Supplementary material to the submission/revision: BJN-22-0692.R1

Manuscript title: "Hydrolysed proteins in infant formula and child neurodevelopment up to the age of 3.5 years: the nationwide ELFE birth cohort"

Table S1. Terms used to classify infant formula according to their protein hydrolysis level

|  |  |  |
| --- | --- | --- |
| IF category | Exemples of claims related to the protein hydrolysis level | Ingredient list related to proteins |
| nHF | - none | Skimmed/whole milk  Whey  Casein  soluble milk proteins  soy protein isolate |
| pHF/non-HA | - none  - slightly hydrolysed soluble proteins | - Skimmed milk + whey + hydrolysed whey proteins  - partially hydrolysed soluble milk protein |
| pHF/HA | - to reduce the risk of cow's milk protein allergy  - hypoallergenic infant formula  - recommended in cases of increased risk of allergy, and minor digestive problems  - 100% partially hydrolysed protein; no casein  - 100% hydrolysed rice protein  - hypoallergenic milk, containing short-chain peptides, which reduces the allergic risk compared to a standard formula | - hydrolysed whey proteins  - casein hydrolysate (from milk)  - Partially hydrolysed protein from skimmed milk and concentrated whey  - Enzymatic hydrolysate of partially demineralised whey enriched with protein  - milk protein hydrolysate  - partial rice protein hydrolysate |
| eHF/AA | contains no protein but only free amino acids | L-aspartate, L-leucine, L-lysine hydrochloride, L-proline, L-alanine, L-valine, glutamate monosodique, L-isoleucine, L-serine, L-thréonine, L-tyrosine, L-arginine, L-phénylalanine, L-histidine, L-cystine, glycine, L-tryptophane, L-méthionine, L-glutamine |
| - Balanced complete food substitute for milk in protein, carbohydrate and fat malabsorption syndromes  - in case of proven allergy to cow's milk proteins  - in cases of acute or chronic diarrhoea, malabsorption, severe undernutrition and allergy to cow's milk proteins | - high hydrolysate of casein  - whey protein extended hydrolysate |

Table S2. Unadjusted estimates of summary developmental scores at 1, 2 and 3.5 years across formulas with increasing degree of protein hydrolysis consumed at 2 months, complete-case analyses

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Summary developmental scores (on a continuous scale)** | | | | | | |  |
|  |  | **N** | **CDI-1** | **N** | **MB-2** | **N** | **CDI-3.5** | **N** | **PS-3.5** |
| *Main analyses, unadjusted* | | *6977* |  | *6145* |  | *5696* |  | *4511* |  |
|  | nHF | 6430 | 0 [Ref] | 5649 | 0 [Ref] | 5238 | 0 [Ref] | 4146 | 0 [Ref] |
|  | pHF/non-HA | 189 | -0.76 [-1.56; 0.04] | 175 | -1.42 [-5.19; 2.34] | 158 | 0.40 [-0.43; 1.23] | 127 | 0.00 [-2.81; 2.80] |
|  | pHF/HA | 288 | -0.21 [-0.87; 0.44] | 258 | 2.35 [-0.77; 5.48] | 241 | -0.43 [-1.10; 0.25] | 196 | 0.44 [-1.83; 2.72] |
|  | eHF/AA | 70 | -0.20 [-1.50; 1.11] | 63 | 0.62 [-5.60; 6.83] | 59 | -0.13 [-1.47; 1.21] | 42 | 0.63 [-4.20; 5.45] |

CDI-1: 1-year Child Development Inventory; MB-2: 2-year MacArthur-Bates Communicative Development Inventory; CDI-3.5: 3.5-year Child Development Inventory; PS-3.5: 3.5-year Picture Similarities ability score form the British Ability Scale.

pHF/non-HA: Partially hydrolysed formula/non-HA; pHF/HA: Partially hydrolysed formula/HA; eHF/AA: extensively hydrolysed formula, or formula based on amino-acids.

Values are estimates [95% CI] from linear regression models.

Varying sample sizes due to missing data in the respective neurodevelopmental score.

Table S3. Unadjusted Odds Ratios (ORs) of having a poor developmental sub-score at 1 and 3.5 years across formulas with increasing degree of protein hydrolysis consumed at 2 months, complete-case analyses

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | **Poor developmental sub-score (lowest quartile vs three other quartiles)** | | | | | |
|  |  |  | N | Social skills | Self-help | Gross motor skills | Fine motor skills | Language expression | Language comprehension |
| **1-year follow-up** | | |  |  |  |  |  |  |  |
|  | *Main analysis* | | *6977* |  |  |  |  |  |  |
|  |  | nHF | 6430 | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] |
|  |  | pHF/non-HA | 189 | 1.10 [0.76; 1.59] | 1.42 [0.94; 2.15] | 1.19 [0.83; 1.69] | 1.10 [0.79; 1.52] | 1.22 [0.85; 1.77] | 1.13 [0.79; 1.62] |
|  |  | pHF/HA | 288 | 1.08 [0.80; 1.46] | 1.07 [0.73; 1.55] | 1.50 [1.14; 1.98] | 1.18 [0.91; 1.53] | 0.84 [0.60; 1.18] | 0.87 [0.64; 1.20] |
|  |  | eHF/AA | 70 | 0.78 [0.40; 1.53] | 1.59 [0.83; 3.04] | 1.01 [0.55; 1.85] | 0.88 [0.50; 1.54] | 1.07 [0.58; 2.01] | 0.48 [0.22; 1.06] |
| **3.5-year follow-up** | | |  |  |  |  |  |  |  |
|  | *Main analysis* | | *5696* |  |  |  |  |  |  |
|  |  | nHF | 5238 | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] |
|  |  | pHF/non-HA | 158 | 0.59 [0.34; 1.01] | 1.36 [0.88; 2.10] | 1.15 [0.70; 1.87] | 1.22 [0.84; 1.76] | 0.71 [0.44; 1.12] | 0.68 [0.42; 1.11] |
|  |  | pHF/HA | 241 | 0.92 [0.64; 1.34] | 1.07 [0.73; 1.57] | 1.06 [0.70; 1.59] | 1.16 [0.86; 1.58] | 1.06 [0.76; 1.47] | 0.97 [0.68; 1.37] |
|  |  | eHF/AA | 59 | 0.88 [0.42; 1.86] | 1.30 [0.64; 2.66] | 0.78 [0.31; 1.95] | 0.60 [0.29; 1.28] | 1.43 [0.78; 2.62] | 0.90 [0.44; 1.84] |

pHF/non-HA: Partially hydrolysed formula/non-HA; pHF/HA: Partially hydrolysed formula/HA; eHF/AA: extensively hydrolysed formula, or formula based on amino-acids.

Values are odds-ratios [95% CI] from logistic regression models.

Varying sample sizes due to missing data in the respective neurodevelopmental score.

Table S4. Adjusted estimates of summary developmental scores at 1, 2 and 3.5 years across formulas with increasing degree of protein hydrolysis consumed at 2 months and, specific sub-samples and analyses after multiple imputations

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Summary developmental scores (on a continuous scale)** | | | | | | | |
|  |  |  | N | CDI-1 | N | MB-2 | N | CDI-3.5 | N | PS-3.5 |
|  | *SS infants without congenital malformations* | | *6711* |  | *5907* |  | *5476* |  | *4333* |  |
|  |  | nHF | 6188 | 0.00 [Ref] | 5434 | 0.00 [Ref] | 5038 | 0.00 [Ref] | 3985 | 0.00 [Ref] |
|  |  | pHF/non-HA | 179 | -0.76 [-1.52; 0.00] | 165 | -1.07 [-4.77; 2.62] | 150 | 0.47 [-0.33; 1.27] | 120 | -0.57 [-3.38; 2.25] |
|  |  | pHF/HA | 276 | -0.29 [-0.91; 0.33] | 247 | 1.98 [-1.07; 5.02] | 231 | -0.40 [-1.05; 0.25] | 187 | 0.07 [-2.22; 2.36] |
|  |  | eHF/AA | 68 | 0.03 [-1.36; 1.41] | 61 | 3.38 [-3.48; 10.24] | 57 | 1.08 [-0.39; 2.55] | 41 | -0.96 [-6.31; 4.39] |
|  | *SS term infants* | | *6602* |  | *5828* |  | *5399* |  | *4281* |  |
|  |  | nHF | 6082 | 0.00 [Ref] | 5357 | 0.00 [Ref] | 4965 | 0.00 [Ref] | 3933 | 0.00 [Ref] |
|  |  | pHF/non-HA | 175 | -0.65 [-1.41; 0.12] | 162 | -1.49 [-5.23; 2.25] | 146 | 0.49 [-0.32; 1.31] | 118 | -0.56 [-3.39; 2.27] |
|  |  | pHF/HA | 278 | -0.09 [-0.70; 0.53] | 248 | 2.10 [-0.95; 5.16] | 232 | -0.43 [-1.09; 0.22] | 190 | 0.21 [-2.06; 2.47] |
|  |  | eHF/AA | 67 | -0.20 [-1.59; 1.18] | 61 | 1.98 [-4.90; 8.86] | 56 | 0.86 [-0.62; 2.34] | 40 | -1.18 [-6.51; 4.16] |
|  | *SS among infants not having changed infant formula up to 2 months* | | *3679* |  | *3213* |  | *2998* |  | *2355* |  |
|  |  | nHF | 3436 | 0.00 [Ref] | 2992 | 0.00 [Ref] | 2788 | 0.00 [Ref] | 2184 | 0.00 [Ref] |
|  |  | pHF/non-HA | 44 | -1.24 [-2.78; 0.30] | 41 | 2.21 [-5.25; 9.67] | 36 | -0.07 [-1.73; 1.58] | 33 | 3.41 [-1.88; 8.69] |
|  |  | pHF/HA | 185 | -0.56 [-1.34; 0.21] | 168 | 0.31 [-3.51; 4.13] | 162 | -0.64 [-1.45; 0.17] | 128 | 0.08 [-2.71; 2.87] |
|  |  | eHF/AA | 14 | -1.36 [-4.20; 1.49] | 12 | -0.07 [-14.40; 14.26] | 12 | -1.44 [-4.44; 1.55] | 10 | -2.68 [-12.64; 7.28] |
|  | *SS among infants not having changed infant formula between 2 and 6 months* | | *3970* |  | *3682* |  | *3480* |  | *2801* |  |
|  |  | nHF | 3790 | 0.00 [Ref] | *3510* | 0.00 [Ref] | 3321 | 0.00 [Ref] | 2671 | 0.00 [Ref] |
|  |  | pHF/non-HA | 64 | -0.83 [-2.11; 0.45] | 62 | -1.23 [-7.33; 4.87] | 55 | 0.52 [-0.81; 1.85] | 43 | 0.46 [-4.25; 5.17] |
|  |  | pHF/HA | 93 | -1.03 [-2.10; 0.04] | 88 | 0.59 [-4.56; 5.74] | 83 | -0.21 [-1.31; 0.88] | 72 | 0.39 [-3.30; 4.07] |
|  |  | eHF/AA | 23 | -0.01 [-2.39; 2.37] | 22 | 0.25 [-11.05; 11.56] | 21 | 1.02 [-1.41; 3.44] | 15 | 1.47 [-7.14; 10.09] |
|  | *Analyses after multiple imputations* | | *8980* |  | *7962* |  | *7334* |  | *5695* |  |
|  |  | nHF | 8295 | 0.00 [Ref] | 7336 | 0.00 [Ref] | 6755 | 0.00 [Ref] | 5240 | 0.00 [Ref] |
|  |  | pHF/non-HA | 246 | -0.46 [-1.11; 0.20] | 230 | -0.37 [-3.53; 2.80] | 206 | 0.63 [-0.06; 1.33] | 159 | -0.61 [-3.06; 1.84] |
|  |  | pHF/HA | 347 | -0.32 [-0.87; 0.24] | 311 | 1.46 [-1.27; 4.20] | 293 | -0.32 [-0.90; 0.27] | 236 | 0.71 [-1.32; 2.74] |
|  |  | eHF/AA | 92 | -0.56 [-1.72; 0.60] | 85 | 2.02 [-3.67; 7.72] | 80 | 0.61 [-0.62; 1.84] | 60 | 0.86 [-3.42; 5.14] |

CDI-1: 1-year Child Development Inventory; MB-2: 2-year MacArthur-Bates Communicative Development Inventory; CDI-3.5: 3.5-year Child Development Inventory; PS-3.5: 3.5-year Picture Similarities ability score form the British Ability Scale.

pHF/non-HA: Partially hydrolysed formula/non-HA; pHF/HA: Partially hydrolysed formula/HA; eHF/AA: extensively hydrolysed formula, or formula based on amino-acids.

Values are estimates [95% CI] from linear regression models adjusted for child age at each assessment, mother’s age, education, employment, and migration status, household income, maternal smoking during pregnancy, parental and sibling history of allergy, mother’s dietary quality during pregnancy, urban/rural are of living, region of residence, parental stimulation, child sex, gestational age, and size according to gestational age, physician consulted between hospital discharge and 2 months post-partum, allergy to cow milk, any breastfeeding duration.

Varying sample sizes due to missing data in the respective neurodevelopmental score.

Table S5. Adjusted Odds Ratios (ORs) of having a poor developmental sub-score at 1 and 3.5 years across formulas with increasing degree of protein hydrolysis consumed at 2 months, specific sub-samples and analyses after multiple imputations

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | **Poor developmental sub-score (lowest quartile vs three other quartiles)** | | | | | |
|  |  |  | N | Social skills | Self-help | Gross motor skills | Fine motor skills | Language expression | Language comprehension |
| **1-year follow-up** | | |  |  |  |  |  |  |  |
|  | *Infants without congenital malformations* | | *6711* |  |  |  |  |  |  |
|  |  | nHF | 6188 | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] |
|  |  | pHF/non-HA | 179 | 1.13 [0.76; 1.66] | 1.50 [0.97; 2.30] | 1.21 [0.83; 1.77] | 1.20 [0.85; 1.68] | 1.16 [0.78; 1.72] | 1.19 [0.82; 1.74] |
|  |  | pHF/HA | 276 | 1.09 [0.79; 1.50] | 1.05 [0.71; 1.56] | 1.64 [1.23; 2.19] | 1.25 [0.95; 1.65] | 0.85 [0.60; 1.22] | 0.93 [0.67; 1.29] |
|  |  | eHF/AA | 68 | 0.66 [0.29; 1.48] | 1.50 [0.69; 3.28] | 1.11 [0.54; 2.27] | 0.99 [0.51; 1.92] | 0.73 [0.33; 1.60] | 0.41 [0.16; 1.03] |
|  | *Term infants* | | *6602* |  |  |  |  |  |  |
|  |  | nHF | 6082 | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] |
|  |  | pHF/non-HA | 175 | 1.02 [0.67; 1.53] | 1.47 [0.94; 2.30] | 1.14 [0.77; 1.69] | 1.13 [0.79; 1.61] | 1.27 [0.85; 1.89] | 1.19 [0.80; 1.75] |
|  |  | pHF/HA | 278 | 1.00 [0.72; 1.38] | 1.00 [0.67; 1.49] | 1.54 [1.15; 2.06] | 1.16 [0.87; 1.53] | 0.82 [0.57; 1.18] | 0.87 [0.62; 1.23] |
|  |  | eHF/AA | 67 | 0.74 [0.33; 1.66] | 1.28 [0.55; 2.97] | 1.09 [0.52; 2.27] | 1.01 [0.51; 1.99] | 1.08 [0.50; 2.31] | 0.40 [0.16; 1.00] |
|  | *Infants not having changed infant formula up to 2 months* | | *3679* |  |  |  |  |  |  |
|  |  | nHF | 3436 | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] |
|  |  | pHF/non-HA | 44 | 2.29 [1.18; 4.47] | 0.86 [0.30; 2.49] | 1.95 [0.99; 3.86] | 0.92 [0.44; 1.92] | 1.28 [0.60; 2.76] | 1.41 [0.67; 2.96] |
|  |  | pHF/HA | 185 | 1.21 [0.82; 1.80] | 0.96 [0.58; 1.58] | 1.64 [1.16; 2.34] | 1.33 [0.95; 1.87] | 0.88 [0.57; 1.35] | 0.94 [0.62; 1.41] |
|  |  | eHF/AA | 14 | 1.05 [0.25; 4.35] | 0.49 [0.06; 4.16] | 4.43 [1.40; 14.06] | 1.07 [0.30; 3.78] | 0.86 [0.20; 3.60] | 1.31 [0.32; 5.41] |
|  | *Infants not having changed infant formula between 2 and 6 months* | | *3970* |  |  |  |  |  |  |
|  |  | nHF | 3790 | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] |
|  |  | pHF/non-HA | 64 | 0.72 [0.35; 1.50] | 1.50 [0.74; 3.05] | 1.47 [0.81; 2.66] | 1.46 [0.85; 2.52] | 1.23 [0.65; 2.34] | 1.22 [0.65; 2.27] |
|  |  | pHF/HA | 93 | 1.04 [0.6; 1.78] | 1.16 [0.62; 2.15] | 2.00 [1.26; 3.18] | 1.42 [0.90; 2.24] | 1.20 [0.70; 2.06] | 1.72 [1.06; 2.80] |
|  |  | eHF/AA | 23 | 0.49 [0.12; 1.92] | 1.07 [0.26; 4.32] | 0.62 [0.16; 2.43] | 1.94 [0.67; 5.59] | 0.79 [0.23; 2.79] | 0.33 [0.07; 1.58] |
|  | *Multiple imputation of missing data* | | *8980* |  |  |  |  |  |  |
|  |  | nHF | 8295 | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] |
|  |  | pHF/non-HA | 246 | 1.19 [0.86; 1.65] | 1.19 [0.80; 1.78] | 1.15 [0.83; 1.59] | 1.03 [0.76; 1.39] | 1.08 [0.76; 1.53] | 1.13 [0. 82; 1.56] |
|  |  | pHF/HA | 347 | 1.11 [0.84; 1.47] | 0.94 [0.65; 1.36] | 1.37 [1.05; 1.79] | 1.27 [0.99; 1.62] | 0.96 [0.70; 1.30] | 1.00 [0.75; 1.33] |
|  |  | eHF/AA | 92 | 0.92 [0.50; 1.71] | 1.63 [0.85; 3.13] | 1.23 [0.69; 2.18] | 0.93 [0.52; 1.64] | 0.98 [0.52; 1.85] | 0.59 [0.29; 1.17] |
| **3.5-year follow-up** | | |  |  |  |  |  |  |  |
|  | *Infants without congenital malformations* | | *5476* |  |  |  |  |  |  |
|  |  | nHF | 5038 | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] |
|  |  | pHF/non-HA | 150 | 0.56 [0.32; 0.99] | 1.29 [0.81; 2.04] | 1.16 [0.69; 1.96] | 1.13 [0.75; 1.70] | 0.63 [0.38; 1.06] | 0.71 [0.42; 1.18] |
|  |  | pHF/HA | 231 | 0.94 [0.63; 1.40] | 0.97 [0.64; 1.45] | 1.18 [0.78; 1.80] | 1.15 [0.82; 1.60] | 1.11 [0.78; 1.59] | 0.99 [0.68; 1.45] |
|  |  | eHF/AA | 57 | 0.82 [0.35; 1.96] | 1.12 [0.47; 2.65] | 0.67 [0.23; 1.95] | 0.32 [0.13; 0.81] | 0.97 [0.46; 2.05] | 0.74 [0.32; 1.70] |
|  | *Term infants* | | *5399* |  |  |  |  |  |  |
|  |  | nHF | 4965 | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] |
|  |  | pHF/non-HA | 146 | 0.59 [0.33; 1.03] | 1.14 [0.70; 1.87] | 1.21 [0.72; 2.04] | 1.08 [0.71; 1.64] | 0.64 [0.38; 1.07] | 0.69 [0.41; 1.16] |
|  |  | pHF/HA | 232 | 1.00 [0.68; 1.47] | 0.93 [0.62; 1.40] | 1.14 [0.75; 1.74] | 1.16 [0.84; 1.61] | 1.11 [0.78; 1.57] | 0.99 [0.69; 1.44] |
|  |  | eHF/AA | 56 | 0.75 [0.30; 1.84] | 1.30 [0.55; 3.06] | 0.80 [0.28; 2.30] | 0.41 [0.17; 1.01] | 1.02 [0.49; 2.14] | 0.65 [0.27; 1.55] |
|  | *Infants not having changed infant formula up to 2 months* | | *2998* |  |  |  |  |  |  |
|  |  | nHF | 2788 | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] |
|  |  | pHF/non-HA | 36 | 0.35 [0.08; 1.47] | 0.97 [0.33; 2.85] | 0.76 [0.23; 2.57] | 1.29 [0.57; 2.88] | 0.72 [0.28; 1.90] | 1.56 [0.69; 3.54] |
|  |  | pHF/HA | 162 | 1.09 [0.69; 1.71] | 1.04 [0.63; 1.70] | 1.33 [0.81; 2.17] | 1.07 [0.71; 1.60] | 1.28 [0.85; 1.91] | 1.14 [0.74; 1.75] |
|  |  | eHF/AA | 12 | 1.26 [0.30; 5.37] | 2.13 [0.49; 9.31] | 3.16 [0.74; 13.51] | 0.66 [0.13; 3.38] | 1.52 [0.40; 5.79] | 0.84 [0.17; 4.26] |
|  | *Infants not having changed infant formula between 2 and 6 months* | | *3480* |  |  |  |  |  |  |
|  |  | nHF | 3321 | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] |
|  |  | pHF/non-HA | 55 | 0.80 [0.35; 1.82] | 1.45 [0.70; 3.00] | 1.21 [0.53; 2.74] | 1.26 [0.67; 2.34] | 0.70 [0.32; 1.55] | 0.34 [0.12; 0.99] |
|  |  | pHF/HA | 83 | 1.10 [0.59; 2.05] | 0.97 [0.50; 1.89] | 0.47 [0.19; 1.18] | 1.01 [0.58; 1.78] | 0.96 [0.53; 1.74] | 1.10 [0.60; 1.99] |
|  |  | eHF/AA | 21 | 1.00 [0.24; 4.12] | 0.79 [0.15; 4.15] | 0.99 [0.23; 4.38] | 0.50 [0.14; 1.81] | 0.95 [0.29; 3.09] | 0.58 [0.14; 2.38] |
|  | *Multiple imputation of missing data* | | *7334* |  |  |  |  |  |  |
|  |  | nHF | 6755 | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] | 1.00 [Ref] |
|  |  | pHF/non-HA | 206 | 0.57 [0.35; 0.91] | 1.06 [0.70; 1.62] | 0.94 [0.59; 1.52] | 1.00 [0.70; 1.43] | 0.74 [0.49; 1.11] | 0.66 [0.42; 1.03] |
|  |  | pHF/HA | 293 | 0.89 [0.63; 1.27] | 0.87 [0.60; 1.27] | 1.14 [0.78; 1.66] | 1.09 [0.81; 1.46] | 1.06 [0.77; 1.45] | 0.95 [0.68; 1.34] |
|  |  | eHF/AA | 80 | 1.14 [0.59; 2.23] | 0.71 [0.32; 1.59] | 0.67 [0.27; 1.70] | 0.63 [0.32; 1.23] | 1.13 [0.62; 2.05] | 1.02 [0.53; 1.97] |

pHF/non-HA: Partially hydrolysed formula/non-HA; pHF/HA: Partially hydrolysed formula/HA; eHF/AA: extensively hydrolysed formula, or formula based on amino-acids.

Values are estimates [95% CI] from linear regression models adjusted for child age at each assessment, mother’s age, education, employment, and migration status, household income, maternal smoking during pregnancy, parental and sibling history of allergy, mother’s dietary quality during pregnancy, urban/rural are of living, region of residence, parental stimulation, child sex, gestational age, and size according to gestational age, physician consulted between hospital discharge and 2 months post-partum, allergy to cow milk, any breastfeeding duration.

Varying sample sizes due to missing data in the respective neurodevelopmental score.