ONLINE SUPPLEMENTARY MATERIAL

Is an antioxidant-rich or a pro-inflammatory diet during pregnancy associated with allergic and respiratory multimorbidity in children from the ELFE birth cohort?

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Summary

Supplementary Table S1. Food items included in the Dietary Total Antioxidant Capacity scores calculation.

Food groups	**Details of included foods**
Cooked vegetables	Green beans; cooked endives, chicory, radicchio, spinach; leeks; cabbage (cauliflower, broccoli); cooked carrots; zucchinis, eggplants, peppers, tomatoes (sauce); peas; artichokes, fennel, asparagus, celery; mushroom; corn; pumpkin
Raw vegetables	Green salad, arugula, spinach; grated carrots; avocado; other raw vegetables (tomato, beet, green cabbage, cucumber, radish, chicory, endive, radicchio, turnip tops)
Citrus fruits	Orange, clementine, grapefruit, tangerine
Berries	Strawberries, raspberries
Exotic fruits	Pineapple, loquat, prickly pears
Dried fruits	Dried apricot, fig, prune, raisin
Other fruits	Apricot, peach, plum, cherries; grapes; melon, watermelon; banana; kiwi; apple or pear
Nuts	Walnuts, hazelnuts, almonds, pistachios; peanuts
Pulses	Lentils, dried beans, chickpeas, broad beans
Starch	Boiled or baked potatoes; mashed potatoes; potato gratin; potato chips; roasted or fried potatoes; French fries
Cereal products	Bread (white bread or sandwich bread); wholegrain or other special breads; breakfast cereals (puffed barley, cornflakes, whole meal oat puffed with honey, white puffed rice, extruded wheat bran); pasta (macaroni, spaghetti, coquillettes); rice; semolina, wheat
Chocolate and cocoa	Chocolate (dark, milk, Gianduja)
Sweetened products	Ice cream, sorbet; honey, jam; chocolate spread
Sauces	Dressing sauce (red vinegar, extra virgin olive, olive oil, sunflower oil)
Fruit juices	Orange juice, grapefruit juice, pineapple juice, apple juice, mixed fruit juice, pear juice, apricot juice, peach juice, tropical juice
Soda	Sugar-sweetened cola or sodas; artificially sweetened cola or sodas
Coffee	Coffee
Tea	Tea
Alcohol	Cider or beer; white, red, rosé wine; whisky, gin, vodka

Foods separated with a "," are from the same item, foods separated with a ";" are from different items

Supplementary Table S2. Pearson correlation coefficients between the E-DII, the different DTAC score versions and daily coffee consumption (n=14,314).

	E-DII	TEAC without coffee	TRAP without coffee	FRAP without coffee	TEAC with coffee	TRAP with coffee	FRAP with coffee	Coffee consumption (ml/day)
E-DII	1	-0.61	-0.61	-0.65	-0.20	-0.09	-0.16	0.04
TEAC without coffee		1	0.97	0.97	0.23	0.05	0.14	-0.16
TRAP without coffee			1	0.97	0.22	0.06	0.15	-0.15
FRAP without coffee				1	0.24	0.07	0.18	-0.13
TEAC with coffee					1	0.98	0.99	0.92
TRAP with coffee						1	0.99	0.95
FRAP with coffee							1	0.98
Coffee consumption (ml/day)								1

E-DII: energy-adjusted Dietary Inflammatory Index; DTAC: Dietary Total Antioxidant Capacity; TEAC: Trolox equivalent antioxidant capacity; TRAP: Total radical trapping antioxidant parameter; FRAP: Ferric reducing-antioxidant power.

Supplementary Table S3. Food components included in the Dietary Inflammatory Index score and their inflammatory weights.

Food components in the DII (Shivappa et *al.*, 2014)	Included in the E-DII	Inflammatory weight (Shivappa et *al.*, 2014)
Energy (kcal/d)[1]	✗	0.180
Protein (g/d)	✓	0.021
Total fat (g/d)	✓	0.298
Saturated fat (g/d)	✓	0.373
MUFAs (g/d)	✓	-0.009
PUFAs (g/d)	✓	-0.337
Trans fat (g/d)	✗	0.229
n-3 PUFAs (g/d)	✓	-0.436
n-6 PUFAs (g/d)	✓	-0.159
Cholesterol (mg/d)	✓	0.110
Carbohydrate (g/d)	✓	0.097
Fiber (g/d)	✓	-0.663
Vitamin A (µg/d)	✓	-0.401
β-Carotene (µg/d)	✓	-0.584
Thiamin (mg/d)	✓	-0.098
Riboflavin (mg/d)	✓	-0.068
Niacin (mg/d)	✓	-0.246
Vitamin B6 (µg/d)	✓	-0.365
Folic acid (µg/d)	✓	-0.190
Vitamin B12 (µg/d)	✓	0.106
Vitamin C (mg/d)	✓	-0.424
Vitamin D (µg/d)	✓	-0.446
Vitamin E (mg/d)	✓	-0.419
Iron (mg/d)	✓	0.032
Magnesium (mg/d)	✓	-0.484
Zinc (mg/d)	✓	-0.313
Selenium (µg/d)	✓	-0.191
Eugenol (mg/d)	✗	-0.140
Flavonols (mg/d)	✗	-0.467
Flavonones (mg/d)	✗	-0.250
Isoflavones (mg/d)	✗	-0.593
Flavones (mg/d)	✗	-0.616
Flavan-3-ol (mg)	✗	-0.415
Anthocyanidins (mg/d)	✗	-0.131

Alcohol (g/d)	✓	-0.278
Caffeine (g/d)	✓	-0.110
Tea (g/d)	✓	-0.536
Garlic (g/d)	✗	-0.412
Ginger (g/d)	✗	-0.453
Onion (g/d)	✗	-0.301
Saffron (g/d)	✗	-0.140
Pepper (mg/d)	✗	-0.131
Turmeric (mg/d)	✗	-0.785
Thyme/oregano (mg/d)	✗	-0.102
Rosemary (mg/d)	✗	-0.013

kcal/d: kilocalorie per day; g/d: gram per day; mg/d: milligram per day; µg/d: microgram per day; MUFAs: mono-unsaturated fatty acids; PUFAs: polyunsaturated fatty acids.

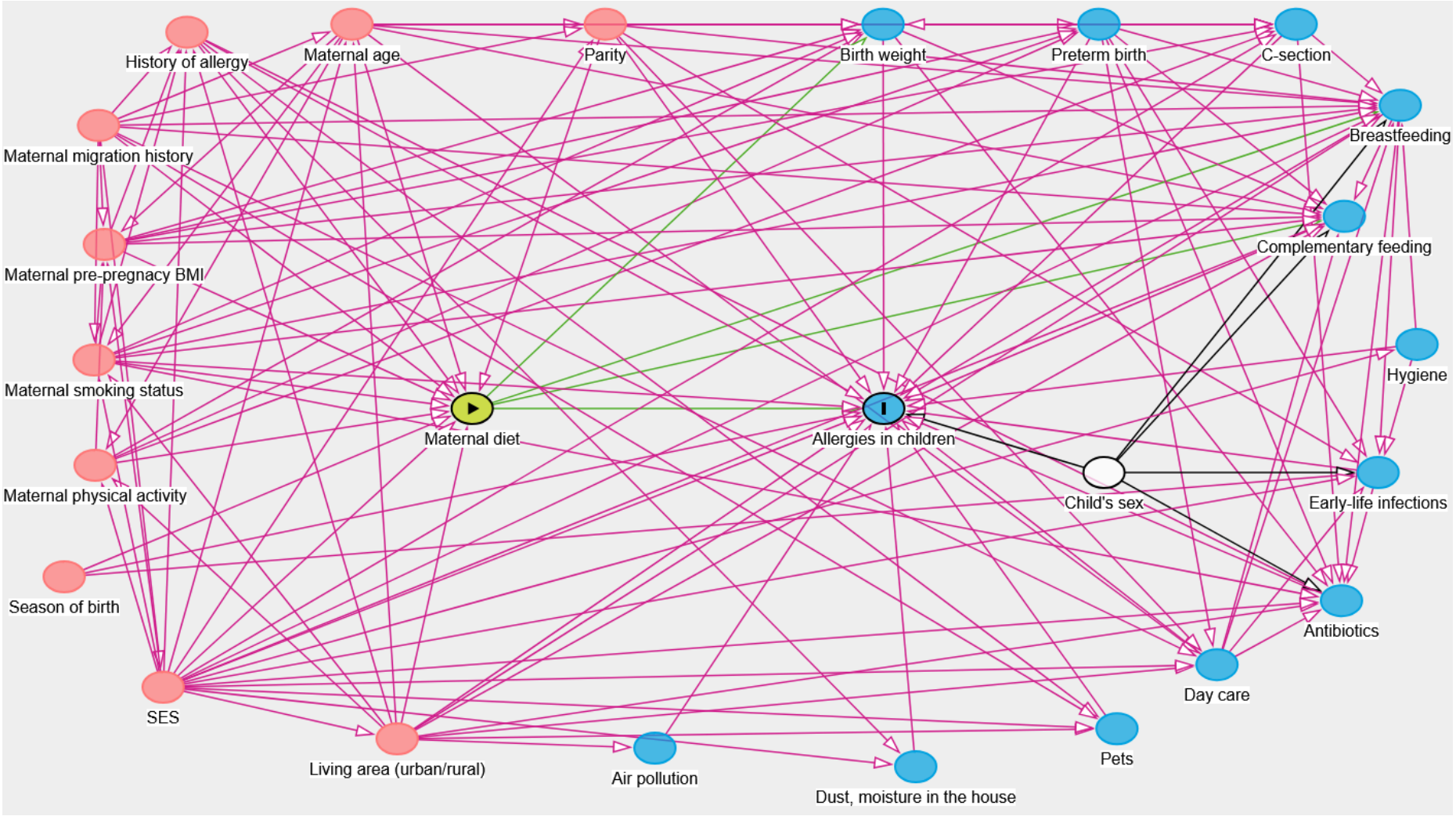
[1] Total energy intake was not included as a food component in the score calculation because the score was adjusted on total energy intake.

Inflammatory weights range between [-1 ; 1], the more pro-inflammatory the food component, the higher the inflammatory weight.

Supplementary Table S4. Description of allergic and respiratory multimorbidity clusters of children up to 5.5 years in the ELFE study (n=11,246).

		Allergic and respiratory multimorbidity clusters				
	Total	**Asymptomatic**	**Early wheeze without asthma**	**Asthma only**	**Allergies without asthma**	**Multi-allergic**
	n=11,246	n=4841	n=3785	n=829	n=804	n=987
Ever food allergy (0-5.5 years)	7.4% (837)	4.2% (205)	5.2% (195)	0.4% (3)	18.7% (150)	28.8% (284)
Ever rash (0-5.5 years)	53.6% (6028)	45.5% (2201)	53.2% (2012)	35.6% (295)	75.4% (606)	92.6% (914)
Ever wheeze (0-5.5 years)	45.3% (5093)	2.6% (128)	79.5% (3010)	91.9% (762)	31.5% (253)	95.2% (940)
Ever night cough (0-5.5 years)	82.3% (9260)	65.6% (3178)	96.6% (3655)	92.3% (765)	84.6% (680)	99.5% (982)
Ever medication for asthma (0-3.5 years)	40.7% (4581)	3.3% (159)	69.8% (2642)	95.2% (789)	15.4% (124)	87.8% (867)
Ever consultation for asthma (2-5.5 years)	15.7% (1771)	0.7% (33)	0.1% (2)	100.0% (829)	15.9% (128)	78.9% (779)
Ever allergic conjunctivitis (3.5-5.5 years)	36.7% (4130)	28.7% (1391)	34.7% (1314)	26.8% (222)	62.7% (504)	70.8% (699)
Allergic rhinitis (5.5 years)	12.1% (1366)	2.7% (130)	0.7% (25)	11.8% (98)	76.5% (615)	50.5% (498)

Values are in % (n) and are the prevalence of the variables included in the cluster construction.



Supplementary Figure S1. Directed Acyclic Graph (DAG) of the maternal inflammatory or antioxidant diet during pregnancy and allergic and respiratory diseases in children, used for the selection of confounders.

Graph made with DAGitty v3.1. The triangle in the **green circle** represents the **main exposure** (maternal diet during pregnancy) and the I in the **blue circle** is the **outcome** (allergic and respiratory diseases in children). **Red circles** represent **potential confounders** (i.e., ancestors of exposure and outcome). **Intermediate factors** (i.e., ancestor of the outcome but not of the exposure) are represented with **blue circles**. Variables included in the adjustment that are not confounders are represented with white circles. Arrows indicate the direction of causal paths. SES: socio-economic status.

Supplementary Table S5. Details on multiple imputation (n=9679).

Variables of interest	Type	Models for imputation	Missing values n (%)
Allergic and respiratory clusters	Categorical *(5 categories)*	No missing data	0 (0.0%)
E-DII	Continuous	No missing data	0 (0.0%)
DTAC	Continuous	No missing data	0 (0.0%)
Size of maternity unit	Ordinal *(5 categories)*	No missing data	0 (0.0%)
Period of enrolment	Categorical *(4 categories)*	No missing data	0 (0.0%)
Child's sex	Binary	No missing data	0 (0.0%)
Living area	Binary	No missing data	0 (0.0%)
Region	Categorical *(9 categories)*	No missing data	0 (0.0%)
Maternal age at delivery	Continuous	Linear regression	1 (0.0%)
Maternal smoking status during pregnancy	Ordinal *(4 categories)*	Logistic regression	79 (0.8%)
Physical activity level during pregnancy	Continuous	Linear regression	80 (0.8%)
Maternal pre-pregnancy BMI	Continuous	Linear regression	97 (1.0%)
Number of older children	Ordinal *(3 categories)*	Logistic regression	110 (1.1%)
Maternal migration status	Categorical *(3 categories)*	Multinomial regression	141 (1.5%)
Family history of allergy	Binary	Logistic regression	150 (1.6%)
Maternal education level	Categorical *(5 categories)*	Logistic regression	275 (2.8%)
Household income	Continuous	Linear regression	375 (3.3%)

E-DII: energy-adjusted Dietary Inflammatory Index, DTAC: Dietary Total Antioxidant Capacity. Multiple imputation on covariates was performed to address missing data. Missing values were considered as missing at random and five independent datasets were generated with the Fully Conditional Specification method (SAS, MI procedure, FCS method). Missing values were imputed using linear regression for continuous variables (regpmm option), logistic regression for ordinal or binary variables (logistic option) and multinomial model (discrim option) for categorical variables. Pooled effects were estimates calculated with the MIANALYZE procedure (V9.4 SAS).

Supplementary Table S6. Associations between dietary total antioxidant capacity scores including coffee of maternal diet during pregnancy and allergic and respiratory multimorbidity clusters in children from the ELFE cohort.

	Allergic and respiratory multimorbidity clusters			
	Early wheeze without asthma	**Asthma only**	**Allergies without asthma**	**Multi-allergic**
Imputed sample, n=9679				
Unadjusted model	n=3281	n=711	n=659	n=850
TEAC (per SD)	1.03 (0.98;1.07)	1.02 (0.94;1.10)	0.94 (0.86;1.02)	1.00 (0.92;1.07)
TRAP (per SD)	1.04 (1.00;1.09)	1.03 (0.95;1.11)	0.96 (0.88;1.04)	1.00 (0.93;1.07)
FRAP (per SD)	1.03 (0.99;1.08)	1.02 (0.95;1.11)	0.95 (0.87;1.04)	1.00 (0.93;1.07)
Adjusted model[1]	n=3281	n=711	n=659	n=850
TEAC (per SD)	1.00 (0.96;1.05)	0.99 (0.91;1.07)	0.98 (0.89;1.07)	1.00 (0.93;1.08)
TRAP (per SD)	1.02 (0.97;1.07)	1.00 (0.92;1.08)	0.99 (0.91;1.08)	1.00 (0.92;1.08)
FRAP (per SD)	1.01 (0.96;1.06)	0.99 (0.91;1.08)	0.99 (0.90;1.08)	1.00 (0.93;1.08)
Imputed and weighted sample, n=9677				
Adjusted model[1]	n=3280	n=711	n=659	n=849
TEAC (per SD)	0.98 (0.92;1.04)	0.96 (0.86;1.06)	1.02 (0.91;1.15)	0.99 (0.90;1.09)
TRAP (per SD)	0.99 (0.93;1.06)	0.95 (0.86;1.06)	1.04 (0.92;1.16)	1.00 (0.91;1.10)
FRAP (per SD)	0.99 (0.93;1.05)	0.96 (0.86;1.06)	1.03 (0.92;1.16)	0.99 (0.90;1.10)
Complete-case sample, n=8939				
Adjusted model[1]	n=3075	n=664	n=591	n=787
TEAC (per SD)	1.02 (0.97;1.07)	1.01 (0.93;1.10)	0.99 (0.90;1.09)	1.01 (0.93;1.10)
TRAP (per SD)	1.03 (0.98;1.09)	1.02 (0.93;1.11)	1.00 (0.91;1.10)	1.00 (0.92;1.09)
FRAP (per SD)	1.03 (0.98;1.08)	1.01 (0.93;1.10)	1.00 (0.90;1.10)	1.01 (0.93;1.10)

*p-value < 0.05

TRAP: Total radical trapping ant<oxidant parameter; FRAP: Ferric reducing-antioxidant power. Each score was considered in a separate model.

Cluster of reference: “asymptomatic”.

OR (95%CI) from multinomial logistic regressions. OR, odds ratio; CI, confidence interval; SD: standard deviation.

[1]Models were adjusted for maternal characteristics (maternal age at delivery, level of education, household income, migration status, smoking status during pregnancy, pre-pregnancy body mass index, physical activity during pregnancy, number of older children, living area (urban/rural), region, total energy intake), child characteristics (sex and family history of allergy), and study design characteristics (period of enrolment, size of maternity unit).