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"Temporal change in maternal dietary intake during pregnancy and lactation between and within two pregnancy cohorts assembled in the United Kingdom"

Kate Maslin, PhD, Carina Venter, PhD, Michaela Palumbo, MSc, Deborah Glueck, PhD, Frances Mitchell, MSc, Stephen Potter, Jane Grundy, RN, Gill Glasbey, Tara Dean, PhD, Syed Hasan Arshad, PhD.

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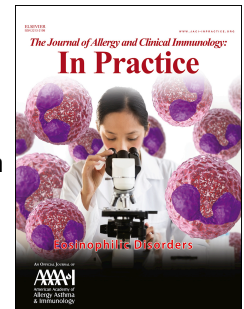
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1 **"Temporal change in maternal dietary intake during pregnancy and lactation between and**
2 **within two pregnancy cohorts assembled in the United Kingdom"**

3 Kate Maslin^{1,2} PhD, Carina Venter^{2,3,4} PhD, Michaela Palumbo⁵ MSc, Deborah Glueck^{4,5} PhD,
4 Frances Mitchell² MSc, Stephen Potter², Jane Grundy² RN, Gill Glasbey², Tara Dean^{2,6} PhD &
5 Syed Hasan Arshad^{2,7} PhD.

- 6 1. School of Nursing and Midwifery, University of Plymouth, United Kingdom.
7 2. David Hide Asthma and Allergy Centre, Isle of Wight, United Kingdom.
8 3. Children's Hospital Colorado, United States.
9 4. Department of Pediatrics, University of Colorado School of Medicine, United States
10 5. Lifecourse Epidemiology of Adiposity and Diabetes (LEAD) Center, University of
11 Colorado Denver, United States.
12 6. University of Brighton, United Kingdom.
13 7. Clinical and Experimental Sciences, University of Southampton, United Kingdom.

14 **Corresponding author:** Dr. Kate Maslin, School of Nursing and Midwifery, Drake Circus,
15 University of Plymouth, Plymouth, Devon, PL4 8AA, UK.

16 Email address: maslinkate@gmail.com

17 Phone: (+44) 01752 586 500

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23 independent of the funders.

24 **Conflicts of interest:** None declared.

25

26 **Key words:** pregnancy, lactation, allergy prevention, maternal diet, maternal nutrition,
27 peanut, birth cohort.

28 **Clinical implications:**

29 Advice regarding peanut intake during pregnancy has changed over the last 20 years. Future
30 guidance on peanut intake during pregnancy, lactation and complementary feeding should
31 be clearly communicated by the government and professional bodies, to prevent
32 unnecessary dietary exclusion.

33

34 To The Editor

35 The association between maternal and infant dietary exposures and risk of allergic disease
36 development has been an area of considerable scientific uncertainty and debate in recent
37 years (1). Overall research has been largely inconclusive, with no evidence supporting
38 maternal exclusion diets for the prevention of food allergy or atopic disease in the offspring
39 (2). The inconsistency in scientific evidence is reflected in contradictory dietary guidelines
40 about peanut intake over the past 20 years. In the United Kingdom, the Department of
41 Health issued a report in 1998, advising that pregnant mothers with a family history of atopy
42 should avoid peanuts during pregnancy/lactation (3). Ten years later, this advice was no
43 longer deemed appropriate and was rescinded based on data from our group (4, 5) (see
44 Figure 1). Similar advice was recommended internationally. Since then, the concept that
45 exposure to potential food allergens could be protective of allergic disease has now been
46 widely adopted. The aim of this study was to compare dietary habits during pregnancy and
47 lactation in two allergy birth cohorts born in the same geographical location approximately
48 10 years apart.

49 The FAIR cohort is a whole population birth cohort born on the Isle of Wight, United
50 Kingdom, between 2001-2002 (n = 969) (Figure 1). Demographic, socioeconomic and family
51 history of allergy information was collected from pregnant women at 12 weeks gestation.
52 A validated food frequency questionnaire was completed at 36 weeks gestation (6) (see file
53 1 in online repository). Information about infant feeding was collected prospectively via a
54 standardized questionnaire at 3 and 6 months postpartum. The 3rd generation cohort is the
55 offspring of the Isle of Wight Whole Population Birth Cohort (n = 1456), born in 1989.
56 Participants of this cohort were followed up to 27 years of age. Since 2010 their offspring
57 have been enrolled in the 3rd generation study (7). The majority of 3rd generation
58 participants were recruited antenatally at 12 weeks gestation. Dietary data was collected by

questionnaire at 28 weeks gestation using a modified version of the FAIR questionnaire and again at 3 and 6 months postpartum (6). Details of statistical methods are included in Online Repository file 2. Ethical approval for both studies was obtained from the Isle of Wight, Portsmouth and South East Hampshire Research Ethics Committee.

Data was available for 1331 participants (969 FAIR and 362 3rd generation). Maternal characteristics are shown in Table E1. The proportion of mothers that reported excluding peanuts during pregnancy was significantly lower for the 3rd generation compared to the FAIR cohort (16.0% vs. 55.6%, $p < 0.01$). Results of the multivariable logistic regression model showed that cohort membership, primiparity, and maternal education were significantly associated with excluding peanuts during pregnancy (Online Repository file 1, Table E2). Specifically, 3rd generation mothers had 0.18 times the odds of excluding peanuts during pregnancy compared to FAIR mothers (OR: 0.18, 95% CI: 0.12-0.27, $p < 0.01$). First time mothers had 65% greater odds of excluding peanuts during pregnancy (OR: 1.65, 95% CI: 1.25-2.17, $p < 0.01$). Vegetarian diet, maternal food allergy, and maternal age were not significantly associated with exclusion of peanuts during pregnancy.

Figure E1 illustrates differences between the FAIR and 3rd generation cohorts in terms of maternal frequency of consumption of key food allergens during pregnancy. A significantly greater proportion of 3rd generation mothers reported regular consumption (once per week or more) of peanuts, tree nuts, and seeds during pregnancy compared to FAIR mothers (all $p < 0.01$). Information regarding infant feeding and maternal dietary intake during lactation is shown in Table E1. The proportion of mothers who reported excluding any foods during breastfeeding was significantly lower for the 3rd generation compared to the FAIR cohort (22.8% vs. 43.4%, $p < 0.01$).

Figure 2 shows that among participants from the 3rd generation cohort only, exclusion of peanuts during pregnancy showed a decreasing trend over time from 2013 to

2018. The results of the multivariable logistic regression model found an overall significant difference in the proportion of mothers excluding peanuts during pregnancy between any of the offspring years of birth (Wald $\chi^2 = 10.27$, $df = 4$, $p = 0.036$). Results of the pairwise tests (Table E3) found that women who gave birth in 2017 had 0.1 times the odds of excluding peanuts during pregnancy compared to women who gave birth in 2013 (OR: 0.10, 95% CI: 0.02-0.57, $p = 0.01$). Primiparity, maternal education, maternal food allergy, nor maternal age were significantly associated with exclusion of peanuts during pregnancy among the 3rd generation participants.

Dietary data on peanut consumption may not be consistently reported as peanuts are not usually differentiated from tree nuts and may be included under broad categories (e.g. “nuts and seeds”) (8). Qualitative research with mothers of young children suggests that peanuts are considered primarily in the form of whole peanuts, or in the form of peanut butter, rather than being ingredients in food, meaning that study participants may in fact consume more than they realise (8). In both the FAIR and 3rd generation studies, the same validated questionnaire was used (6), which separated peanut, tree nuts and seeds into different categories and gave several examples for each item (Online Repository file 1). Research from the EuroPrevall birth cohort study, a multicentre study in nine European countries indicated wide practices in peanut intake; with only 2.7% of Dutch women avoiding eating peanut in pregnancy, compared to 44.4 % of British women (8). In addition, pregnant women in the UK were the highest avoiders of peanut and tree nuts (16.8%) compared to the other eight countries. The UK was the only country at the time to have any national guidance on peanut consumption during pregnancy, advocating peanut avoidance in high-risk families.

Against a backdrop of changing scientific evidence surrounding food allergy prevention, the importance of providing clear dietary advice to the public, is paramount. In the case of peanut exclusion variations in information provision, a lack of clarity in relation

to risks and the importance of atopy have been highlighted as potential issues (9). Due to this confusion, there has been a concern that the 1998 advice (3) could possibly have *increased* the prevalence of peanut allergy in the UK, as the advice may have been acted upon by non-high-risk families, to whom the advice was not targeted (4, 10). Ongoing data collection by our group of the 3rd generation participants will allow us to assess whether any changes in peanut sensitisation and clinical allergy have occurred as a result of changes in their dietary behaviour.

A strength of this study is that it was conducted in one area of the UK, although this limits external generalization. There were some differences between the two cohorts, meaning there is a risk of residual confounding. Maternal food allergy was self-reported and data was collected at one pregnancy time point. In conclusion, maternal exclusion of peanut during pregnancy was lower for mothers giving birth between 2012-2018 when compared to mothers giving birth between 2001-2002. These results align with the change in government dietary advice in 2008 and a paradigm shift towards exposure to dietary allergens via infant feeding, as a preventative approach to food allergy in infancy.

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Figure legends

Figure 1: Timeline illustrating the two different cohorts and timing of dietary recommendations and new guidance.

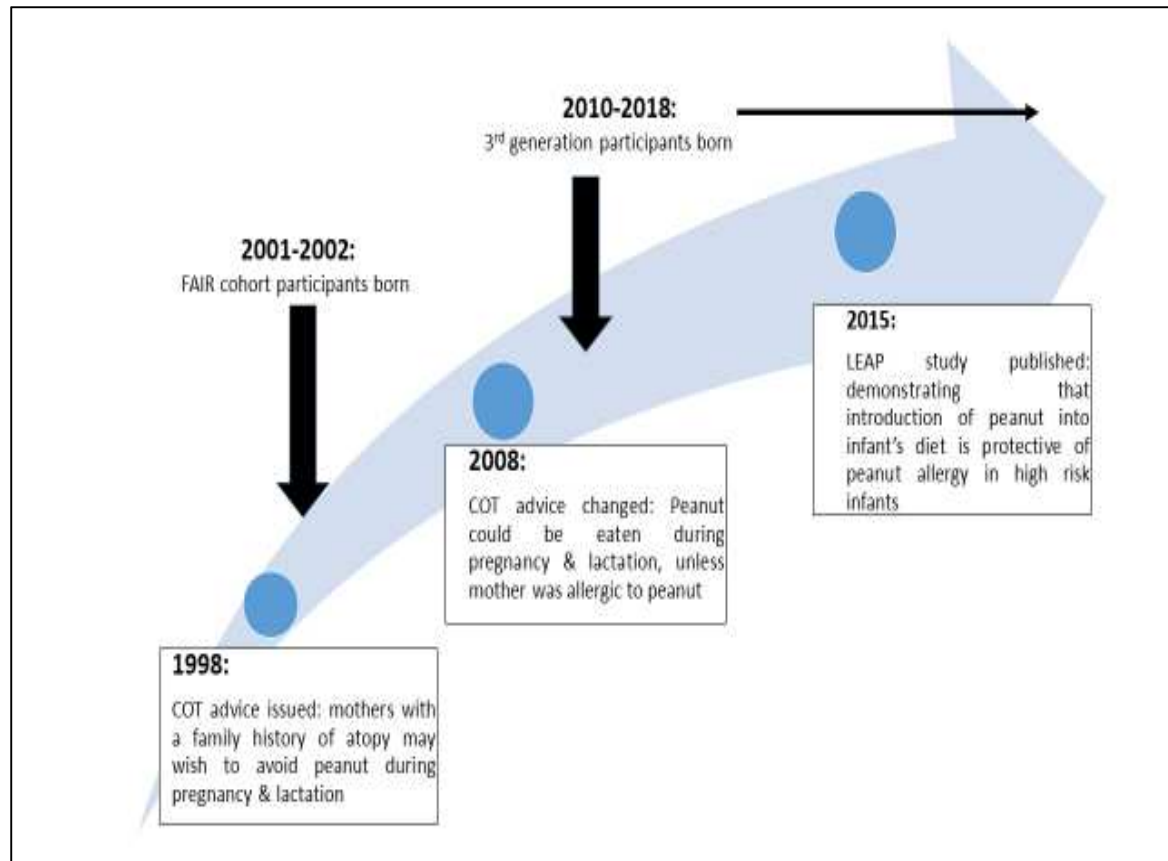
COT: Committee on Toxicity of Chemicals in Food (5).

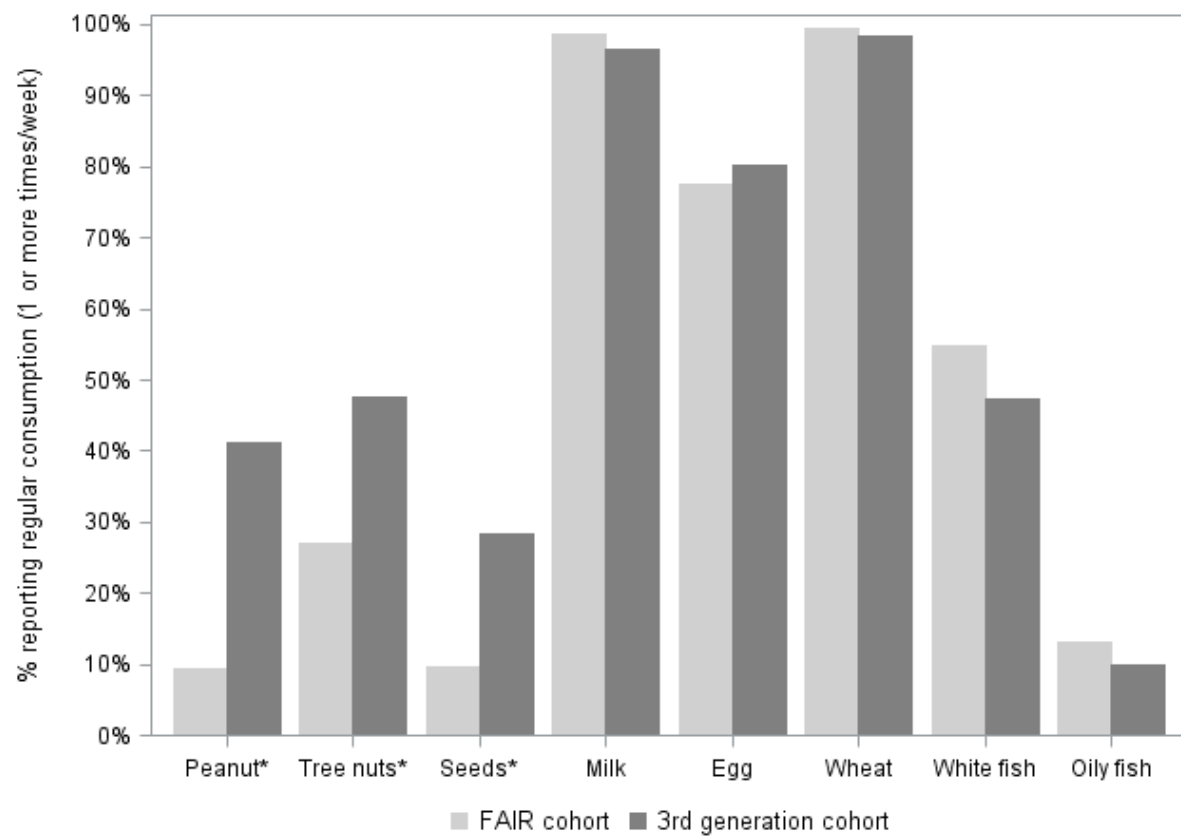
FAIR: Food Allergy and Intolerance Research Study.

LEAP: Learning Early About Peanut Allergy (11).

Figure 2. Percent of 3rd generation cohort participants that excluded peanut during pregnancy by child's year of birth (with exact 95% confidence limits).

Due to a small number of observations (n=2) with a birth year of 2012, Figure 2 only presents data from births between 2013 and 2018.





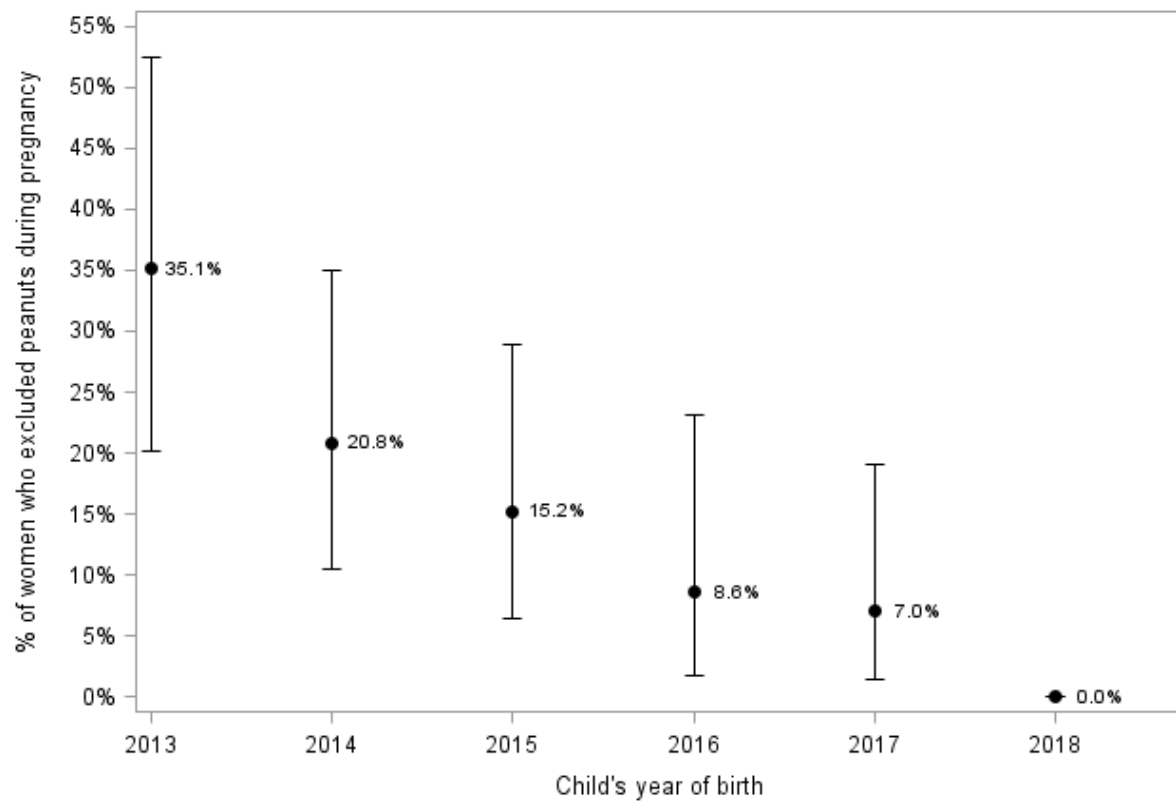


Figure E1. Percent of participants in the FAIR and 3rd generation cohorts that regularly consumed various food allergens during the third trimester of pregnancy.

*Significant difference at Bonferroni-corrected alpha level: $p < 0.0001$

Supplementary file 2: Statistical analysis and Tables E1-E3**Details of statistical analysis**

Descriptive statistics were calculated for the total sample including participants from both cohorts, as well as separately for each of the two cohorts. Differences between the two cohorts in maternal characteristics, pregnancy diet data, and infant feeding data were tested using t-tests and Wilcoxon rank sum tests for continuous variables, and chi-squared and Fisher's exact tests for categorical variables. To compare frequency of intake of key food allergens during pregnancy between the cohorts, frequency categories were collapsed into two categories: rarely (less than once per week) or regularly (once per week or more). Significant differences in frequency of food allergen consumption between the two cohorts were assessed using a multiple comparison-corrected Bonferroni alpha level of $0.5/8 = 0.0625$.

Multivariable logistic regression models were fit to test the association between cohort membership and exclusion of peanuts during pregnancy and exclusion of any foods during breastfeeding. Using only data from the 3rd generation cohort, multivariable logistic regression models were fit to test the association between child's year of birth with exclusion of peanuts during pregnancy and exclusion of any foods during breastfeeding. For the models looking at associations with child's year of birth, year of birth was included as a categorical predictor variable. Covariates were selected on the basis of previous publications and biological rationale. All models adjusted for primiparity (no vs. yes), vegetarian diet (no vs. yes), maternal education (≤ 16 years of age vs. continued education past 16 years of age), maternal food allergy (no vs. yes), and maternal age (years).

Table E1. Maternal and infant feeding characteristics

Maternal characteristics				
	Total	FAIR	3 rd generation	
Continuous variables	mean $\pm$ SD			p-value*
Maternal age (years)	27.70 $\pm$ 5.73	28.81 $\pm$ 6.10	24.77 $\pm$ 3.08	<0.001
Portions fruits and vegetables consumed per day during pregnancy	2.94 $\pm$ 1.49	2.86 $\pm$ 1.50	3.23 $\pm$ 1.43	<0.001
Categorical variables	n (%)			p-value [§]
Maternal education greater than 16 years	781 (64.4%)	589 (60.8%)	192 (79.0%)	<0.001
Maternal food allergy	243 (18.7%)	189 (19.6%)	54 (16.1%)	0.150
Primiparous	526 (44.4%)	378 (42.0%)	148 (52.1%)	0.003
Multivitamin/mineral supplement during pregnancy	369 (30.8%)	241 (25.8%)	128 (48.3%)	<0.001
Vegetarian diet	77 (6.4%)	69 (7.4%)	8 (3.0%)	0.011
Vegan diet	3 (0.3%)	2 (0.2%)	1 (0.4%)	0.527
Excluding peanuts during pregnancy	559 (47.6%)	521 (55.6%)	38 (16.0%)	<0.001
Infant feeding characteristics				
Continuous variables	median (IQR)			p-value**
Breastfeeding duration (days), capped at 3 months	56.0 (14.0-98.0)	77.0 (21.0-98.0)	21.0 (7.0-49.0)	<0.001
Age of introduction of solid foods (weeks)	16.0 (13.0-16.0)	16.0 (13.0-16.0)	17.0 (17.0-21.0)	<0.001
Categorical variables	n (%)			p-value [§]
Any breastfeeding	901 (75.6%)	706 (76.5%)	195 (72.5%)	0.179
Exclusion of any foods during breastfeeding	307 (38.6%)	265 (43.4%)	42 (22.8%)	<0.001
Feeding method at 3 months				0.398
Breastmilk only	252 (21.1%)	198 (21.4%)	54 (20.4%)	
Formula only	783 (65.7%)	601 (64.8%)	182 (68.7%)	
Mixed feeding	157 (13.2%)	128 (13.8%)	29 (10.9%)	

*For t-test of difference in means between the FAIR and 3rd generation cohorts.

**For testing differences between the FAIR and 3rd generation cohorts using non-parametric Wilcoxon rank sum tests as the distributions for breastfeeding duration and age of introduction of solids were not normally distributed.

§For chi-Squared or Fisher's Exact test of difference in proportions between the FAIR and 3rd generation cohorts.

Table E2. Multivariable logistic regression model of log odds of peanut exclusion during pregnancy

Variable	Odds ratio	95% CI	p-value
Cohort: FAIR (ref) vs. 3 rd generation	0.179	0.117, 0.273	<0.001
Primiparous: No (ref) vs. yes	1.645	1.248, 2.166	<0.001
Vegetarian: No (ref) vs. yes	0.663	0.406, 1.084	0.101
Maternal education: ≤16 years (ref) vs. >16 years	0.750	0.571, 0.984	0.038
Maternal food allergy: No (ref) vs. yes	1.077	0.780, 1.486	0.652
Maternal age: Continuous (per one year increase)	1.006	0.982, 1.030	0.629

Table E3. Multivariable logistic regression model of log odds of peanut exclusion during pregnancy in 3rd generation participants only

Variable	Odds ratio	95% CI	p-value
Child's year of birth*			
2013 (ref) vs. 2014	0.542	0.185, 1.586	0.264
2013 (ref) vs. 2015	0.391	0.122, 1.252	0.114
2013 (ref) vs. 2016	0.109	0.020, 0.607	0.011
2013 (ref) vs. 2017	0.097	0.017, 0.566	0.010
Primiparous: No (ref) vs. yes	1.125	0.478, 2.645	0.788
Maternal education: ≤16 years (ref) vs. >16 years	0.644	0.242, 1.718	0.380
Maternal food allergy: No (ref) vs. yes	1.833	0.696, 4.828	0.220
Maternal age: Continuous (per one year increase)	1.176	0.987, 1.401	0.070
*Child's year of birth was modeled as a categorical predictor. The table presents pairwise comparisons with statistical significance assessed at a Bonferroni corrected alpha level of 0.05/4=0.0125.			

Supplementary file 1
Excerpt from FAIR pregnancy questionnaire

Q1. Please tick all of the following statements that are applicable to you:

- a. I am following a normal diet ☐ Yes ☐ No
- b. I am following a vegetarian diet ☐ Yes ☐ No
- c. I am following a vegan diet ☐ Yes ☐ No
- d. I am excluding raw eggs, unpasteurised soft cheese, to my pregnancy ☐ Yes ☐ No liver etc. due
- e. I am excluding PEANUTS due to my pregnancy ☐ Yes ☐ No
- f. I am following a special diet due to medical reasons (medical condition) ☐ Yes ☐ No (please state
- g. I am excluding certain foods due to personal choice (please list foods) ☐ Yes ☐ No
-

Q2. On average, how often have you eaten these foods during pregnancy?

	Never	Rarely (1-2 or less per month)	Occasionally (1-3 per week)	4 or more times per week	Uncertain
Milk and milk products (e.g. custard, yoghurt, ice cream, chocolate, butter, margarine, cheese – pizza, cheese sauce, lasagne, cheesy biscuits)					
Egg (e.g. omelettes, flans, meringues, cakes, cookies, batter mixes, egg pasta, quorn, mayonnaise, quiches)					
Wheat (e.g. bread, cereals, pasta, pizza, cakes, pies, pastry)					
White fish (e.g. tuna, fish cakes, battered fish, fish fingers)					
Shellfish (e.g. crab, prawns, shrimp, lobster, crayfish)					
Oily fish (e.g. mackerel, salmon, sardines, pilchards, herring, kipper, white bait, trout, crab, FRESH tuna)					
Peanuts (e.g. Bombay mix, peanut butter, peanut brittle, peanut cookies, sate, some vegetarian meals)					
Tree nuts - almonds, brazil nuts, pecan nuts, hazel nuts, walnuts etc (e.g. in chocolate, crunchy nut cornflakes, stuffing mix, sweet mincemeat, choc chip cookies, almond slice, marzipan, pesto sauce. Vegetarian meals, Greek desserts like baklava)					
Seeds – sesame, poppy, sunflower (e.g. on bread rolls, tahini paste)					
Citrus Fruits (e.g. orange, tangerine, grapefruit, lemon, lime)					