of cases

[a] Values are odd ratios [95% confidence intervals] adjusted for child characteristics (sex, gestational age, caesarean section, birth weight category, child's physician type, presence of siblings, age at infant formula introduction), maternal and household characteristics (age, education level, city size, region of residence, employment status in early pregnancy, pre-pregnancy body mass index, smoking status, diet quality during pregnancy, n-3 PUFA supplementation during pregnancy, household income and family history of allergy) and Elfe study design variables (recruitment wave, maternity size). Separate logistic regressions for each outcome and LCPUFA variable.

[b] DHA and EPA enrichment levels were categorized using the median value.

Table 3 Adjusted associations between consumption of LCPUFA-enriched formula at 2 months and risk of allergies in the overall sample and among exclusively formula-fed infants, Elfe study [a]

		Wheezing		Asthma medications		Itchy rash		Food allergy	
	N	OR [95% CI]	NC	OR [95% CI]	NC	OR [95% CI]	NC	OR [95% CI]	NC
Overall sample (n=8,389)									
LCPUFA enrichment									
DHA-ARA									
Not enriched		1.00 [Ref]	2190	1.00 [Ref]	2165	1.00 [Ref]	2403	1.00 [Ref]	327
Enriched	3134	1.08 [0.98; 1.18]	1366	1.04 [0.95; 1.15]	1326	1.00 [0.91; 1.09]	1446	1.01 [0.84; 1.21]	198
DHA-ARA-EPA									
Not enriched		1.00 [Ref]	3182	1.00 [Ref]	3139	1.00 [Ref]	3415	1.00 [Ref]	480
Enriched	927	0.91 [0.79; 1.05]	374	**0.84 [0.73; 0.97]**	352	1.02 [0.89; 1.18]	434	0.73 [0.53; 1.00]	45
LCPUFA content [b]									
DHA									
Not enriched		1.00 [Ref]	2190	1.00 [Ref]	2165	1.00 [Ref]	2403	1.00 [Ref]	327
DHA <10 mg/100 kcal	1433	**1.20 [1.07; 1.36]**	658	1.13 [1.00; 1.28]	631	0.98 [0.87; 1.10]	654	1.12 [0.89; 1.42]	99
DHA ≥10 mg/100 kcal	1024	0.93 [0.81; 1.07]	415	0.88 [0.76; 1.01]	394	1.00 [0.87; 1.14]	474	0.80 [0.59; 1.09]	53
Enriched but DHA content unknown	677	1.06 [0.89; 1.25]	293	1.14 [0.96; 1.34]	301	1.04 [0.88; 1.22]	318	1.09 [0.79; 1.50]	46
EPA									
Not enriched		1.00 [Ref]	3182	1.00 [Ref]	3139	1.00 [Ref]	3415	1.00 [Ref]	480
EPA <3.2 mg/100 kcal	295	0.90 [0.71; 1.15]	117	0.91 [0.71; 1.16]	117	0.91 [0.71; 1.15]	128	0.62 [0.34; 1.11]	12
EPA ≥3.2 mg/100 kcal	560	0.85 [0.71; 1.01]	218	**0.73 [0.61; 0.88]**	196	1.05 [0.88; 1.25]	267	0.80 [0.54; 1.17]	30
Enriched but EPA content unknown	72	1.59 [0.99; 2.56]	39	1.64 [1.02; 2.64]	39	1.42 [0.88; 2.27]	39	0.63 [0.20; 2.03]	3
Exclusively formula-fed infants (n =6,251)									
LCPUFA enrichment									
DHA-ARA									
Not enriched		1.00 [Ref]	1664	1.00 [Ref]	1684	1.00 [Ref]	1816	1.00 [Ref]	239
Enriched	2199	1.05 [0.94; 1.17]	929	0.98 [0.88; 1.09]	905	1.03 [0.92; 1.14]	1012	1.03 [0.83; 1.29]	133
DHA-ARA-EPA									
Not enriched		1.00 [Ref]	2348	1.00 [Ref]	2354	1.00 [Ref]	2530	1.00 [Ref]	340
Enriched	612	0.94 [0.79; 1.12]	245	0.87 [0.73; 1.03]	235	1.15 [0.97; 1.36]	298	0.85 [0.58; 1.24]	32
LCPUFA content [b]									
DHA									
Not enriched		1.00 [Ref]	1664	1.00 [Ref]	1684	1.00 [Ref]	1816	1.00 [Ref]	239
DHA <10 mg/100 kcal	1139	**1.16 [1.01; 1.33]**	509	1.04 [0.91; 1.20]	484	1.00 [0.88; 1.15]	519	1.06 [0.81; 1.40]	72
DHA ≥10 mg/100 kcal	635	0.93 [0.78; 1.11]	251	0.86 [0.72; 1.02]	242	1.00 [0.84; 1.19]	288	0.85 [0.58; 1.25]	32
Enriched but DHA content unknown	425	0.94 [0.76; 1.16]	169	1.02 [0.82; 1.25]	179	1.14 [0.93; 1.40]	205	1.22 [0.81; 1.83]	29
EPA									
Not enriched		1.00 [Ref]	2348	1.00 [Ref]	2354	1.00 [Ref]	2530	1.00 [Ref]	340
EPA <3.2 mg/100 kcal	231	0.98 [0.74; 1.28]	95	0.94 [0.72; 1.24]	94	1.04 [0.80; 1.37]	106	0.69 [0.36; 1.33]	10
EPA ≥3.2 mg/100 kcal	317	0.83 [0.65; 1.06]	117	**0.72 [0.56; 0.92]**	108	1.18 [0.94; 1.49]	158	1.04 [0.65; 1.68]	20
Enriched but EPA content unknown	64	1.47 [0.89; 2.44]	33	1.50 [0.90; 2.48]	33	1.40 [0.85; 2.31]	34	0.50 [0.12; 2.07]	2

DHA docosahexaenoic acid; *EPA* eicosapentaenoic acid; *LCPUFA* polyunsaturated fatty acids; *NC* number of cases

[a] Values are odd ratios [95% confidence intervals] adjusted for child characteristics (sex, gestational age, caesarean section, birth weight category, child's physician type, presence of siblings, age at infant formula introduction), maternal and household characteristics (age, education level, city size, region of residence, employment status in early pregnancy, pre-pregnancy body mass index, smoking status, diet quality during pregnancy, n-3 PUFA supplementation during pregnancy, household income and family history of allergy) and Elfe study design variables (recruitment wave, maternity size). Separate logistic regressions for each outcome and LCPUFA variable.

[b] DHA and EPA enrichment levels were categorized using the median value.