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Chapter 2.1

Macronutrient composition and gestational weight gain: a systematic review


* Contributed equally

Supplementary material 2.1.1. Search strategy

Relevant articles, published before 12 August 2015, were identified through eight electronic databases (Embase (in embase.com), Medline (in OvidSP), Cochrane central (in Wiley), Web-of-Science, CINAHL (in EBSCOhost), PsycINFO (in OvidSP), PubMed as supplied by publisher, and Google Scholar). The following search terms were used without language restriction:

**Embase**

('weight gain'/de OR 'weight change'/de OR (((weight OR 'body mass' OR bmi OR quetelet) NEAR/3 (gain* OR increase* OR chang*))):ab,ti) AND (((maternal nutrition'/de OR ((nutrition* OR malnutrition* OR diet* OR intake OR consum* OR color* OR feeding OR food OR glycemic* OR eating OR meal* OR fasting OR macronutrient* OR nutrient* OR eating) NEAR/6 (matern* OR pregnan* OR mother* OR prenatal OR gravid* OR gestation*)):ab,ti) OR ((pregnancy/exp OR 'pregnant woman'/de OR (pregnan*):ab,ti) AND (nutrition/exp OR diet/exp OR 'dietary intake'/exp OR (nutrit* OR diet* OR eating):ab,ti))) NOT ([animals]/lim NOT [humans]/lim)

**Medline (in OvidSP)**

("weight gain"/ OR "Body Weight Changes"/ OR (((weight OR "body mass" OR bmi OR quetelet) ADJ3 (gain* OR increase* OR chang*))):ab,ti) AND ((("Maternal Nutritional Physiological Phenomena"/ OR ((nutrition* OR malnutrition* OR diet* OR intake OR consum* OR color* OR feeding OR food OR glycemic* OR eating OR meal* OR fasting OR macronutrient* OR nutrient* OR eating) ADJ6 (matern* OR pregnan* OR mother* OR prenatal OR gravid* OR gestation*)):ab,ti) OR (exp pregnancy/ OR "pregnant women"/ OR exp "Pregnancy Trimesters"/ OR (pregnan*):ab,ti) AND (exp "Nutritional Physiological Phenomena"/ OR "Diet Records"/ OR (nutrit* OR diet* OR eating):ab,ti))) NOT (exp animals/ NOT humans/)

**Cochrane Central**

(((weight OR 'body mass' OR bmi OR quetelet) NEAR/3 (gain* OR increase* OR chang*))):ab,ti) AND (((nutrition* OR malnutrition* OR diet* OR intake OR consum* OR color* OR feeding OR food OR glycemic* OR eating OR meal* OR fasting OR macronutrient* OR nutrient* OR eating) NEAR/6 (matern* OR pregnan* OR mother* OR prenatal OR gravid* OR gestation*)):ab,ti)

**Web-of-Science**

TS=(((weight OR "body mass" OR bmi OR quetelet) NEAR/3 (gain* OR increase* OR chang*)))))) AND (((nutrition* OR malnutrition* OR diet* OR intake OR consum* OR color* OR feeding OR food OR glycemic* OR eating OR meal* OR fasting OR macronutrient* OR nutrient* OR eating) NEAR/6 (matern* OR pregnan* OR mother* OR prenatal OR gravid* OR gestation*))))) NOT ((animal* OR sheep OR rat OR rats OR ovine* OR rodent* OR baboon* OR monkey* OR primate* OR cattle OR swine OR horse* OR sow OR sows OR cow OR cows OR rabbit* OR mare OR mares OR goat* OR hamster*)) NOT (human* OR wom?n OR patient*))

**CINAHL**

(MH "weight gain"+ OR MH "Body Weight Changes" OR TX (((weight OR "body mass" OR bmi OR quetelet) N3 (gain* OR increase* OR chang*))))) AND (((MH "Maternal Nutritional Physiology"+ OR TX ((nutrition* OR malnutrition* OR diet* OR intake OR consum* OR color* OR feeding OR food OR glycemic* OR eating OR meal* OR fasting OR macronutrient* OR nutrient* OR eating) N6 (matern* OR pregnan* OR mother* OR prenatal OR gravid* OR gestation*))))) OR ((MH pregnancy+ OR MH "Expectant Mothers"+ OR MH "Pregnancy Trimesters"+ OR TX (pregnan*)) AND (MH "Nutrition"+ OR MH "Diet"+ OR TX (nutrit* OR diet* OR eating))) NOT (MH animals+ NOT human+)

**PsycINFO (in OvidSP)**

("weight gain"/ OR (((weight OR "body mass" OR bmi OR quetelet) ADJ3 (gain* OR increase* OR chang*))):ab,ti.) AND (((nutrition* OR malnutrition* OR diet* OR intake OR consum* OR color* OR feeding OR food OR glycemic* OR eating OR meal* OR fasting OR macronutrient* OR nutrient* OR eating) ADJ6 (matern* OR pregnan* OR mother* OR prenatal OR gravid* OR gestation*)):ab,ti.) OR (exp pregnancy/ OR (pregnan*):ab,ti.) AND ((nutrit* OR diet* OR eating):ab,ti.)) NOT (exp animals/ NOT humans/)

**PubMed as supplied by publisher**

Supplementary material 2.1.2. Quality score

This quality score was used to assess the quality of included studies in this systematic review and is applicable to both interventional and observational studies. The score was designed based on previously published scoring systems (1, 2). The quality score consists of 5 items, and each item is allocated 0, 1 or 2 points. This allows a total score between 0 and 10 points, 10 representing the highest quality.

1. Study design
   0 for studies with cross-sectional data collection
   1 for studies with longitudinal data collection
   2 for intervention studies

2. Study size
   Observational studies
   Intervention studies
   0 if n<500
   1 if n 500 to 2000
   2 if >2000
   0 if n<50
   1 if n 50 to 100
   2 if n>100

3. Exposure
   Observational studies
   0 if the study used no appropriate standard diet assessment or if not reported
   1 if the study used a one-day food record, a one-day 24h recall or an inappropriate FFQ
   2 if the study used an appropriate FFQ, multiple day food records, or multiple 24h recalls
   Intervention studies
   0 if the intervention was not described or not blinded
   1 if the intervention was adequately single-blinded
   2 if the intervention was adequately double-blinded

4. Outcome
   0 if the study used no appropriate outcome measurement method or if not reported
   1 if the study used a self-reported (pre-pregnancy) weight and a measured weight (at end of observation) or a self-reported gestational weight gain
   2 if the study used a measured weight at start and end of the study to calculate gestational weight gain

5. Adjustments
   0 if findings are not controlled for at least the two key covariates† mentioned below
   1 if findings are controlled for:
   - Pre-pregnancy body mass index or pre-pregnancy weight
   - Maternal age
   2 if an intervention study is adequately randomized or if findings are additionally controlled for at least two of the following covariates†:
   - Total energy intake
   - Birth weight
   - Ethnicity
   - Gestational age at delivery
   - Parity
   - Physical activity
   - Social economic status

† Either adjusted for in the statistical analyses; stratified for in the analyses; or not applicable (e.g., a study in nulliparous women only does not require controlling for parity).

Abbreviation: FFQ, food-frequency questionnaire.
### Supplementary Table 2.1.1 Associations between energy intake and gestational weight gain (N=42)

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<td>Bompiani, 1986 (3)</td>
<td>Unpaired student t-test</td>
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<td>Gaillard, 2013 (12)</td>
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<td>Energy intake per SD (1 SD = 563 kcal) and the odds of excessive GWG</td>
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<td>Ali, 2002 (26)</td>
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<td>Age, pre-pregnancy weight and height, weight-for-height ratio index, weight-height-product index, mid-arm circumference</td>
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<td>2.24 (1.16, 3.32)</td>
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<td>1.70 (0.86, 2.54)</td>
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<td>Ebrahami, 2015 (continued)</td>
<td>Logistic regression</td>
<td>Energy intake (kcal) and the odds of adequate (vs. excessive) GWG</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
<td></td>
<td></td>
<td>$1.00 (&lt;1.00, 1.00)$</td>
<td>$\geq 0.05$</td>
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<tr>
<td></td>
<td>Cumulative Logit Model for Ordinal Responses</td>
<td>Odd ratio between energy intake (kcal) and adequacy of GWG (inadequate, adequate and excessive GWG)</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
<td></td>
<td></td>
<td>$1.00 (1.00, 1.00)$</td>
<td>$0.25$</td>
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<td>Ho, 2005 (32)</td>
<td>ANOVA</td>
<td>Difference in GWG (kg) per energy intake (in tertiles)</td>
<td>null</td>
<td>T1</td>
<td>0.20</td>
<td>&lt;0.01</td>
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<td></td>
<td>Pearson</td>
<td>Correlation between energy intake (kcal/day) and GWG (kg)</td>
<td></td>
<td>T2</td>
<td>0.19</td>
<td>&lt;0.01</td>
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<td></td>
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<td></td>
<td>T3</td>
<td>0.22</td>
<td>&lt;0.01</td>
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<tr>
<td>Jaruratanasiriku, 2009 (34)</td>
<td>Logistic regression</td>
<td>Energy intake (kcal) and the odds of inadequate (vs. adequate) GWG</td>
<td>Pre-pregnancy BMI, maternal education, family income, intake of calcium and iron</td>
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<td>$0.91 (0.62, 2.72)$</td>
<td>0.33</td>
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<tr>
<td>Kardjati, 1990 (35)</td>
<td>Regression</td>
<td>Association between energy intake (kcal) and GWG (kg)</td>
<td>Parity, pre-pregnancy BMI, gender of the child, protein intake, compliance to the supplementation intake</td>
<td>T2</td>
<td>NR</td>
<td>NS</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>T3</td>
<td>NR</td>
<td>NS</td>
<td></td>
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<tr>
<td></td>
<td>Correlation</td>
<td>Correlation between energy intake (kcal) and GWG (kg)</td>
<td></td>
<td>T2</td>
<td>0.15</td>
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<td>T3</td>
<td>0.08</td>
<td>NS</td>
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<td>Lechtig, 1978 (36)</td>
<td>Student t-test</td>
<td>Difference in percentage mothers with a monthly adequate GWG per energy intake (high energy supplemented vs. low energy supplemented)</td>
<td>null</td>
<td></td>
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<td>$&lt;0.10$</td>
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<tr>
<td>Popa, 2014 (37)</td>
<td>Chi-square test</td>
<td>Difference in energy intake (kcal) between women with inadequate GWG and adequate GWG</td>
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<td>$&lt;0.01$</td>
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<tr>
<td></td>
<td>Chi-square test</td>
<td>Difference in energy intake (kcal) between women with adequate GWG and excessive GWG</td>
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<td>$&lt;0.01$</td>
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<tr>
<td></td>
<td>Multinomial logistic regression</td>
<td>Energy intake (quartiles) and the odds of inadequate GWG (vs. adequate GWG)</td>
<td>Age, pre-pregnancy BMI, adequacy of prenatal care utilization index, area of residence</td>
<td></td>
<td></td>
<td>Q1: 1.41 (0.73, 2.72) Q2+Q3: reference Q4: 1.82 (0.89, 3.74)</td>
<td>0.31</td>
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Supplementary Table 2.1.1 (continued). Associations between energy intake and gestational weight gain (N=42)
### Supplementary Table 2.1.1 (continued). Associations between energy intake and gestational weight gain (N=42)

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Statistical analysis</th>
<th>Measure of association</th>
<th>Covariate adjustments</th>
<th>Subgroups</th>
<th>Trimester</th>
<th>Effect estimate ± (95% CI)</th>
<th>P-value</th>
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<tr>
<td>Popa, 2014 (continued)</td>
<td>Multinomial logistic regression</td>
<td>Energy intake (quartiles) and the odds of excessive GWG (vs. adequate GWG)</td>
<td>Age, pre-pregnancy BMI, adequacy of prenatal care utilization index, area of residence</td>
<td>Q1: 0.66 (0.35, 1.23)</td>
<td>0.19</td>
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<tr>
<td>Rodrigues, 2008 (38)</td>
<td>Linear mixed model</td>
<td>Adequacy of energy intake (%) and change in weight (kg)</td>
<td>Age, gestational age at delivery, age at menarche, triglycerides, blood glucose</td>
<td>-0.06 (-0.10, -0.03)</td>
<td>&lt;0.01</td>
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<tr>
<td>Saowakontha, 1992 (39)</td>
<td>Linear regression</td>
<td>Explained variance of GWG (R²) by energy intake (kcal)</td>
<td>Rural T1 NR</td>
<td>NS</td>
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<tr>
<td>Rodribes, 1993 (39)</td>
<td>Linear regression</td>
<td>Explained variance of GWG (R²) by energy intake (kcal)</td>
<td>Rural T2 NR</td>
<td>NS</td>
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<td>Rodrigues, 2008 (38)</td>
<td>Linear mixed model</td>
<td>Adequacy of energy intake (%) and change in weight (kg)</td>
<td>Rural T3 NR</td>
<td>NS</td>
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<td>Rodrigues, 2008 (38)</td>
<td>Linear mixed model</td>
<td>Adequacy of energy intake (%) and change in weight (kg)</td>
<td>Urban T1 14.0</td>
<td>≤0.05</td>
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<td>Rodrigues, 2008 (38)</td>
<td>Linear mixed model</td>
<td>Adequacy of energy intake (%) and change in weight (kg)</td>
<td>Urban T2 26.3</td>
<td>≤0.05</td>
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<td>Rodrigues, 2008 (38)</td>
<td>Linear mixed model</td>
<td>Adequacy of energy intake (%) and change in weight (kg)</td>
<td>Urban T3 28.1</td>
<td>≤0.05</td>
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<tr>
<td>Siega-Riz, 1993 (40)</td>
<td>Linear regression</td>
<td>Association between energy intake (kJ) and GWG (kg)</td>
<td>Maternal age, parity, pre-pregnancy BMI, gestational age at delivery, physical activity</td>
<td>0.50 (0.05, 0.95)</td>
<td>&lt;0.05</td>
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<tr>
<td>Smith, 1997 (41)</td>
<td>Stepwise regression analysis</td>
<td>Association between energy intake and GWG (kg)</td>
<td>NR</td>
<td>NS</td>
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<tr>
<td>Wagner, 1975 (42)</td>
<td>Student t-test</td>
<td>Difference in GWG (g/week) between energy intake (3 categories)</td>
<td>+10</td>
<td>&lt;0.05</td>
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<tr>
<td>Zulfiqar, 2011 (43)</td>
<td>Regression</td>
<td>Association between energy intake (kcal/day) and GWG (g/week)</td>
<td>0.05 (NR)</td>
<td>0.33</td>
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**Case control study**

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<tr>
<th>First author, year</th>
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<th>Measure of association</th>
<th>Covariate adjustments</th>
<th>Trimester</th>
<th>Effect estimate ± (95% CI)</th>
<th>P-value</th>
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<td>Costa, 2011 (44)</td>
<td>Spearman correlation</td>
<td>Correlation between energy intake (kcal) and adequacy of GWG</td>
<td>Maternal age, pre-pregnancy BMI, protein intake, total cholesterol, several micronutrients</td>
<td>0.15</td>
<td>0.04</td>
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<tr>
<td>Linear regression</td>
<td>Association between energy intake (kcal) and adequacy of GWG</td>
<td>Maternal age, pre-pregnancy BMI, protein intake, total cholesterol, several micronutrients</td>
<td>0.04 (NR)</td>
<td>0.87</td>
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1: Parameter estimate of the used statistical method, + = positive value, - = negative value, null = no association; 2: Slightly different macronutrient composition among the two diets; 3: Only descriptive, no statistical analysis. Based on reported numbers and the assumption of a normal distribution of carbohydrate intake, we have a Welch t-test performed; 4: p for trend; 5: 95% confidence interval calculated using reported mean and standard error; 6: Change in energy intake as compared with previous dietary assessment (cT1: change during 1st trimester of pregnancy, cT1-3: change during 3rd until 8th month of pregnancy); 7: Recommended energy intake based on IOM 2009 recommendation and uses maternal age, weight, height and physical activity level (45); 8: Category 1 (lowest caloric intake) versus all other 4 categories; 9: Living location of the
women (rural vs. urban); 10. Highest category of energy intake compared with lowest category energy intake (in total 3 categories). **Abbreviations:** ANOVA, Analysis of Variance; BMI, body mass index (kg/m²); CI, confidence interval; GEE, generalized estimating equation; GWG, gestational weight gain; lbs, pounds; NR, not reported; NS, not significant; OC, oral contraceptive; Q, quartile; SD, standard deviation; T, trimester of pregnancy.
**Supplementary Table 2.1.2. Associations between macronutrient supplementation and gestational weight gain (N=11)**

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Statistical analysis</th>
<th>Measure of association</th>
<th>Details supplementation</th>
<th>Subgroups</th>
<th>Trimester</th>
<th>Effect estimate</th>
<th>P-value</th>
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<tr>
<td><strong>High-income countries</strong></td>
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<td></td>
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<tr>
<td>Viegas, 1982a (46)</td>
<td>NR</td>
<td>Difference in GWG (g/week) between 3 groups (En/Pr/Vi vs. En/Vi vs. Vi)</td>
<td>En/Pr/Vi: 273 kcal/day (11% protein) En/Vi: 273 kcal/day (100% carbohydrate) Supplemented during T2 and T3</td>
<td>T2 T3</td>
<td>+²</td>
<td>&lt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>Viegas, 1982b (47)</td>
<td>NR</td>
<td>Difference in GWG (g/week) between 3 groups (En/Pr/Vi vs. En/Vi vs. Vi)</td>
<td>En/Pr/Vi: 425 kcal/day (10% protein) En/Vi: 425 kcal/day (100% carbohydrate) Supplemented during T3</td>
<td>T3</td>
<td>null²</td>
<td>&gt;0.05</td>
<td>NS</td>
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<tr>
<td><strong>Low- and middle-income countries</strong></td>
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<tr>
<td>Adair, 1984 (48)</td>
<td>NR</td>
<td>Different in GWG (kg) between 2 groups (En vs. placebo)</td>
<td>En: 400 kcal/day (50% carbohydrate, 20% protein, 30% fat) Placebo (&lt;June 1971): 3 kcal/day; Placebo (≥June 1971): 43 kcal/day (93% carbohydrate, trace protein and fat) Supplemented during T1, T2 and T3</td>
<td>null</td>
<td>NS</td>
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<tr>
<td>Begum, 1991 (49)</td>
<td>NR</td>
<td>Difference in GWG (kg and kg/week) between 2 groups (En vs. NoS)</td>
<td>En: 520 kcal (13% protein, 31% fat) Supplemented during T1, T2 and T3 (subgroup: T2 and T3)</td>
<td>+</td>
<td>&lt;0.05</td>
<td></td>
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<tr>
<td>Hussain, 1988 (50)</td>
<td>NR</td>
<td>Difference in GWG (kg/week) between 2 groups (En vs. NoS)</td>
<td>En: 488 kcal (14% protein, 27% fat) Supplemented during T2 and T3 (duration: 12 weeks)</td>
<td>+</td>
<td>&lt;0.05</td>
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<tr>
<td>Hussain, 1988 (50)</td>
<td>NR</td>
<td>Difference in GWG (kg) between 2 groups (En vs. NoS)</td>
<td>En: 488 kcal (14% protein, 27% fat) Supplemented during T2 and T3 (duration: 12 weeks)</td>
<td>null</td>
<td>NS</td>
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<td></td>
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<tr>
<td>Kardjati, 1990 (35)</td>
<td>ANOVA</td>
<td>Difference in GWG (kg) between 2 groups (HEN vs. LEn) and divided into categories based on compliance supplement intake</td>
<td>HEn: 465 kcal/day (40% carbohydrate, 10% protein, 50% fat) LEn: 52 kcal/day (25% carbohydrate, 50% protein) Supplemented during T3</td>
<td>T2 T3</td>
<td>null</td>
<td>NS</td>
<td>NS</td>
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<td>Kaseb, 2002 (51)</td>
<td>Students t-test</td>
<td>Difference in GWG (kg) between 2 groups (En/Pr vs. NoS)</td>
<td>En/Pr: 400 kcal/day (5 days/week; 15% protein) Supplemented during T2 and T3</td>
<td>+</td>
<td>&lt;0.02</td>
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### Supplementary Table 2.1.2. (continued) Associations between macronutrient supplementation and gestational weight gain (N=11)

<table>
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<tr>
<th>First author, year</th>
<th>Statistical analysis</th>
<th>Measure of association</th>
<th>Details supplementation</th>
<th>Subgroups</th>
<th>Trimester</th>
<th>Effect estimate$^1$</th>
<th>P-value</th>
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<tr>
<td>Nahar, 2009 (52)</td>
<td>ANOVA</td>
<td>Difference in GWG (kg) between 2 groups (En vs. NoS)</td>
<td>En: 600 kcal/day (6 days/week; 80% carbohydrate, 12% protein, 8% fat) Supplemented during T2 and T3</td>
<td>BMI &lt;18.5</td>
<td>NR</td>
<td>NR</td>
<td>NS</td>
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<tr>
<td>Ortolano, 2003 (53)</td>
<td>Two-sided t-test</td>
<td>Difference in GWG (kg/month) between 2 groups$^5$ (En vs NoS)</td>
<td>En: 600 kcal/day Supplemented period NR</td>
<td>+</td>
<td>&lt;0.01</td>
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<tr>
<td>Ortolano, 2003 (53)</td>
<td>Two-sided t-test</td>
<td>Difference in GWG adequacy between 2 groups$^5$ (En vs NoS)</td>
<td>En: 600 kcal/day Supplemented period NR</td>
<td>+</td>
<td>&lt;0.01</td>
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<td>Qureshi, 1973 (54)</td>
<td>None$^6$</td>
<td>Difference in GWG (kg) between 2 groups (En/Pr/MiN vs MiN supplementation)</td>
<td>En/Pr/MiN: 500 kcal/day (16% protein) Supplemented during T2 and T3</td>
<td>null</td>
<td>0.09</td>
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<td>Tontisirin, 1986 (55)</td>
<td>Unpaired t-test</td>
<td>Difference in GWG (kg/week) between 3 groups (I (En/Pr) and II (En/Pr) vs. III (NoS))</td>
<td>En/Pr (group I and II): 350 kcal/day (15% protein) Supplemented during T3</td>
<td>+$^7$</td>
<td>&lt;0.01</td>
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$^1$ Parameter estimate of the used statistical method, + = positive value, - = negative value, null = no association; $^2$ Pr/En/Vi supplementation compared with Vi supplementation; $^3$ Adequacy of fat accretion was based on increase in triceps skinfold thickness increment during the second trimester; $^4$ Pr/En/Vi supplementation compared with En/Vi supplementation and Vi supplementation; $^5$ Significant difference in BMI between supplemented group and control group (BMI resp. 17 and 20 kg/m$^2$); $^6$ Results were only descriptive. Using reported mean weight gains and standard deviations, we calculated a p-value using an independent sample t-test; $^7$ Group I and group II vs group III (supplemented groups vs not-supplemented group); **Abbreviations:** ANOVA, analysis of variance; BMI, body mass index (kg/m$^2$); En, energy supplementation; En/Pr, energy/protein supplementation; En/Pr/MiN, energy/protein and micronutrient supplementation; En/Pr/Vi, energy/protein/vitamin supplementation; GWG, gestational weight gain; HEn, high energy supplementation; Len, low energy supplementation; MiN, micronutrient supplementation; NoS, no supplementation; NR, not reported; NS, not significant; T, trimester of pregnancy; Vi, vitamin supplementation.
### Supplementary Table 2.1.3: Associations between protein intake and gestational weight gain (N=29)

<table>
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<tr>
<th>First author, year</th>
<th>Statistical analysis</th>
<th>Measure of association</th>
<th>Covariate adjustments</th>
<th>Subgroups</th>
<th>Trimester</th>
<th>Effect estimate $^1$ (95% CI)</th>
<th>P-value</th>
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<td><strong>Longitudinal studies</strong></td>
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<td>Ancri, 1977 (6)</td>
<td>Rank correlation</td>
<td>Correlation between protein intake (g) and GWG (kg)</td>
<td>Stratified by age</td>
<td>18-19 y, 20-24 y, 25-32 y</td>
<td>NR, NR, +0.47</td>
<td>NR, NS, &lt;0.05</td>
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<tr>
<td>Anderson, 1986 (7)</td>
<td>None $^2$</td>
<td>Difference in protein intake (E%) between categories of GWG adequacy</td>
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<td>Blumfield, 2015 (10)</td>
<td>Kruskal-Wallis test</td>
<td>Difference in protein intake (E%) between categories of GWG adequacy</td>
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<td>Gaillard, 2013 (12)</td>
<td>Logistic regression</td>
<td>Protein intake per SD (1 SD = 2.6 E%) and the odds of excessive GWG</td>
<td>Age, parity, pre-pregnancy BMI, maternal education, ethnicity, smoking during pregnancy, energy intake, folic acid supplementation, alcohol consumption during pregnancy</td>
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<td>1.91 (1.26, 2.88)</td>
<td>&lt;0.01</td>
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<td>Lagiou, 2004 (14)</td>
<td>Linear regression</td>
<td>Association between protein intake (per SD increase) and GWG (kg)</td>
<td>Age, parity, pre-pregnancy BMI, maternal education, smoking during pregnancy, energy intake, gestational age at delivery, gender of the baby, maternal height, pre-pregnancy OC use</td>
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<td>3.11 (1.72, 4.50) $^3$</td>
<td>&lt;0.01 $^*$</td>
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<tr>
<td>Maple-Brown, 2013 (16)</td>
<td>Pearson correlation</td>
<td>Correlation between protein intake and GWG (kg)</td>
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<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NS</td>
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<tr>
<td>Maslova, 2015 (56)</td>
<td>Linear regression</td>
<td>Difference in GWG (g/week) when substituting energy-adjusted carbohydrate for energy-adjusted protein (in quintiles)</td>
<td>Age, parity, pre-pregnancy BMI, socio-economic indicators, smoking during pregnancy, physical activity, maternal height, fat intake</td>
<td>Q1: reference</td>
<td>Q2: -10 (-17, -4)</td>
<td>&lt;0.01 $^*$</td>
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<td></td>
<td>Linear regression</td>
<td>Difference in GWG (g/week) when substituting energy-adjusted fat for energy-adjusted protein</td>
<td>Age, parity, pre-pregnancy BMI, socio-economic indicators, smoking during pregnancy, physical activity, maternal height, carbohydrate intake</td>
<td>NR</td>
<td>NR</td>
<td>&lt;0.05</td>
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**Supplementary Table 2.1.3** (continued). Associations between protein intake and gestational weight gain (N=29)

<table>
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<th>First author, year</th>
<th>Statistical analysis</th>
<th>Measure of association</th>
<th>Covariate adjustments</th>
<th>Subgroups</th>
<th>Trimester</th>
<th>Effect estimate&lt;sup&gt;1&lt;/sup&gt; (95% CI)</th>
<th>P-value</th>
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<tr>
<td><strong>Maslova, 2015</strong> (cont’d)</td>
<td>Linear regression</td>
<td>Difference in GWG (g/week) for energy-adjusted protein: carbohydrate ratio z-score (in quintiles)</td>
<td>Age, parity, pre-pregnancy BMI, socio-economic indicators, smoking during pregnancy, physical activity, maternal height, fat intake</td>
<td>Normal weight</td>
<td>Q1: reference</td>
<td>Q5: -15 (-12, -8)</td>
<td>&lt;0.01&lt;sup&gt;4&lt;/sup&gt;</td>
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<td>Linear regression</td>
<td>Difference in GWG (g/week) for &lt;12 E% protein vs. ≥12 E% protein</td>
<td>Age, parity, pre-pregnancy BMI, socio-economic indicators, smoking during pregnancy, physical activity, maternal height, carbohydrate intake</td>
<td>Overweight</td>
<td>Q1: reference</td>
<td>Q5: -26 (-43, -10)</td>
<td>&lt;0.01&lt;sup&gt;4&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>Linear regression</td>
<td>Difference in GWG (g/week) for &gt;20 E% protein vs. ≤20 E% protein</td>
<td>Age, parity, pre-pregnancy BMI, socio-economic indicators, smoking during pregnancy, physical activity, maternal height, carbohydrate intake</td>
<td>Obese</td>
<td>Q1: reference</td>
<td>Q5: 11 (-21, 43)</td>
<td>0.57&lt;sup&gt;4&lt;/sup&gt;</td>
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<tr>
<td>Olafsdottir, 2006 (18)</td>
<td>ANOVA</td>
<td>Difference in protein intake (E%) between categories of GWG adequacy</td>
<td>BMI &lt; 25 BMI ≥ 25</td>
<td>NR</td>
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<td>NS</td>
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<td>Ostachowska-Gasior, 2003 (19)</td>
<td>NR</td>
<td>Difference in protein intake (E%) between adequate and excessive GWG</td>
<td>T1</td>
<td>null</td>
<td>NS</td>
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<tr>
<td>Papoz, 1980 (20)</td>
<td>Pearson correlation</td>
<td>Correlation between protein intake (g) and GWG (kg)</td>
<td>T1&lt;sup&gt;5&lt;/sup&gt; cT1&lt;sup&gt;5&lt;/sup&gt; cT1-3&lt;sup&gt;5&lt;/sup&gt;</td>
<td>0.19 0.27 -0.21</td>
<td>&lt;0.01 &lt;0.01 &lt;0.01</td>
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<td>Picone, 1982 (21)</td>
<td>ANOVA</td>
<td>Difference in protein intake (g) between categories of GWG adequacy</td>
<td>null</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td>Renault, 2015 (57)</td>
<td>Linear regression</td>
<td>Difference in GWG (kg) when substituting carbohydrates (E%) for protein (E%) (in quartiles)</td>
<td>Age, parity, pre-pregnancy BMI, smoking during pregnancy, energy intake, intervention group</td>
<td>Q1: reference</td>
<td>Q2: 0.4 (-1.5, 2.2) Q3: 0.9 (-1.0, 2.7) Q4: 0.0 (-1.9, 1.9)</td>
<td>0.86&lt;sup&gt;4&lt;/sup&gt;</td>
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### Supplementary Table 2.1.3 (continued). Associations between protein intake and gestational weight gain (N=29)

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Statistical analysis</th>
<th>Measure of association</th>
<th>Covariate adjustments</th>
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<th>Effect estimate 1 (95% CI)</th>
<th>P-value</th>
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<td>Shin, 2014 (23)</td>
<td>Wald F test</td>
<td>Difference in protein intake (E%) between categories of GWG adequacy (inadequate vs. adequate GWG)</td>
<td>Age, pre-pregnancy BMI, education, family poverty income ratio, ethnicity, smoking during pregnancy, physical activity, trimester of gestation, marital status, daily supplement use</td>
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<td>+</td>
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<td>Sloan, 2001 (58)</td>
<td>NR</td>
<td>Difference in GWG (kg) between protein intake (categories; g/day)</td>
<td>null</td>
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<td>Stuebe, 2009 (24)</td>
<td>Logistic regression</td>
<td>Protein intake (per 5 E% compared to carbohydrates) and the odds of excessive (vs. not excessive) GWG</td>
<td>Age, pre-pregnancy BMI, ethnicity, smoking, gestational age at delivery, nausea during first trimester of pregnancy, other macronutrients (E%)</td>
<td></td>
<td></td>
<td>1.10 (0.86, 1.42)</td>
<td>NS</td>
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<td>Uusitalo, 2009 (25)</td>
<td>Linear regression</td>
<td>Association between protein intake (E%) and GWG (kg)</td>
<td>Age, parity, pre-pregnancy BMI, maternal education, smoking, birth weight, living area, gestational duration at first weight measurement</td>
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<td>-0.00 (NR)</td>
<td>&lt;0.01</td>
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### Low- and middle-income countries

#### Longitudinal studies

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<th>Trimester</th>
<th>Effect estimate 1 (95% CI)</th>
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<tr>
<td>Ali, 2002 (26)</td>
<td>Linear regression</td>
<td>Association between protein intake and GWG (kg)</td>
<td>Age, pre-pregnancy weight and height, energy intake, weight for height ratio index, weight-height-product index, mid arm circumference</td>
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<td></td>
<td>1.92 (1.42, 2.42)</td>
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<td>Changamire, 2014 (28)</td>
<td>GEE</td>
<td>Difference in GWG (g/month) when substituting 5E% from fat with protein</td>
<td>Parity, pre-pregnancy BMI, maternal education, socio-economic position indicator, energy intake, maternal height, baseline haemoglobin level, marital status, season, trimester of pregnancy, multivitamin regimen assignment, other macronutrients</td>
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<td>-72 (-140, -6)</td>
<td>0.03</td>
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**Supplementary Table 2.1.3 (continued). Associations between protein intake and gestational weight gain (N=29)**

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<td>Changamire, 2014 (cont’d)</td>
<td>GEE</td>
<td>Difference in GWG (g/month) when substituting 5E% from carbohydrate with protein</td>
<td>Parity, pre-pregnancy BMI, maternal education, socio-economic position indicator, energy intake, maternal height, baseline haemoglobin level, marital status, season, trimester of pregnancy, multivitamin regimen assignment, other macronutrients</td>
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<td>-70 (-12.4, -15)</td>
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<td>Das, 1976 (29)</td>
<td>ANOVA</td>
<td>Difference in GWG (kg) per protein intake category</td>
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<td>NR</td>
<td>NS</td>
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<td>Ebrahimi, 2015 (31)</td>
<td>Logistic regression</td>
<td>Protein intake (g) and the odds of inadequate (vs. adequate) GWG</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
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<td>&lt;1.00 (0.97, 1.00)</td>
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<td>Logistic regression</td>
<td>Protein intake (g) and the odds of inadequate (vs. excessive) GWG</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
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<td></td>
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<td>0.99 (0.97, 1.01)</td>
<td>≥0.05</td>
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<td>Logistic regression</td>
<td>Protein intake (g) and the odds of adequate (vs. excessive) GWG</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
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<td>1.00 (0.99, 1.01)</td>
<td>≥0.05</td>
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<tr>
<td>Cumulative Logit Model for Ordinal Responses</td>
<td>Odds ratio between protein intake (g) and adequacy of GWG (inadequate, adequate and excessive GWG)</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
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<td>1.00 (0.99, 1.01)</td>
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<td>Hsu, 2013 (33)</td>
<td>Pearson correlation</td>
<td>Correlation between protein intake (g/day) and GWG (kg)</td>
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<td>T1</td>
<td>0.21</td>
<td>&lt;0.01</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T2</td>
<td>0.17</td>
<td>&lt;0.01</td>
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<td></td>
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<td></td>
<td>T3</td>
<td>0.20</td>
<td>&lt;0.01</td>
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<tr>
<td>Jaruratanasirikul, 2009 (34)</td>
<td>Logistic regression</td>
<td>Protein intake (g) and the odds of Inadequate (vs. adequate) GWG</td>
<td>Pre-pregnancy BMI, maternal education, energy intake, family income, intake of calcium and iron</td>
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<td>0.57 (0.21, 1.54)</td>
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<td>Kardjati, 1990 (35)</td>
<td>Regression</td>
<td>Association between protein intake (g) and GWG (kg)</td>
<td>Parity, pre-pregnancy BMI, energy intake, gender of the child, compliance to the supplementation intake</td>
<td>T2</td>
<td>0.04 (NR)</td>
<td>&lt;0.01</td>
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<td></td>
<td>Correlation</td>
<td>Correlation between protein intake (g) and GWG (kg)</td>
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<td>Popa, 2014 (37)</td>
<td>Chi-square test</td>
<td>Difference in protein intake (E%) between women with inadequate GWG and excessive GWG</td>
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<td>0.02</td>
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### Supplementary Table 2.1.3 (continued). Associations between protein intake and gestational weight gain (N=29)

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<td>Popa, 2014 (cont’d)</td>
<td>Chi-square test</td>
<td>Difference in protein intake (E%) between women with adequate GWG and excessive GWG</td>
<td>null</td>
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<td>-0.01 (-0.04,0.03)</td>
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<tr>
<td>Rodrigues, 2008 (38)</td>
<td>Linear regression</td>
<td>Association between protein intake (g/day) and GWG (kg)</td>
<td>Rural</td>
<td>T1</td>
<td>NR</td>
<td>NS</td>
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<td>Rural</td>
<td>T2</td>
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<td>T3</td>
<td>NR</td>
<td>NS</td>
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<td></td>
<td></td>
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<td>Urban</td>
<td>T1</td>
<td>NR</td>
<td>NS</td>
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<tr>
<td></td>
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<td>Urban</td>
<td>T2</td>
<td>27.8</td>
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<td>Urban</td>
<td>T3</td>
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<tr>
<td>Saowakontha, 1992 (39)</td>
<td>Linear regression</td>
<td>Explained variance of GWG (R²) by protein intake (g)</td>
<td>Rural</td>
<td>T1</td>
<td>NR</td>
<td>NS</td>
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<td>T2</td>
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<td>Rural</td>
<td>T3</td>
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<td></td>
<td></td>
<td></td>
<td>Urban</td>
<td>T1</td>
<td>NR</td>
<td>NS</td>
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<td></td>
<td></td>
<td></td>
<td>Urban</td>
<td>T2</td>
<td>27.8</td>
<td>≤0.05</td>
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<td></td>
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<td>T3</td>
<td>20.6</td>
<td>≤0.05</td>
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<tr>
<td>Wagner, 1975 (42)</td>
<td>Student t-test</td>
<td>Difference in GWG (g/week) between protein intake (3 categories)</td>
<td>null</td>
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<td>NS</td>
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<tr>
<td>Zulfiqar, 2011 (43)</td>
<td>Regression</td>
<td>Association between protein intake (g/day) and GWG (g/week)</td>
<td>Rural</td>
<td>T1</td>
<td>NR</td>
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<tr>
<td>Case control study</td>
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<td>Rural</td>
<td>T2</td>
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<td>Costa, 2011 (44)</td>
<td>Spearman correlation</td>
<td>Correlation between protein intake (g) and GWG (kg)</td>
<td>Age, pre-pregnancy BMI, energy intake, total cholesterol, several micronutrients</td>
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<td>0.48 (NR)</td>
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<td>Linear regression</td>
<td>Association between protein intake (g/day) and adequacy of GWG</td>
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¹ Parameter estimate of the used statistical method, + = positive value, - = negative value, null = no association; ² Only descriptive, no statistical analysis. Based on reported numbers and the assumption of a normal distribution of carbohydrate intake, we have a Welch t-test performed; ³ 95% confidence interval calculated using reported mean and standard error; ⁴ p for trend; ⁵ Change in protein intake as compared with previous dietary assessment (cT1: change during 1st trimester of pregnancy, cT1-3: change during 3rd until 8th month of pregnancy); ⁶ Reported p-value and mean, however calculated 95% CI (based on reported standard error) is in disagreement with this reported p-value. ⁷ Living location of the women (rural vs. urban); **Abbreviations**: ANOVA, Analysis of Variance; BMI, body mass index (kg/m²); CI, confidence interval; E%, energy percent; GEE, generalized estimating equation; GWG, gestational weight gain; NR, not reported; NS, not significant; OC, oral contraceptive; Q, quartiles or quintiles; SD, standard deviation; T: trimester of pregnancy.
### Supplementary Table 2.1.4: Associations between source of protein and gestational weight gain (N=2)

<table>
<thead>
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<th>Measure of association</th>
<th>Covariate adjustments</th>
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<td><strong>Longitudinal studies, high-income countries</strong></td>
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<tr>
<td>Maslova, 2015 (56)</td>
<td>Linear regression</td>
<td>Difference in GWG (g/week) when substituting carbohydrate for animal protein (in quintiles)</td>
<td>Age, parity, pre-pregnancy BMI, socioeconomic indicators, smoking during pregnancy, physical activity, maternal height, fat intake, subtypes of protein</td>
<td>Q1: reference Q2: -6 (-13, 0) Q3: -5 (-12, 1) Q4: -9 (-16, -2) Q5: -10 (-17, -3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Renault, 2015 (57)</td>
<td>Linear regression</td>
<td>Difference in GWG (g/week) when substituting carbohydrate for meat protein (in quintiles)</td>
<td>Age, parity, pre-pregnancy BMI, socioeconomic indicators, smoking during pregnancy, physical activity, maternal height, fat intake, subtypes of protein</td>
<td>Q1: reference Q2: -6 (-12, 0) Q3: -11 (-18, -5) Q4: -11 (-17, -4) Q5: -17 (-24, -11)</td>
<td>&lt;0.01</td>
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<tr>
<td>Renault, 2015 (57)</td>
<td>Linear regression</td>
<td>Difference in GWG (g/week) when substituting carbohydrate for fish protein (in quintiles)</td>
<td>Age, parity, pre-pregnancy BMI, socioeconomic indicators, smoking during pregnancy, physical activity, maternal height, fat intake, subtypes of protein</td>
<td>Q1: reference Q2: -7 (-13, -1) Q3: -10 (-17, -4) Q4: -14 (-20, -7) Q5: -19 (-26, -13)</td>
<td>&lt;0.01</td>
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<tr>
<td>Renault, 2015 (57)</td>
<td>Linear regression</td>
<td>Difference in GWG (g/week) when substituting carbohydrate for dairy protein (in quintiles)</td>
<td>Age, parity, pre-pregnancy BMI, socioeconomic indicators, smoking during pregnancy, physical activity, maternal height, fat intake, subtypes of protein</td>
<td>Q1: reference Q2: 4 (-3, 10) Q3: 0 (-6, 7) Q4: -3 (-10, 4) Q5: 0 (-7, 7)</td>
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<tr>
<td>Maslova, 2015 (56)</td>
<td>Linear regression</td>
<td>Difference in GWG (g/week) when substituting carbohydrate for vegetable protein (in quintiles)</td>
<td>Age, parity, pre-pregnancy BMI, socioeconomic indicators, smoking during pregnancy, physical activity, maternal height, fat intake, subtypes of protein</td>
<td>Q1: reference Q2: 8 (1, 14) Q3: -2 (-8, 5) Q4: 0 (-7, 7) Q5: -10 (-17, -2)</td>
<td>&lt;0.01</td>
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<tr>
<td>Renault, 2015 (57)</td>
<td>Linear regression</td>
<td>Difference in GWG (kg) when substituting carbohydrates (E%) for animal protein (E%) (in quartiles)</td>
<td>Age, parity, pre-pregnancy BMI, smoking during pregnancy, energy intake, intervention group</td>
<td>Q1: reference Q2: -0.1 (-1.9, 1.8) Q3: 0.4 (-1.4, 2.2) Q4: 0.0 (-1.9, 1.9)</td>
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<td>Difference in GWG (kg) when substituting carbohydrates (E%) for vegetable protein (E%) (in quartiles)</td>
<td>Age, parity, pre-pregnancy BMI, smoking during pregnancy, energy intake, intervention group</td>
<td>Q1: reference Q2: 0.9 (-0.9, 2.7) Q3: 1.4 (-0.4, 3.3) Q4: -0.2 (-2.1, 1.7)</td>
<td>0.99</td>
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*P for trend. Abbreviations: BMI, body mass index; CI, confidence interval; E%, energy percentage; Q, quartile or quintile.
**Supplementary Table 2.1.5: Associations between total fat intake and gestational weight gain (N=21)**

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Statistical analysis</th>
<th>Measure of association</th>
<th>Covariate adjustments</th>
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<th>Trimester</th>
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</tr>
<tr>
<td>Althuizen, 2009 (5)</td>
<td>Linear regression</td>
<td>Association between fat intake (E%) and GWG (kg)</td>
<td>Gestational age at delivery</td>
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<td></td>
<td>-0.01 (NR)</td>
<td>0.9</td>
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<td></td>
<td>Logistic regression</td>
<td>Fat intake (E%) and the odds of excessive GWG (vs. inadequate and adequate GWG)</td>
<td>Gestational age at delivery</td>
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<td></td>
<td>0.98 (NR)</td>
<td>0.6</td>
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<td>Anderson, 1986 (7)</td>
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<td>Difference in fat intake (E%) between categories of GWG adequacy</td>
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<td>Blumfield, 2015 (10)</td>
<td>Kruskal-Wallis test</td>
<td>Difference in fat intake (E%) between categories of GWG adequacy</td>
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<td>≥0.05</td>
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<tr>
<td>Gaillard, 2013 (12)</td>
<td>Logistic regression</td>
<td>Fat intake per SD (1 SD = 5.6 E%) and the odds of excessive GWG</td>
<td>Age, parity, pre-pregnancy BMI, maternal education, ethnicity, smoking during pregnancy, energy intake, folic acid supplementation, alcohol consumption during pregnancy</td>
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<td></td>
<td>4.00 (1.62, 9.83)</td>
<td>&lt;0.01</td>
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<td>Maple-Brown, 2013 (16)</td>
<td>Pearson correlation</td>
<td>Correlation between total fat intake and GWG (kg)</td>
<td>NR</td>
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<td>Olafsdottir, 2006 (18)</td>
<td>ANOVA</td>
<td>Difference in fat intake (E%) between categories of GWG adequacy</td>
<td>BMI &lt; 25 BMI ≥ 25</td>
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<td>Ostachowska-Gasior, 2003 (19)</td>
<td>NR</td>
<td>Difference in fat intake (E%) between adequate and excessive GWG</td>
<td>T1 T2 T3</td>
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<td>Papoz, 1980 (20)</td>
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## Supplementary Table 2.1.5 (continued) Associations between total fat intake and gestational weight gain (N=21)

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<th>Effect estimate&lt;sup&gt;1&lt;/sup&gt; (95% CI)</th>
<th>P-value</th>
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<tr>
<td>Changamire, 2014 (28)</td>
<td>GEE</td>
<td>Difference in GWG (g/month) when substituting 5E% from protein with fat</td>
<td>Parity, pre-pregnancy BMI, maternal education, socio-economic position indicator, energy intake maternal height, baseline haemoglobin level, marital status, season, trimester of pregnancy, multivitamin regimen assignment, other macronutrients</td>
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<td>72 (6, 140)</td>
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<tr>
<td></td>
<td>GEE</td>
<td>Difference in GWG (g/month) when substituting 5E% from carbohydrate with fat</td>
<td>Parity, pre-pregnancy BMI, maternal education, socio-economic position indicator, energy intake maternal height, baseline haemoglobin level, marital status, season, trimester of pregnancy, multivitamin regimen assignment, other macronutrients</td>
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<td>1 (-20.21)</td>
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<td>Ebrahimi, 2015 (31)</td>
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<td>Fat intake (g) and the odds of inadequate (vs. adequate) GWG</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
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<td>1.00 (0.99, 1.02)</td>
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<td>Fat intake (g) and the odds of inadequate (vs. excessive) GWG</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
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<td>1.00 (0.98, 1.02)</td>
<td>≥0.05</td>
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<td>Fat intake (g) and the odds of adequate (vs. excessive) GWG</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
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<td>&lt;1.00 (0.98, 1.01)</td>
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<td>Cumulative Logit Model for Ordinal Responses</td>
<td>Odds ratio between fat intake (g) and adequacy of GWG (inadequate, adequate and excessive GWG)</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
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<td>1.00 (0.99, 1.01)</td>
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<td>Hsu, 2013 (33)</td>
<td>Pearson correlation</td>
<td>Correlation between total fat intake (g/day) and GWG (kg)</td>
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<td></td>
<td>&lt;0.01</td>
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<tr>
<td></td>
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<td></td>
<td>T2 0.14</td>
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<td></td>
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<td>&lt;0.01</td>
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<td></td>
<td></td>
<td></td>
<td>T3 0.20</td>
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<td>Jaruratanasirikul, 2009 (34)</td>
<td>Logistic regression</td>
<td>Fat intake (g) and the odds of inadequate (vs. adequate) GWG</td>
<td>Pre-pregnancy BMI, maternal education, energy intake, family income, intake of calcium and iron</td>
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<td>0.80 (0.52, 3.27)</td>
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<tr>
<td>Kardjati, 1990 (35)</td>
<td>Correlation</td>
<td>Correlation between fat intake (g) and GWG (kg)</td>
<td>T2 0.14</td>
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<td></td>
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<td>T3 0.10</td>
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### Supplementary Table 2.1.5 (continued) Associations between total fat intake and gestational weight gain (N=21)

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<th>Covariate adjustments</th>
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<th>Trimester</th>
<th>Effect estimate(^1) (95% CI)</th>
<th>P-value</th>
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<tr>
<td>Popa, 2014 (37)</td>
<td>Chi-square test</td>
<td>Difference in fat intake (E%) between inadequate, adequate and excessive GWG</td>
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<td>null</td>
<td>T1-3</td>
<td>-0.01 (-0.05, 0.03)(^*)</td>
<td>0.64</td>
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<tr>
<td>Rodrigues, 2008 (38)</td>
<td>Linear regression</td>
<td>Association between fat intake (g/day) and GWG (kg)</td>
<td>Rural(^2)</td>
<td>T1</td>
<td>NR</td>
<td>NS</td>
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<td></td>
<td></td>
<td></td>
<td>Rural</td>
<td>T2</td>
<td>NR</td>
<td>NS</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Rural</td>
<td>T3</td>
<td>NR</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Urban(^3)</td>
<td>T1</td>
<td>NR</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Urban</td>
<td>T2</td>
<td>NR</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Urban</td>
<td>T3</td>
<td>20.7</td>
<td>≤0.05</td>
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<tr>
<td>Saowakontha, 1992 (39)</td>
<td>Linear regression</td>
<td>Explained variance of GWG (R(^2)) by fat intake (g)</td>
<td>Rural(^2)</td>
<td>T1</td>
<td>NR</td>
<td>NS</td>
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<tr>
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<td></td>
<td></td>
<td>Rural</td>
<td>T2</td>
<td>NR</td>
<td>NS</td>
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<tr>
<td></td>
<td></td>
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<td>Rural</td>
<td>T3</td>
<td>NR</td>
<td>NS</td>
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<td></td>
<td></td>
<td></td>
<td>Urban(^3)</td>
<td>T1</td>
<td>NR</td>
<td>NS</td>
<td></td>
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<tr>
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<td></td>
<td></td>
<td>Urban</td>
<td>T2</td>
<td>NR</td>
<td>NS</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Urban</td>
<td>T3</td>
<td>20.7</td>
<td>≤0.05</td>
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<tr>
<td>Zulfiqar, 2011 (43)</td>
<td>Regression</td>
<td>Association between fat intake (g/day) and GWG (g/week)</td>
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<td>2.06 (NR)</td>
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<td>Costa, 2011 (44)</td>
<td>Spearman correlation</td>
<td>Correlation between fat intake (g) and total GWG</td>
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<td></td>
<td></td>
<td>0.11</td>
<td>0.11</td>
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</tbody>
</table>

\(^1\) Parameter estimate of the used statistical method, + = positive value, - = negative value, null = no association; \(^2\) Only descriptive, no statistical analysis. Based on reported numbers and the assumption of a normal distribution of carbohydrate intake, we have a Welch t-test performed; \(^3\) Change in fat intake as compared with previous dietary assessment (cT1: change during 1st trimester of pregnancy, cT1-3: change during 3rd until 8th month of pregnancy); \(^4\) 95% confidence interval calculated using reported mean and standard error; \(^5\) Living location of the women (rural vs. urban); **Abbreviations:** ANOVA, Analysis of Variance; BMI, body mass index (kg/m\(^2\)); CI, confidence interval; E%, energy percentage; GEE, generalized estimating equation; GWG, gestational weight gain; NR, not reported; NS, not significant; OC, oral contraceptive; SD, standard deviation; T: trimester of pregnancy.
**Supplementary Table 2.1.6:** Associations between types of fat intake and gestational weight gain (N=9)

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Statistical analysis</th>
<th>Measure of association</th>
<th>Covariate adjustments</th>
<th>Subgroups</th>
<th>Effect estimate</th>
<th>P-value</th>
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<tr>
<td>Saturated fat intake</td>
<td><strong>Longitudinal studies, high-income countries</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Althuizen, 2009 (5)</td>
<td>Linear regression</td>
<td>Association between saturated fat intake (E%) and GWG (kg)</td>
<td>Gestational age at delivery</td>
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<td>0.02 (NR)</td>
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<tr>
<td></td>
<td>Logistic regression</td>
<td>Saturated fat intake (E%) and the odds of excessive GWG (vs. inadequate and adequate GWG)</td>
<td>Gestational age at delivery</td>
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<td>0.98 (NR)</td>
<td>0.7</td>
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<tr>
<td>Blumfield, 2015 (10)</td>
<td>Kruskal-Wallis test</td>
<td>Difference in saturated fat intake (E%) between categories of GWG adequacy</td>
<td>null</td>
<td></td>
<td>≥0.05</td>
<td></td>
</tr>
<tr>
<td>Maple-Brown, 2013 (16)</td>
<td>Pearson correlation</td>
<td>Correlation between saturated fat intake and GWG (kg)</td>
<td></td>
<td>NR</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Renault, 2015 (57)</td>
<td>Linear regression</td>
<td>Difference in GWG (kg) when substituting monounsaturated or polyunsaturated fat (E%) for saturated fat (E%) (in quartiles)</td>
<td>Age, parity, pre-pregnancy BMI, smoking during pregnancy, energy intake, intervention group</td>
<td>Q1: reference</td>
<td>0.83*</td>
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<tr>
<td>Shin, 2014 (23)</td>
<td>Logistic regression</td>
<td>&lt;10E% of saturated fat intake (vs. ≥10E%) and odds of inadequate GWG (vs. adequate GWG)</td>
<td>Age, pre-pregnancy BMI, education, family poverty income ratio, ethnicity, smoking during pregnancy, physical activity, trimester of gestation, marital status, daily supplement use</td>
<td>1.3 (0.2, 7.0)</td>
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<td>Logistic regression</td>
<td>&lt;10E% of saturated fat intake (vs. ≥10E%) and odds of excessive GWG (vs. adequate GWG)</td>
<td>Age, pre-pregnancy BMI, education, family poverty income ratio, ethnicity, smoking during pregnancy, physical activity, trimester of gestation, marital status, daily supplement use</td>
<td>0.8 (0.2, 3.5)</td>
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<td>Stuebe, 2009 (24)</td>
<td>Logistic regression</td>
<td>Saturated fat intake (per 5 E%, compared to carbohydrates) and the odds of excessive GWG</td>
<td>Age, pre-pregnancy BMI, ethnicity, smoking during pregnancy, gestational age at delivery, nausea during first trimester of pregnancy, other macronutrients (E%)</td>
<td>1.33 (0.87, 2.02)</td>
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<td>Uusitalo, 2009 (25)</td>
<td>Linear regression</td>
<td>Association between saturated fat intake (E%) and GWG (kg)</td>
<td>Age, parity, pre-pregnancy BMI, maternal education, smoking during pregnancy, birth weight, living area, gestational age at first weight measurement</td>
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### Supplementary Table 2.1.6 (continued). Associations between types of fat intake and gestational weight gain (N=9)

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<td>Martins, 2011 (59)</td>
<td>Linear regression</td>
<td>Association between saturated fat intake (g, in tertiles) and weight retention (kg)</td>
<td>Age, pre-pregnancy BMI, maternal education, smoking during pregnancy, height, per capita family income</td>
<td>Tertile 1</td>
<td>Reference</td>
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<td>Tertile 2</td>
<td>2.63 (NR)</td>
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<td>Tertile 3</td>
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<td>Costa, 2011 (44)</td>
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<td>Correlation between saturated fat intake (g) and total GWG</td>
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<td><strong>Longitudinal studies, high-income countries</strong></td>
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<tr>
<td>Blumfield, 2015 (10)</td>
<td>Kruskal-Wallis test</td>
<td>Difference in monounsaturated fat intake (E%) between categories of GWG adequacy</td>
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<tr>
<td></td>
<td>Kruskal-Wallis test</td>
<td>Difference in polyunsaturated fat intake (E%) between categories of GWG adequacy</td>
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<td>≥0.05</td>
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<td>Maple-Brown, 2013 (16)</td>
<td>Pearson correlation</td>
<td>Correlation between monounsaturated fat intake and GWG (kg)</td>
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<td>NR</td>
<td>NS</td>
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<td>Pearson correlation</td>
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<td>NS</td>
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<tr>
<td>Renault, 2015 (57)</td>
<td>Linear regression</td>
<td>Difference in GWG (kg) when substituting monounsaturated or saturated fat (E%) for polyunsaturated fat (E%) (in quartiles)</td>
<td>Age, parity, pre-pregnancy BMI, smoking during pregnancy, energy intake, intervention group</td>
<td>Q1: reference</td>
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<td></td>
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<td>Q2: 1.0 (-2.8, 0.8)</td>
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<td>Q3: 1.3 (-0.5, 3.1)</td>
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<td>Q4: -0.4 (-2.2, 1.4)</td>
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<td>Monounsaturated fat intake (per 5 E%, compared to carbohydrates) and the odds of excessive GWG</td>
<td>Age, pre-pregnancy BMI, ethnicity, smoking during pregnancy, gestational age at delivery, nausea during first trimester of pregnancy, other macronutrients (E%)</td>
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<td>0.63 (0.40, 0.99)</td>
<td>NR</td>
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<td>Logistic regression</td>
<td>Polysaturated fat intake (per 5 E%, compared to carbohydrates) and the odds of excessive GWG</td>
<td>Age, pre-pregnancy BMI, ethnicity, smoking during pregnancy, gestational age at delivery, nausea during first trimester of pregnancy, other macronutrients (E%)</td>
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<td>1.32 (0.80, 2.18)</td>
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**Supplementary Table 2.1.6 (continued).** Associations between types of fat intake and gestational weight gain (N=9)

<table>
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<th>First author, year</th>
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<th>Measure of association</th>
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<td>Costa, 2011 (44)</td>
<td>Spearman correlation</td>
<td>Correlation between unsaturated fat intake (g) and total GWG</td>
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<td>0.09 (0.19)</td>
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<td><strong>Trans-fat intake</strong></td>
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<td>Logistic regression</td>
<td>Trans-fat intake (per 2E%, compared with carbohydrates) and the odds of excessive GWG</td>
<td>Age, pre-pregnancy BMI, ethnicity, smoking during pregnancy, gestational age at delivery, nausea during first trimester of pregnancy, other macronutrients (E%)</td>
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<td>1.27 (0.39, 4.13)</td>
<td>NS</td>
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\(^1\) Parameter estimate of the used statistical method, + = positive value, - = negative value, null = no association; \(^2\) p for trend. **Abbreviations:** BMI, body mass index (kg/m\(^2\)); CI, confidence interval; E%, energy percentage; GWG, gestational weight gain; NR, not reported; NS, not significant; Q, quartile.
### Supplementary Table 2.17: Associations between source of fat and gestational weight gain (N=1)

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<td>Lagiou, 2004 (14)</td>
<td>Linear regression</td>
<td>Association between fat intake from animal sources (per SD increase) and GWG (kg)</td>
<td>Age, parity, pre-pregnancy BMI, maternal education, smoking, energy intake, gestational age at delivery, gender of the baby, maternal height, pre-pregnancy OC use</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.56 (1.64, 3.48)(^1) &lt;0.01(^2)</td>
</tr>
<tr>
<td><strong>Vegetable source</strong></td>
<td></td>
<td>Association between fat intake from vegetable sources (per SD increase) and GWG (kg)</td>
<td>Age, parity, pre-pregnancy BMI, maternal education, smoking, energy intake, gestational age at delivery, gender of the baby, maternal height, pre-pregnancy OC use</td>
</tr>
<tr>
<td>Lagiou, 2004 (14)</td>
<td>Linear regression</td>
<td></td>
<td>0.77 (-0.17, 1.71)(^1) 0.11(^2)</td>
</tr>
</tbody>
</table>

\(^1\) 95% confidence interval calculated using reported mean and standard error; \(^2\) \(p\) for trend. **Abbreviations**: BMI, body mass index (kg/m\(^2\)); CI, confidence interval; GWG, gestational weight gain; OC, oral contraceptive; SD, standard deviation.
**Supplemental Table 2.1.8: Associations between carbohydrate intake and gestational weight gain (N=18)**

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Statistical analysis</th>
<th>Measure of association</th>
<th>Covariate adjustments</th>
<th>Subgroups</th>
<th>Trimester</th>
<th>Effect estimate$^*$ (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High-income countries</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Longitudinal studies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anderson, 1986 (7)</td>
<td>None$^*$</td>
<td>Difference in carbohydrate intake (E%) between categories of GWG</td>
<td>null</td>
<td>null</td>
<td>≥0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blumfield, 2015 (10)</td>
<td>Kruskal-Wallis test</td>
<td>Difference in carbohydrate intake (E%) between categories of GWG adequacy</td>
<td>null</td>
<td>null</td>
<td>≥0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gaillard, 2013 (12)</td>
<td>Logistic regression</td>
<td>Carbohydrate intake per SD (1 SD = 6.5 E%) and the odds of excessive GWG</td>
<td>Age, parity, pre-pregnancy BMI, maternal education, smoking during pregnancy, energy intake, folic acid supplementation, alcohol consumption during pregnancy</td>
<td>null</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lagiou, 2004 (14)</td>
<td>Linear regression</td>
<td>Association between carbohydrate intake (per SD increase) and GWG (kg)</td>
<td>Age, parity, pre-pregnancy BMI, maternal education, smoking, energy intake, gestational age at delivery, gender of the baby, height, pre-pregnancy OC use</td>
<td>null</td>
<td>&lt;0.01$^*$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maple-Brown, 2013 (16)</td>
<td>Pearson correlation</td>
<td>Correlation between carbohydrate intake and GWG (kg)</td>
<td>BMI &lt;25</td>
<td>NR</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olafsdottir, 2006 (18)</td>
<td>ANOVA</td>
<td>Difference in carbohydrate intake (E%) between categories of GWG adequacy</td>
<td>BMI ≥ 25</td>
<td>NR</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ostachowska-Gasior, 2003 (19)</td>
<td>NR</td>
<td>Difference in carbohydrate intake (E%) between adequate and excessive GWG</td>
<td>T1</td>
<td>null</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T2</td>
<td>null</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T3</td>
<td>null</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papoz, 1980 (20)</td>
<td>Pearson correlation</td>
<td>Correlation between carbohydrate intake (g) and GWG (kg)</td>
<td>T1</td>
<td>0.24</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>cT1$^5$</td>
<td>0.17</td>
<td>&lt;0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>cT1-3$^5$</td>
<td>-0.15</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Picone, 1982 (21)</td>
<td>ANOVA</td>
<td>Difference in carbohydrate intake (g) between categories of GWG adequacy</td>
<td>null</td>
<td>null</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shin, 2014 (23)</td>
<td>Wald F test</td>
<td>Difference in carbohydrate intake (E%) between categories of GWG adequacy</td>
<td>Age, pre-pregnancy BMI, education, family poverty income ratio, ethnicity, smoking during pregnancy, physical activity, trimester of gestation, marital status, daily supplement use</td>
<td>null</td>
<td>0.90</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Supplemental Table 2.1.8 (continued) Associations between carbohydrate intake and gestational weight gain (N=18)

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Statistical analysis</th>
<th>Measure of association</th>
<th>Covariate adjustments</th>
<th>Subgroups</th>
<th>Trimester</th>
<th>Effect estimate (^1) (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low- and middle-income countries</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changamire, 2014 (28)</td>
<td>GEE</td>
<td>Difference in GWG (g/month) when substituting 5% from fat with carbohydrate</td>
<td>Parity, pre-pregnancy BMI, maternal education, socio-economic position indicator, energy intake, maternal height, baseline haemoglobin level, marital status, season, trimester of pregnancy, multivitamin regimen assignment, other macronutrients</td>
<td>null</td>
<td>null</td>
<td>-1 (-21, 20)</td>
<td>0.96</td>
</tr>
<tr>
<td></td>
<td>GEE</td>
<td>Difference in GWG (g/month) when substituting 5% from protein with carbohydrate</td>
<td>Parity, pre-pregnancy BMI, maternal education, socio-economic position indicator, energy intake, maternal height, baseline haemoglobin level, marital status, season, trimester of pregnancy, multivitamin regimen assignment, other macronutrients</td>
<td>null</td>
<td>null</td>
<td>70 (15, 124)</td>
<td>0.01</td>
</tr>
<tr>
<td>Ebrahimi, 2015 (31)</td>
<td>Logistic regression</td>
<td>Carbohydrate intake (g) and the odds of inadequate (vs. adequate) GWG</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
<td>null</td>
<td>null</td>
<td>1.00 (&lt;1.00, 1.01)</td>
<td>≥0.05</td>
</tr>
<tr>
<td></td>
<td>Logistic regression</td>
<td>Carbohydrate intake (g) and the odds of inadequate (vs. excessive) GWG</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
<td>null</td>
<td>null</td>
<td>1.00 (&lt;1.00, 1.01)</td>
<td>≥0.05</td>
</tr>
<tr>
<td></td>
<td>Logistic regression</td>
<td>Carbohydrate intake (g) and the odds of adequate (vs. excessive) GWG</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
<td>null</td>
<td>null</td>
<td>&lt;1.00 (0.99, 1.00)</td>
<td>≥0.05</td>
</tr>
<tr>
<td></td>
<td>Cumulative Logit Model for Ordinal Responses</td>
<td>Odds ratio between carbohydrate intake (g) and adequacy of GWG (inadequate, adequate and excessive GWG)</td>
<td>Age, pre-pregnancy BMI, maternal education, household income, physical activity, gravidity</td>
<td>null</td>
<td>null</td>
<td>1.00 (&lt;1.00, 1.01)</td>
<td>0.32</td>
</tr>
<tr>
<td>Jaruratanasirikul, 2009 (34)</td>
<td>Logistic regression</td>
<td>Carbohydrate intake (g) and the odds of inadequate (vs. adequate) GWG</td>
<td>Pre-pregnancy BMI, maternal education, energy intake, family income, intake of calcium and iron</td>
<td>null</td>
<td>null</td>
<td>0.67 (0.25, 1.72)</td>
<td>0.39</td>
</tr>
<tr>
<td>Popa, 2014 (37)</td>
<td>Chi-square test</td>
<td>Difference in carbohydrate intake (E%) between inadequate, adequate and excessive GWG</td>
<td>null</td>
<td>null</td>
<td>null</td>
<td>null</td>
<td>NS</td>
</tr>
</tbody>
</table>
Supplemental Table 2.1.8 (continued) Associations between carbohydrate intake and gestational weight gain (N=18)

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Statistical analysis</th>
<th>Measure of association</th>
<th>Covariate adjustments</th>
<th>Subgroups</th>
<th>Trimester</th>
<th>Effect estimate (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rodrigues, 2008 (38)</td>
<td>Linear regression</td>
<td>Association between carbohydrate intake (g/day) and GWG (kg)</td>
<td></td>
<td>Rural* NR</td>
<td>T1</td>
<td>-0.00 (-0.01, 0.01)</td>
<td>0.98</td>
</tr>
<tr>
<td>Saowakontha, 1992 (39)</td>
<td>Linear regression</td>
<td>Explained variance of GWG ($R^2$) by carbohydrate intake (g)</td>
<td></td>
<td>Rural* NR</td>
<td>T1</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Rural* NR</td>
<td>T2</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Rural* NR</td>
<td>T3</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Urban* T1</td>
<td></td>
<td>18.8</td>
<td>≤0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Urban* T2</td>
<td></td>
<td>25.8</td>
<td>≤0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Urban* T3</td>
<td></td>
<td>19.0</td>
<td>≤0.05</td>
</tr>
<tr>
<td>Zulfiqar, 2011 (43)</td>
<td>Regression</td>
<td>Association between carbohydrate intake (g/day) and GWG (g/week)</td>
<td></td>
<td></td>
<td></td>
<td>0.52 (NR)</td>
<td>0.01</td>
</tr>
<tr>
<td>Case control study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costa, 2011 (44)</td>
<td>Spearman correlation</td>
<td>Correlation between carbohydrate intake (g) and GWG (kg)</td>
<td></td>
<td></td>
<td></td>
<td>0.13</td>
<td>0.07</td>
</tr>
</tbody>
</table>

1. Parameter estimate of the used statistical method, + = positive value, - = negative value, null = no association; 2. Only descriptive, no statistical analysis. Based on reported numbers and the assumption of a normal distribution of carbohydrate intake, we have a Welch t-test performed; 3. 95% confidence interval calculated using reported mean and standard error; 4. p for trend; 5. Change of carbohydrate intake as compared with previous dietary assessment (cT1: change during 1st trimester of pregnancy, cT1-3: change during 3rd until 8th month of pregnancy); 6. Living location of the women (rural vs. urban); Abbreviations: ANOVA, Analysis of Variance; BMI, body mass index (kg/m²); CI, confidence interval; E%, energy percent; GEE, generalized estimating equation; GWG, gestational weight gain; NR, not reported; NS, not significant; OC, oral contraceptive; SD, standard deviation; T, trimester of pregnancy.
References: supplementary material chapter 2.1


31. Ebrahimi F, Shariff ZM, Tabatabaei SZ, Fathollahi MS, Mun CY, Nazari M. Relationship between sociodemographics, dietary intake, and physical activity with gestational weight gain among pregnant women in Rafsanjan City, Iran. J Health Popul Nutr 2015;33:168-76.

Chapter 2.2

A Priori and a posteriori dietary patterns during pregnancy and gestational weight gain: The Generation R Study

Myrte J. Tielemans, Nicole S. Erler, Elisabeth T.M. Leermakers, Marion van den Broek, Vincent W.V. Jaddoe, Eric A.P. Steegers, Jessica C. Kiefte-de Jong, Oscar H. Franco

Nutrients. 2015 Nov; 7, 9383-9399
**Supplementary Figure 2.2.1.** Bland Altman plots for self-reported pre-pregnancy weight and maximum weight in pregnancy.

A. Bland-Altman plot for pre-pregnancy weight and weight during the first visit (n = 2425)

B. Bland-Altman plot for maximum weight in pregnancy and weight during the third visit (n = 2177)
**Supplementary Table 2.2.1. Food groups and its food components**

<table>
<thead>
<tr>
<th>Food Group</th>
<th>Food Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potatoes and other tubers</td>
<td>Potatoes (cooked or fried) and French fries</td>
</tr>
<tr>
<td>Vegetables</td>
<td>Endive, purslane, turnip tops, lettuce, chard, spinach, chicory, eggplant,</td>
</tr>
<tr>
<td></td>
<td>avocado, cucumber, paprika, corn, pickle, tomatoes, beans, snow peas,</td>
</tr>
<tr>
<td></td>
<td>courgette, tomato sauce, carrots, beetroot, cabbages, mushrooms, green</td>
</tr>
<tr>
<td></td>
<td>peas, onions, leek, garlic, bean sprouts, celery, atjar tjampoer and crudités</td>
</tr>
<tr>
<td>Fruits</td>
<td>Apple, strawberries, apricot, pineapple, red berries, banana, blackberries,</td>
</tr>
<tr>
<td></td>
<td>lemon, grapes, raspberries, cherries, grapefruit, tangerine, peach, pear,</td>
</tr>
<tr>
<td></td>
<td>prunes, orange, applesauce, kiwi, mango, rhubarb, melon, nectarine, canned</td>
</tr>
<tr>
<td></td>
<td>fruit and dried fruit</td>
</tr>
<tr>
<td>Dairy products—high fat</td>
<td>Whole milk, full-fat yoghurt drink, full-fat yogurt,</td>
</tr>
<tr>
<td></td>
<td>cheese 40–60+, cream cheese, full-fat quark, pudding,</td>
</tr>
<tr>
<td></td>
<td>sour cream, whipped cream and crème fraiche</td>
</tr>
<tr>
<td>Dairy products—low fat</td>
<td>Skimmed and semi-skinned milk, skimmed and</td>
</tr>
<tr>
<td></td>
<td>semi-skinned yoghurt drink, skimmed and</td>
</tr>
<tr>
<td></td>
<td>semi-skinned yogurt, cheese 20–30+ and low-fat quark</td>
</tr>
<tr>
<td>Cereals—high fibre</td>
<td>Brown rice, whole wheat pasta, whole wheat/brown/rye bread, muesli,</td>
</tr>
<tr>
<td></td>
<td>seitan, oatmeal, wheat germ, and bran</td>
</tr>
<tr>
<td>Cereals—low fibre</td>
<td>White rice, couscous, bulgur, white bread, rusk, croissants,</td>
</tr>
<tr>
<td></td>
<td>corn flakes, crackers, rice cake, toast, pancakes,</td>
</tr>
<tr>
<td></td>
<td>raisin bread, bami and white pasta</td>
</tr>
<tr>
<td>Meat and meat products</td>
<td>Red meat, poultry, organ meat and meat products</td>
</tr>
<tr>
<td>Fish and shellfish</td>
<td>Fish, fish products and shellfish</td>
</tr>
<tr>
<td>Eggs and egg products</td>
<td>Egg (cooked or fried)</td>
</tr>
<tr>
<td>Vegetable oils</td>
<td>Olive oil, nut oil, salad oil, sesame oil,</td>
</tr>
<tr>
<td></td>
<td>sunflower oil, soybean oil and peanut oil</td>
</tr>
<tr>
<td>Margarine and butter</td>
<td>Margarine (solid and liquid) and butter</td>
</tr>
<tr>
<td>Sugar and confectionary and cakes</td>
<td>Chocolate, candy, chocolate sprinkles, cake, pastry and biscuits</td>
</tr>
<tr>
<td>Snacks</td>
<td>Peanuts, beer nuts, trail mix, pretzels and chips</td>
</tr>
<tr>
<td>Coffee and tea</td>
<td>Coffee, cappuccino, espresso, English tea, green tea and herbal tea</td>
</tr>
<tr>
<td>Sugar-containing beverages</td>
<td>Coke/Fanta/Sprite soft drinks, isotonic drinks, fruit juices and vegetable</td>
</tr>
<tr>
<td></td>
<td>juices</td>
</tr>
<tr>
<td>Light soft drinks</td>
<td>Coke/Fanta/Sprite light soft drinks and water</td>
</tr>
<tr>
<td>Alcoholic beverages</td>
<td>Beer, wine, mixed drinks and liquor</td>
</tr>
<tr>
<td>Condiments and sauces</td>
<td>Chili/tomato/barbecue/shaslick/peanut/garlic/whisky/soy/salad sauce, salad</td>
</tr>
<tr>
<td></td>
<td>dressing, mayonnaise, fish/egg/meat/Russian salad, sandwich spread, marmite,</td>
</tr>
<tr>
<td></td>
<td>salt, spices/herbs and flavour powder</td>
</tr>
<tr>
<td>Soups and bouillon</td>
<td>Soup or bouillon with or without meat, meal soup and lentil soup</td>
</tr>
<tr>
<td>Nuts, seeds and olives</td>
<td>Nut butter, tahini, poppy seed, sesame, pumpkin seeds,</td>
</tr>
<tr>
<td></td>
<td>sunflower seeds, pine nuts, mixed seeds and olives</td>
</tr>
<tr>
<td>Soy products</td>
<td>Tofu, tempeh, soymilk, soy chunks, soy</td>
</tr>
<tr>
<td></td>
<td>dessert, vegetable burgers and Quorn</td>
</tr>
<tr>
<td>Legumes</td>
<td>Legumes and tempeh</td>
</tr>
</tbody>
</table>

1 Reprinted with permission from van den Broek et al., [1]. The food groups were primarily created based on the Dutch National Food Consumption Survey.
**Supplementary Table 2.2.2.** Modified version of the Dutch Healthy Diet-index

<table>
<thead>
<tr>
<th>Components of the Dutch Healthy Diet-Index</th>
<th>Minimum Score (0)</th>
<th>Maximum Score (10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Physical activity (daily)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>2 Vegetable (g/day)</td>
<td>0</td>
<td>≥200</td>
</tr>
<tr>
<td>3 Fruit (g/day)</td>
<td>0</td>
<td>≥200</td>
</tr>
<tr>
<td>4 Fiber (g/4.2MJ/day)</td>
<td>0</td>
<td>≥14</td>
</tr>
<tr>
<td>5 Fish (g/day)</td>
<td>0</td>
<td>34.3 (1)</td>
</tr>
<tr>
<td>6 Saturated fat (E%)</td>
<td>≥16.6</td>
<td>&lt;10</td>
</tr>
<tr>
<td>7 Trans fatty acid (E%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>8 Acidic drinks and foods (servings/day)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>9 Sodium (mg/day)</td>
<td>≥2450</td>
<td>&lt;1680</td>
</tr>
<tr>
<td>10 Alcohol (g/day)</td>
<td>NI</td>
<td>NI</td>
</tr>
</tbody>
</table>

1 Adapted from van Lee et al., [2]; a Fruit without fruit juices; b Based on two portions of 120 g fish per week [3]; Abbreviations: NA: not available; NI: not included.
### Supplementary Table 2.2.3. Sensitivity analyses in normal weight women (n = 2141)

<table>
<thead>
<tr>
<th>Dietary Pattern</th>
<th>Gestational Weight Gain until Early Third Trimester of Pregnancy</th>
<th>1. Additionally Adjusted for Energy Intake</th>
<th>2. Additional Adjustment for Estimated Foetal Weight</th>
<th>3. Excluding Women with Comorbidities or Pregnancy Complications</th>
<th>4. Excluding Women Vomiting &gt; 1 Times per Week in Previous Three Months</th>
<th>Maximal Gestational Weight Gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 (low)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Q2</td>
<td>16 (−0; 31)</td>
<td>14 (−1; 30)</td>
<td>16 (0; 32)</td>
<td>20 (3; 36)</td>
<td>13 (−4; 30)</td>
<td>14 (−12; 41)</td>
</tr>
<tr>
<td>Q3</td>
<td>5 (−11; 21)</td>
<td>2 (−15; 18)</td>
<td>5 (−11; 21)</td>
<td>7 (−10; 23)</td>
<td>2 (−15; 19)</td>
<td>4 (−23; 31)</td>
</tr>
<tr>
<td>Q4 (high)</td>
<td>25 (9; 42) *</td>
<td>18 (0; 35)</td>
<td>25 (9; 41) *</td>
<td>27 (11; 44) *</td>
<td>20 (3; 37)</td>
<td>29 (2; 57)</td>
</tr>
<tr>
<td>Per SD</td>
<td>p = 0.02</td>
<td>p = 0.29</td>
<td>p = 0.02</td>
<td>p &lt; 0.01 *</td>
<td>p = 0.11</td>
<td>p = 0.19</td>
</tr>
<tr>
<td>&quot;Vegetable, Oil and Fish&quot; Pattern</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 (low)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Q2</td>
<td>10 (−6; 26)</td>
<td>7 (−9; 23)</td>
<td>11 (−5; 26)</td>
<td>12 (−4; 29)</td>
<td>11 (−6; 28)</td>
<td>16 (−12; 44)</td>
</tr>
<tr>
<td>Q3</td>
<td>−3 (−19; 14)</td>
<td>−6 (−23; 10)</td>
<td>0 (−16; 16)</td>
<td>0 (−17; 17)</td>
<td>−1 (−18; 16)</td>
<td>25 (−3; 54)</td>
</tr>
<tr>
<td>Q4 (high)</td>
<td>−5 (−22; 11)</td>
<td>−12 (−29; 5)</td>
<td>−5 (−21; 11)</td>
<td>−2 (−19; 15)</td>
<td>−7 (−24; 10)</td>
<td>10 (−19; 38)</td>
</tr>
<tr>
<td>Per SD</td>
<td>p = 0.51</td>
<td>p = 0.14</td>
<td>p = 0.36</td>
<td>p = 0.66</td>
<td>p = 0.48</td>
<td>p = 0.20</td>
</tr>
<tr>
<td>&quot;Nuts, High-Fibre Cereals and Soy&quot; Pattern</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 (low)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Q2</td>
<td>6 (−9; 21)</td>
<td>−1 (−19; 16)</td>
<td>3 (−12; 18)</td>
<td>6 (−10; 22)</td>
<td>4 (−12; 20)</td>
<td>27 (1; 53)</td>
</tr>
<tr>
<td>Q3</td>
<td>−0 (−16; 16)</td>
<td>−14 (−35; 7)</td>
<td>−2 (−17; 13)</td>
<td>1 (−15; 17)</td>
<td>−3 (−20; 13)</td>
<td>26 (0; 53)</td>
</tr>
<tr>
<td>Q4 (high)</td>
<td>11 (−5; 26)</td>
<td>−11 (−40; 17)</td>
<td>9 (−7; 24)</td>
<td>10 (−6; 26)</td>
<td>7 (−9; 23)</td>
<td>24 (−2; 50)</td>
</tr>
<tr>
<td>Per SD</td>
<td>p = 0.37</td>
<td>p = 0.06</td>
<td>p = 0.48</td>
<td>p = 0.82</td>
<td>p = 0.12</td>
<td></td>
</tr>
<tr>
<td>&quot;Margarine, Sugar and Snacks&quot; Pattern</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 (low)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Q2</td>
<td>−9 (−24; 7)</td>
<td>−10 (−25; 6)</td>
<td>−8 (−23; 8)</td>
<td>−13 (−29; 3)</td>
<td>−12 (−28; 4)</td>
<td>−10 (−35; 16)</td>
</tr>
<tr>
<td>Q3</td>
<td>−2 (−18; 13)</td>
<td>−3 (−19; 12)</td>
<td>−3 (−18; 13)</td>
<td>−4 (−20; 12)</td>
<td>−6 (−22; 10)</td>
<td>4 (−22; 29)</td>
</tr>
<tr>
<td>Q4 (high)</td>
<td>−11 (−27; 5)</td>
<td>−11 (−27; 5)</td>
<td>−9 (−25; 6)</td>
<td>−16 (−33; 1)</td>
<td>−13 (−29; 4)</td>
<td>−28 (−55; −1)</td>
</tr>
<tr>
<td>Per SD</td>
<td>p = 0.13</td>
<td>p = 0.13</td>
<td>p = 0.19</td>
<td>p = 0.06</td>
<td>p = 0.08</td>
<td>p = 0.05</td>
</tr>
</tbody>
</table>

1 Values (regression coefficients with 95%-confidence interval) reflect the difference in gestational weight gain until early-third trimester (g/week) for quartile 2 until 4 relative to quartile 1 in normal weight women. p-Values correspond to the effect of 1SD increase in dietary pattern score. Adjusted for pre-pregnancy BMI, median gestational age at follow-up, age, educational level, household income, parity, smoking during pregnancy, alcohol consumption during pregnancy, stress during pregnancy, and fetal sex. 2 Further adjusted for energy intake (kcal/day). 3 Women excluded with pre-existing comorbidities (diabetes mellitus, hypercholesterolemia, hypertension, heart disease, thyroid disease, and systemic lupus erythematosus) and with pregnancy complications (pregnancy-induced hypertension, preeclampsia or gestational diabetes). 4 Gestational weight gain calculated from self-reported pre-pregnancy weight and maximum weight in pregnancy. Significant results are presented in bold (p-value < 0.05) and results with a p-value < 0.0125 with an asterisk (*).
### Supplementary Table 2.2.4. Sensitivity analyses in overweight women (n = 674)

<table>
<thead>
<tr>
<th>Dietary Pattern</th>
<th>Gestational Weight Gain until Early Third Trimester of Pregnancy</th>
<th>1. Additionally Adjusted for Estimated Foetal Weight</th>
<th>2. Additional Adjustment for Energy Intake</th>
<th>3. Excluding Women with Comorbidities or Pregnancy Complications</th>
<th>4. Excluding Women Vomiting &gt; 1 Times per Week in Previous Three Months</th>
<th>Maximal Gestational Weight Gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quartile</td>
<td>n = 674</td>
<td>n = 674</td>
<td>n = 665</td>
<td>n = 532</td>
<td>n = 560</td>
<td>n = 425</td>
</tr>
<tr>
<td>Q1 (low)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Q2</td>
<td>30 (−8; 68)</td>
<td>29 (−8; 67)</td>
<td>28 (−9; 65)</td>
<td>27 (−13; 66)</td>
<td>27 (−14; 68)</td>
<td>11 (−40; 62)</td>
</tr>
<tr>
<td>Q3</td>
<td>40 (1; 79)</td>
<td>38 (−2; 77)</td>
<td>41 (2; 80)</td>
<td>40 (−2; 81)</td>
<td>44 (3; 86)</td>
<td>25 (−27; 77)</td>
</tr>
<tr>
<td>Q4 (high)</td>
<td>26 (−15; 67)</td>
<td>22 (−21; 65)</td>
<td>25 (−15; 66)</td>
<td>19 (−23; 61)</td>
<td>38 (−6; 82)</td>
<td>1 (−54; 55)</td>
</tr>
<tr>
<td>Per SD</td>
<td>p = 0.15</td>
<td>p = 0.22</td>
<td>p = 0.13</td>
<td>p = 0.18</td>
<td>p = 0.07</td>
<td>p = 0.87</td>
</tr>
</tbody>
</table>

#### “Vegetable, Oil and Fish” Pattern

| Quartile        | n = 674                                                       | n = 674                                          | n = 665                                  | n = 532                                          | n = 560                                                   | n = 425                     |
| Q1 (low)        | Reference                                                    | Reference                                       | Reference                               | Reference                                       | Reference                                                | Reference                  |
| Q2              | 1 (−38; 39)                                                  | 0 (−38; 39)                                     | −0 (−38; 38)                           | −23 (−63; 17)                                    | 6 (−38; 49)                                              | 10 (−46; 67)               |
| Q3              | −14 (−53; 25)                                                | −14 (−54; 25)                                   | −19 (−58; 19)                          | −8 (−50; 33)                                     | −14 (−57; 29)                                            | 47 (−9; 102)               |
| Q4 (high)       | −9 (−50; 32)                                                 | −10 (−53; 32)                                   | −12 (−52; 28)                         | −12 (−55; 31)                                    | −11 (−55; 33)                                            | 15 (−41; 72)               |
| Per SD          | p = 0.49                                                    | p = 0.45                                        | p = 0.38                                | p = 0.48                                        | p = 0.38                                                 | p = 0.70                   |

#### “Nuts, High-Fibre Cereals and Soy” Pattern

| Quartile        | n = 674                                                       | n = 674                                          | n = 665                                  | n = 532                                          | n = 560                                                   | n = 425                     |
| Q1 (low)        | Reference                                                    | Reference                                       | Reference                               | Reference                                       | Reference                                                | Reference                  |
| Q2              | 11 (−26; 48)                                                 | 19 (−24; 61)                                    | 10 (−27; 46)                           | 7 (−39; 40)                                     | 7 (−33; 48)                                              | −1 (−50; 48)               |
| Q3              | 18 (20; 55)                                                  | 31 (−21; 83)                                    | 16 (−21; 53)                           | 9 (−31; 49)                                     | 9 (−42; 59)                                              | 8 (−42; 59)                |
| Q4 (high)       | 30 (−8; 68)                                                 | 51 (−17; 120)                                   | 28 (−9; 66)                            | 38 (−2; 79)                                     | 27 (−15; 69)                                             | 22 (−31; 75)               |
| Per SD          | p = 0.36                                                    | p = 0.89                                        | p = 0.41                                | p = 0.20                                        | p = 0.49                                                 | p = 0.51                   |

#### “Margarine, Sugar and Snacks” Pattern

| Quartile        | n = 674                                                       | n = 674                                          | n = 665                                  | n = 532                                          | n = 560                                                   | n = 425                     |
| Q1 (low)        | Reference                                                    | Reference                                       | Reference                               | Reference                                       | Reference                                                | Reference                  |
| Q2              | −3 (−40; 34)                                                 | −4 (−41; 34)                                    | 1 (−36; 38)                            | −6 (−46; 34)                                    | 8 (−32; 47)                                              | −28 (−76; 21)              |
| Q3              | 16 (22; 54)                                                 | 15 (−22; 53)                                    | 15 (−23; 52)                           | 11 (−29; 52)                                    | 28 (−13; 68)                                             | −5 (−55; 44)               |
| Q4 (high)       | 9 (−30; 48)                                                  | 9 (−30; 48)                                     | 9 (−30; 48)                            | 11 (−30; 52)                                    | −3 (−46; 40)                                             | −9 (−62; 44)               |
| Per SD          | p = 0.84                                                    | p = 0.83                                        | p = 0.82                                | p = 0.89                                        | p = 0.50                                                 | p = 0.84                   |

#### “Dutch Healthy Diet-Index” Pattern

| Quartile        | n = 674                                                       | n = 674                                          | n = 665                                  | n = 532                                          | n = 560                                                   | n = 425                     |
| Q1 (low)        | Reference                                                    | Reference                                       | Reference                               | Reference                                       | Reference                                                | Reference                  |
| Q2              | −3 (−40; 34)                                                 | −4 (−41; 34)                                    | 1 (−36; 38)                            | −6 (−46; 34)                                    | 8 (−32; 47)                                              | −28 (−76; 21)              |
| Q3              | 16 (22; 54)                                                 | 15 (−22; 53)                                    | 15 (−23; 52)                           | 11 (−29; 52)                                    | 28 (−13; 68)                                             | −5 (−55; 44)               |
| Q4 (high)       | 9 (−30; 48)                                                  | 9 (−30; 48)                                     | 9 (−30; 48)                            | 11 (−30; 52)                                    | −3 (−46; 40)                                             | −9 (−62; 44)               |
| Per SD          | p = 0.84                                                    | p = 0.83                                        | p = 0.82                                | p = 0.89                                        | p = 0.50                                                 | p = 0.84                   |

1 Values (regression coefficients with 95%-confidence interval) reflect the difference in gestational weight gain until early third trimester (g/week) for quartile 2 until 4 relative to quartile 1 in overweight women. p-Values correspond to the effect of 1SD increase in dietary pattern score. Adjusted for pre-pregnancy BMI, median gestational age at follow-up, age, educational level, household income, parity, smoking during pregnancy, alcohol consumption during pregnancy, stress during pregnancy, and fetal sex. Further adjusted for energy intake (kcal/day). Women excluded with pre-existing comorbidities (diabetes mellitus, hypercholesterolemia, hypertension, heart disease, thyroid disease, and systemic lupus erythematosus) and with pregnancy complications (pregnancy-induced hypertension, preeclampsia or gestational diabetes). Gestational weight gain calculated from self-reported pre-pregnancy weight and maximum weight in pregnancy. Significant results are presented in bold (p-value < 0.05) and results with a p-value < 0.0125 with an asterisk (*).
### Supplementary Table 2.2.5. Gestational weight trajectories in normal weight and overweight women (n = 3374)\(^1\)

<table>
<thead>
<tr>
<th>Normal Weight Women (n=2564)</th>
<th>Mean</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Vegetable, oil and fish” pattern</td>
<td>0.217</td>
<td>−0.010; 0.443</td>
</tr>
<tr>
<td>“Nuts, high-fibre cereals and soy” pattern</td>
<td>0.151</td>
<td>−0.084; 0.395</td>
</tr>
<tr>
<td>“Margarine, sugar and snacks” pattern</td>
<td><em>0.300</em></td>
<td><em>0.074; 0.520</em></td>
</tr>
<tr>
<td>Gestational age (at measurement in weeks)</td>
<td>0.131</td>
<td>0.121; 0.142 *</td>
</tr>
<tr>
<td>Gestational age × gestational age</td>
<td><em>0.008</em></td>
<td><em>0.007; 0.008</em></td>
</tr>
<tr>
<td>“Vegetable, oil and fish” pattern × gestational age</td>
<td><em>−0.001</em></td>
<td><em>−0.007; 0.005</em></td>
</tr>
<tr>
<td>“Nuts, high-fibre cereals and soy” pattern × gestational age</td>
<td><em>−0.010</em></td>
<td><em>−0.016; −0.004</em></td>
</tr>
<tr>
<td>“Margarine, sugar and snacks” pattern × gestational age</td>
<td>0.006</td>
<td>−0.000; 0.012</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overweight women (n=810)</th>
<th>Mean</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Vegetable, oil and fish” pattern</td>
<td>0.263</td>
<td>−0.180; 0.717</td>
</tr>
<tr>
<td>“Nuts, high-fibre cereals and soy” pattern</td>
<td>−0.306</td>
<td>−0.767; 0.140</td>
</tr>
<tr>
<td>“Margarine, sugar and snacks” pattern</td>
<td>0.319</td>
<td>−0.074; 0.714</td>
</tr>
<tr>
<td>Gestational age (at measurement in weeks)</td>
<td><em>0.099</em></td>
<td><em>0.081; 0.118</em></td>
</tr>
<tr>
<td>Gestational age × gestational age</td>
<td><em>0.008</em></td>
<td><em>0.007; 0.008</em></td>
</tr>
<tr>
<td>“Vegetable, oil and fish” pattern × gestational age</td>
<td>0.005</td>
<td>−0.006; 0.016</td>
</tr>
<tr>
<td>“Nuts, high-fibre cereals and soy” pattern × gestational age</td>
<td>0.007</td>
<td>−0.004; 0.018</td>
</tr>
<tr>
<td>“Margarine, sugar and snacks” pattern × gestational age</td>
<td>0.005</td>
<td>−0.005; 0.015</td>
</tr>
</tbody>
</table>

\(^1\) The table shows the posterior mean and 95% credible intervals (95%CI) of the longitudinal analysis of a posteriori-derived dietary patterns and weight development in pregnancy in normal weight and overweight women using Bayesian linear mixed models. The model included the following variables: the a posteriori-derived dietary patterns, gestational age at measurement, gestational age at measurement × gestational age at measurement, interaction terms of the dietary patterns with gestational age at measurement, age, educational level, household income, parity, smoking during pregnancy, alcohol consumption during pregnancy, stress during pregnancy, and fetal sex. Significant results are presented in bold (\(p\)-value < 0.05) and results with a \(p\)-value <0.0125 with an asterisk (*).
**Supplementary Table 2.2.6.** Association of dietary patterns with adequacy of weekly gestational weight gain (n=2745)\(^1\)

<table>
<thead>
<tr>
<th>Dietary Pattern Quartile</th>
<th>Inadequate Weekly GWG (n=437)</th>
<th>Adequate Weekly GWG (n=753)</th>
<th>Excessive Weekly GWG (n=1555)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95%CI)</td>
<td>OR (95%CI)</td>
<td>OR (95%CI)</td>
</tr>
<tr>
<td><strong>“Vegetable, Oil and Fish” Pattern</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 (low)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Q2</td>
<td>0.81 (0.57; 1.16)</td>
<td>Reference</td>
<td>0.99 (0.76; 1.29)</td>
</tr>
<tr>
<td>Q3</td>
<td>0.83 (0.58; 1.18)</td>
<td>Reference</td>
<td>0.89 (0.68; 1.16)</td>
</tr>
<tr>
<td>Q4 (high)</td>
<td>0.97 (0.67; 1.41)</td>
<td>Reference</td>
<td>0.85 (0.64; 1.13)</td>
</tr>
<tr>
<td>Per SD</td>
<td>(p = 0.92)</td>
<td>(p = 0.99)</td>
<td>(p = 0.11)</td>
</tr>
<tr>
<td><strong>“Nuts, High-Fibre Cereals and Soy” Pattern</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 (low)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Q2</td>
<td>1.12 (0.79; 1.59)</td>
<td>Reference</td>
<td>1.16 (0.89; 1.51)</td>
</tr>
<tr>
<td>Q3</td>
<td>0.86 (0.59; 1.24)</td>
<td>Reference</td>
<td>0.99 (0.76; 1.30)</td>
</tr>
<tr>
<td>Q4 (high)</td>
<td>1.10 (0.76; 1.61)</td>
<td>Reference</td>
<td>1.16 (0.87; 1.55)</td>
</tr>
<tr>
<td>Per SD</td>
<td>(p = 0.83)</td>
<td>(p = 0.83)</td>
<td>(p = 0.20)</td>
</tr>
<tr>
<td><strong>“Margarine, Sugar and Snacks” Pattern</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 (low)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Q2</td>
<td>1.17 (0.83; 1.65)</td>
<td>Reference</td>
<td>1.13 (0.88; 1.47)</td>
</tr>
<tr>
<td>Q3</td>
<td>0.92 (0.65; 1.32)</td>
<td>Reference</td>
<td>1.10 (0.85; 1.43)</td>
</tr>
<tr>
<td>Q4 (high)</td>
<td>(1.49) ((1.05; 2.11))</td>
<td>Reference</td>
<td>(1.32) ((1.01; 1.72))</td>
</tr>
<tr>
<td>Per SD</td>
<td>(p = 0.19)</td>
<td>(p = 0.19)</td>
<td>(p = 0.29)</td>
</tr>
<tr>
<td><strong>“Dutch Healthy Diet-Index” Pattern</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 (low)</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Q2</td>
<td>0.79 (0.56;1.11)</td>
<td>Reference</td>
<td>0.93 (0.72;1.20)</td>
</tr>
<tr>
<td>Q3</td>
<td>0.88 (0.62;1.25)</td>
<td>Reference</td>
<td>1.10 (0.85;1.42)</td>
</tr>
<tr>
<td>Q4 (high)</td>
<td>1.00 (0.69;1.43)</td>
<td>Reference</td>
<td>1.02 (0.77;1.34)</td>
</tr>
<tr>
<td>Per SD</td>
<td>(p = 0.84)</td>
<td>(p = 0.84)</td>
<td>(p = 0.63)</td>
</tr>
</tbody>
</table>

\(^1\) Results from multivariable multinomial logistic regression analyses, based on imputed data. Low dietary pattern adherence (Q1) is the reference category for diet and adequate weekly GWG is the reference category for weekly GWG in the multinomial regression model. \(p\)-Values correspond to the effect of 1SD increase in dietary pattern score. Adjusted for pre-pregnancy BMI, gestational age at measurements, age, educational level, household income, parity, smoking during pregnancy, alcohol consumption during pregnancy, stress during pregnancy, and fetal sex. Significant results are presented in bold (\(p\)-value < 0.05) and results with a \(p\)-value <0.0125 with an asterisk (*). Abbreviations: CI: confidence interval; GWG: gestational weight gain; OR: odds ratio; SD: standard deviation; Q: quartile.

**References chapter 2.2**


Chapter 2.3

Dietary acid load and blood pressure development in pregnancy: The Generation R Study

Myrte J. Tielemans, Nicole S. Erler, Oscar H. Franco, Vincent W.V. Jaddoe, Eric A.P. Steegers, Jessica C. Kiefte-de Jong

Submitted for publication
Statistical analysis – Modelling choices for the linear mixed models

In the following, we provide details on the modelling choices for the linear mixed models to evaluate the association between dietary acid load measurements and the development of diastolic blood pressure (DBP) and systolic blood pressure (SBP) during pregnancy.

1. Determining the random effects structure
   First, an extensive fixed effects structure was used to compare a model containing only a random intercept with models containing a random intercept and slope using an adapted likelihood ratio test. This analysis showed that a random intercept model was adequate for DBP, whereas for SBP a model with a random intercept and slope was more appropriate.

2. Simplifying the fixed effects structure
   Second, we evaluated the models with different numbers of df in the spline for gestational age and compared the fit using the Akaike’s Information Criterion (AIC). For DBP, the AIC indicated that a model with 2 df in the natural cubic spline for gestational age was the best fit for all exposures. For SBP, the AIC had no clear preference for a specific number of df. Plots of the non-linear effect of time showed that in the model for SBP at least 4 df were required to allow for enough flexibility to represent the expected physiological development of blood pressure, and we therefore chose to use 4 df in the model for SBP. Analogous comparisons showed that there was no evidence for non-linear effects of the exposures on either DBP or SBP.

3. Testing for interaction
   We tested whether including interaction terms between the exposure and gestational age and between the exposure and smoking would significantly improve the fit of any of the models. Likelihood ratio tests showed that none of the interaction terms significantly improved the model fit.

4. Final models
   The models for the main analysis include

   **Final model DBP:** a random intercept, a natural cubic spline with 2 df for gestational age, linear effects of the exposure (i.e. dPRAL, NEAP, animal protein/potassium ratio, or vegetable protein/potassium ratio), covariates (namely maternal age, educational level, household income, pre-pregnancy BMI, parity, maternal alcohol consumption and maternal smoking), and no interaction terms.

   **Final model SBP:** a random intercept and a random slope, a natural cubic spline with 4 df for gestational age, linear effects of the exposure (i.e. dPRAL, NEAP, animal protein/potassium ratio, or vegetable protein/potassium ratio), covariates (namely maternal age, educational level, household income, pre-pregnancy BMI, parity, maternal alcohol consumption and maternal smoking), and no interaction terms.
Supplementary Figure 2.3.1. Development of diastolic blood pressure during pregnancy

The upper panel shows the estimated average profile of diastolic blood pressure (mmHg) of a subgroup of 200 randomly selected participants. The mean value is presented in black and individual trajectories in color. The lower panel shows a zoomed-in version of the mean diastolic blood pressure during pregnancy in all participants.

The upper panel shows the estimated average profile of diastolic blood pressure (mmHg) of a subgroup of 200 randomly selected participants. The mean value is presented in black and individual trajectories in color. The lower panel shows a zoomed-in version of the mean diastolic blood pressure during pregnancy in all participants.
Supplementary Figure 2.3.2. Development of systolic blood pressure during pregnancy

The upper panel shows the estimated average profile of systolic blood pressure (mmHg) of a subgroup of 200 randomly selected participants. The mean value is presented in black and individual trajectories in color. The lower panel shows a zoomed-in version of the mean systolic blood pressure during pregnancy in all participants.
### Supplementary Table 2.3.1. Details of the multiple imputation process

| Multiple imputation |  
|---------------------|---
| **Software used**   | IBM SPSS statistics version 21  
| **Imputation method and key settings** | Fully conditional specification (Markov chain Monte Carlo method); maximum iterations: 10  
| **No. of imputed data sets created** | 10  
| **Variables included in the imputation procedure as both predictor variable as a variable to be imputed** | Age mother at enrolment; Gravidity at enrolment; Parity at enrolment; Nausea during pregnancy; Vomiting during pregnancy; Pre-pregnancy weight; Pre-pregnancy BMI; Gestational weight gain: Height at enrolment; Maternal educational level at enrolment; Maternal alcohol consumption during pregnancy; Maternal smoking during pregnancy; Folic acid supplementation during pregnancy; Age partner at enrolment; BMI partner; Education level partner at enrolment; Household income at enrolment; Maternal stress during pregnancy; Foetal sex; Gestational age at birth; Preterm birth.  
| **Variables added as predictors (not used in the main analysis) of missing data to increase plausibility of missing at random assumption** | Dietary potential renal acid load (dPRAL); net endogenous acid production (NEAP); Animal protein/potassium ratio (AP/K ratio); Dutch Healthy Diet-Index; Maternal energy intake during pregnancy; Maternal serum folate level 18 weeks of gestation; Height at 2nd and 3rd visit; Weight at 1st, 2nd and 3rd visit; Birthweight; Standardized birth weight (Niklasson); Maternal educational level 6 years after enrolment; Household income 6 years after enrolment; Hypertensive complications in pregnancy; Gestational age at first, second and third visit; Systolic blood pressure during first, second, and third visit; Diastolic blood pressure during first, second, and third visit.  
| **Treatment of not normally distributed variables** | Predictive mean matching  
| **Treatment of binary/categorical variables** | Logistic regression models  
| **Population** | For the multiple imputation we included those mothers of Dutch ancestry, enrolled during pregnancy and with available dietary information (n=3558)  

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### Supplementary Table 2.3.2. Differences between the population of analysis and eligible women not included in the analysis (n=4096)

<table>
<thead>
<tr>
<th></th>
<th>Included (n=3411)</th>
<th>Not included (n=685)</th>
<th>p-value&lt;sup&gt;2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>31.4 ± 4.4</td>
<td>30.7 ± 5.1</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td><strong>Educational level</strong></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low and midlow</td>
<td>505 (15.0)</td>
<td>173 (25.9)</td>
<td></td>
</tr>
<tr>
<td>Midhigh</td>
<td>1712 (50.8)</td>
<td>322 (48.2)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>1150 (34.2)</td>
<td>173 (25.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td>44 (1.3)</td>
<td>17 (2.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Household income (Euros/month)</strong></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt; 2,200</td>
<td>769 (25.2)</td>
<td>182 (34.9)</td>
<td></td>
</tr>
<tr>
<td>≥ 2,200</td>
<td>2281 (74.8)</td>
<td>340 (65.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td>361 (10.6)</td>
<td>163 (23.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Parity</strong></td>
<td></td>
<td></td>
<td>0.40</td>
</tr>
<tr>
<td>0</td>
<td>2038 (59.9)</td>
<td>396 (58.1)</td>
<td></td>
</tr>
<tr>
<td>≥1</td>
<td>1365 (40.1)</td>
<td>285 (41.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td>8 (0.2)</td>
<td>4 (0.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Pre-pregnancy body mass index (kg/m&lt;sup&gt;2&lt;/sup&gt;)</strong></td>
<td></td>
<td></td>
<td>0.16</td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td>467 (13.7)</td>
<td>119 (17.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Never during pregnancy</td>
<td>2346 (74.2)</td>
<td>415 (66.6)</td>
<td></td>
</tr>
<tr>
<td>Until pregnancy was known</td>
<td>280 (8.9)</td>
<td>68 (10.9)</td>
<td></td>
</tr>
<tr>
<td>Continued throughout pregnancy</td>
<td>536 (17.0)</td>
<td>140 (22.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td>249 (7.3)</td>
<td>62 (9.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Alcohol consumption</strong></td>
<td></td>
<td></td>
<td>0.006</td>
</tr>
<tr>
<td>Never during pregnancy</td>
<td>1059 (33.8)</td>
<td>241 (38.9)</td>
<td></td>
</tr>
<tr>
<td>Until pregnancy was known</td>
<td>509 (16.2)</td>
<td>112 (18.1)</td>
<td></td>
</tr>
<tr>
<td>Continued throughout pregnancy</td>
<td>1569 (50.0)</td>
<td>267 (43.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td>274 (8.0)</td>
<td>65 (9.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Folic acid supplementation</strong></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Started periconceptional</td>
<td>1569 (56.1)</td>
<td>267 (48.6)</td>
<td></td>
</tr>
<tr>
<td>Started first 10 weeks</td>
<td>923 (33.0)</td>
<td>191 (34.8)</td>
<td></td>
</tr>
<tr>
<td>No supplementation</td>
<td>304 (10.9)</td>
<td>91 (16.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td>615 (18.0)</td>
<td>136 (19.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Gestational age at enrolment (weeks)</strong></td>
<td></td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td><strong>Diastolic blood pressure at enrolment (mmHg)</strong></td>
<td>68 ± 9</td>
<td>70 ± 11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td>28 (0.8)</td>
<td>11 (1.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Systolic blood pressure at enrolment (mmHg)</strong></td>
<td>117 ± 12</td>
<td>120 ± 14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td>28 (0.8)</td>
<td>11 (1.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Pregnancy-induced hypertension</strong></td>
<td>173 (5.3)</td>
<td>34 (5.0)</td>
<td>0.64</td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td>140 (4.1)</td>
<td>95 (13.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Pre-eclampsia</strong></td>
<td>59 (1.9)</td>
<td>19 (3.3)</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td>254 (7.4)</td>
<td>110 (16.1)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> Values represent n (%), mean ± SD, median (interquartile range). <sup>2</sup> Differences between continuous variables tested using independent student t-test or Mann Whitney U test, and between categorical variables were tested using Chi-square statistics.
**Supplementary Table 2.3.3.** Pooled results of dietary acid load with systolic blood pressure and with diastolic blood pressure, additionally adjusted for the Dutch Healthy Diet-index (n=3411)

<table>
<thead>
<tr>
<th>Dietary acid load</th>
<th>Diastolic blood pressure</th>
<th>Systolic blood pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Difference in mmHg (95% CI)</td>
<td>Difference in mmHg (95% CI)</td>
</tr>
<tr>
<td>dPRAL</td>
<td>Adjusted (per SD)</td>
<td>-0.07 (-0.32; 0.19)</td>
</tr>
<tr>
<td>NEAP</td>
<td>Adjusted (per SD)</td>
<td>-0.13 (-0.39; 0.13)</td>
</tr>
<tr>
<td>Animal protein/potassium ratio</td>
<td>Adjusted (per SD)</td>
<td>0.06 (-0.19; 0.32)</td>
</tr>
<tr>
<td>Vegetable protein/potassium ratio</td>
<td>Adjusted (per SD)</td>
<td><strong>-0.28 (-0.52; 0.04)</strong></td>
</tr>
</tbody>
</table>

1. Results (coefficients with 95% confidence interval (CI)) from linear mixed model analysis. The coefficient reflects the difference in systolic blood pressure (mmHg) or diastolic blood pressure (mmHg) per one standard deviation (SD) increase in dietary acid load. The models include the natural cubic splines for gestational age (2 df for DBP and 4 df for SBP), a random intercept and slope for SBP, maternal age, pre-pregnancy BMI, parity, educational level, household income, alcohol consumption during pregnancy, smoking behavior during pregnancy, and Dutch Health Diet-index. Significant associations (p-value <0.05) are presented with an asterisk (*). **Abbreviations:** DBP: diastolic blood pressure, dPRAL: dietary potential renal acid load, NEAP: net endogenous acid production, SBP: systolic blood pressure.

**Supplementary Table 2.3.4.** Analysis in women without pre-existing comorbidities (n=3290)¹

<table>
<thead>
<tr>
<th>Dietary acid load</th>
<th>Diastolic blood pressure</th>
<th>Systolic blood pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Difference in mmHg (95% CI)</td>
<td>Difference in mmHg (95% CI)</td>
</tr>
<tr>
<td>dPRAL</td>
<td>Adjusted (per SD)</td>
<td>-0.13 (-0.37; 0.11)</td>
</tr>
<tr>
<td>NEAP</td>
<td>Adjusted (per SD)</td>
<td>-0.17 (-0.41; 0.07)</td>
</tr>
<tr>
<td>Animal protein/potassium ratio</td>
<td>Adjusted (per SD)</td>
<td>-0.01 (-0.25; 0.23)</td>
</tr>
<tr>
<td>Vegetable protein/potassium ratio</td>
<td>Adjusted (per SD)</td>
<td><strong>-0.30 (-0.54; -0.05)</strong></td>
</tr>
</tbody>
</table>

¹ Results (coefficients with 95% confidence interval (CI)) from linear mixed model analysis. The coefficient reflects the difference in systolic blood pressure or diastolic blood pressure (mmHg) per one standard deviation (SD) increase in dietary acid load. The models include the natural cubic splines for gestational age (2 df for DBP and 4 df for SBP), a random intercept for DBP and a random intercept and slope for SBP, maternal age, pre-pregnancy BMI, parity, educational level, household income, alcohol consumption during pregnancy and smoking behavior during pregnancy. Significant associations (p-value <0.05) are presented with an asterisk (*). **Abbreviations:** DBP: diastolic blood pressure, dPRAL: dietary potential renal acid load, NEAP: net endogenous acid production, SBP: systolic blood pressure.
Chapter 3.1

Maternal fish consumption, fatty acid levels and angiogenic factors: The Generation R Study


* Contributed equally

Placenta. 2015 Oct;36(10):1178-84
### Supplementary Table 3.1.1. Characteristics of participants (n = 3134)\textsuperscript{a}

<table>
<thead>
<tr>
<th>Maternal characteristics</th>
<th>Unimputed dataset</th>
<th>Imputed dataset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31.4 ± 4.3</td>
<td>31.4 ± 4.3</td>
</tr>
<tr>
<td>Gestational age at enrolment (weeks)</td>
<td>13.2 (9.9-21.6)</td>
<td>No missing</td>
</tr>
<tr>
<td>BMI at enrolment (kg/m\textsuperscript{2})</td>
<td>24.1 ± 3.9</td>
<td>24.1 ± 3.9</td>
</tr>
<tr>
<td>Parity, % (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nullipara</td>
<td>60.1 (1880)</td>
<td>60.1 (1883)</td>
</tr>
<tr>
<td>Multipara</td>
<td>39.9 (1247)</td>
<td>39.9 (1251)</td>
</tr>
<tr>
<td>Highest education finished, % (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>3.1 (97)</td>
<td>3.2 (100)</td>
</tr>
<tr>
<td>Secondary</td>
<td>36.4 (1133)</td>
<td>36.4 (1140)</td>
</tr>
<tr>
<td>Higher</td>
<td>60.5 (1885)</td>
<td>60.5 (1894)</td>
</tr>
<tr>
<td>Smoking during pregnancy, % (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>25.9 (755)</td>
<td>28.5 (894)</td>
</tr>
<tr>
<td>No</td>
<td>74.1 (2160)</td>
<td>71.5 (2240)</td>
</tr>
<tr>
<td>Alcohol use during pregnancy, % (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>67.1 (1944)</td>
<td>67.2 (2105)</td>
</tr>
<tr>
<td>No</td>
<td>32.9 (952)</td>
<td>32.8 (1029)</td>
</tr>
<tr>
<td>Folic acid supplementation use, % (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>89.5 (2310)</td>
<td>89.0 (2789)</td>
</tr>
<tr>
<td>No</td>
<td>10.5 (272)</td>
<td>11.0 (345)</td>
</tr>
<tr>
<td>Pregnancy-induced hypertension, % (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5.3 (164)</td>
<td>Not imputed</td>
</tr>
<tr>
<td>No</td>
<td>94.7 (2914)</td>
<td></td>
</tr>
<tr>
<td>Preeclampsia, % (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.9 (56)</td>
<td>Not imputed</td>
</tr>
<tr>
<td>No</td>
<td>98.1 (2914)</td>
<td></td>
</tr>
<tr>
<td>Season of conception, % (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Winter</td>
<td>28.3 (888)</td>
<td>28.3 (888)</td>
</tr>
<tr>
<td>Spring</td>
<td>23.6 (738)</td>
<td>23.6 (738)</td>
</tr>
<tr>
<td>Summer</td>
<td>21.8 (684)</td>
<td>21.8 (684)</td>
</tr>
<tr>
<td>Fall</td>
<td>26.3 (823)</td>
<td>26.3 (823)</td>
</tr>
<tr>
<td>Total daily energy intake (kJ/day)</td>
<td>8972 ± 2127\textsuperscript{b}</td>
<td>No missing</td>
</tr>
<tr>
<td>Total fish intake (gram/week)\textsuperscript{c}</td>
<td>75 (0-318)</td>
<td>No missing</td>
</tr>
<tr>
<td>Lean fish intake (gram/week)\textsuperscript{c}</td>
<td>24 (0-149)</td>
<td>No missing</td>
</tr>
<tr>
<td>Fatty fish intake (gram/week)\textsuperscript{c}</td>
<td>30 (0-150)</td>
<td>No missing</td>
</tr>
<tr>
<td>Shellfish intake (gram/week)\textsuperscript{c}</td>
<td>0 (0-34.5)</td>
<td>No missing</td>
</tr>
<tr>
<td>Plasma fatty acids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Docosahexaenoic acid (mg/L)</td>
<td>80.1 ± 20.0</td>
<td>Not imputed</td>
</tr>
<tr>
<td>Eicosapentaenoic acid (mg/L)</td>
<td>13.0 ± 4.2</td>
<td>Not imputed</td>
</tr>
<tr>
<td>Alpha-Linolenic acid (mg/L)</td>
<td>5.5 ± 1.8</td>
<td>Not imputed</td>
</tr>
<tr>
<td>Linoleic acid (mg/L)</td>
<td>352.3 ± 59.5</td>
<td>Not imputed</td>
</tr>
</tbody>
</table>
**Supplementary Table 3.1.1. (continued) Characteristics of participants (n = 3134)**

<table>
<thead>
<tr>
<th>Maternal characteristics</th>
<th>Unimputed dataset</th>
<th>Imputed dataset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arachidonic acid (mg/L)</td>
<td>154.5 ± 31.2</td>
<td>Not imputed</td>
</tr>
<tr>
<td>Omega-3/omega-6 ratio</td>
<td>0.2 ± 0.05</td>
<td>Not imputed</td>
</tr>
<tr>
<td>EPA/AA ratio</td>
<td>0.06 ± 0.04</td>
<td>Not imputed</td>
</tr>
<tr>
<td>DHA/AA ratio</td>
<td>0.5 ± 0.14</td>
<td>Not imputed</td>
</tr>
</tbody>
</table>

**Angiogenic factors levels**

*First trimester*
- PI GF (pg/mL) 37.8 (14.4-154.7) Not imputed
- sFlt-1 (ng/mL) 4.9 (1.9-12.8) Not imputed
- sFlt-1/PI GF ratio 0.13 (0.02-0.43) Not imputed

*Second trimester*
- PI GF (pg/mL) 185.9 (73.2-569.3) Not imputed
- sFlt-1 (ng/mL) 4.7 (1.5-16.0) Not imputed
- sFlt-1/PI GF ratio 0.02 (0.01-0.11) Not imputed

*Cord blood*
- PI GF (pg/mL) 8.6 (0.0-20.7) Not imputed
- sFlt-1 (ng/mL) 0.45 (0.08-4.01) Not imputed
- sFlt-1/PI GF ratio 0.05 (0.01-0.42) Not imputed

**Child characteristics**

<table>
<thead>
<tr>
<th>Sex, % (n)</th>
<th>Unimputed dataset</th>
<th>Imputed dataset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boy</td>
<td>50.8 (1592)</td>
<td>50.8 (1592)</td>
</tr>
<tr>
<td>Girl</td>
<td>49.2 (1541)</td>
<td>49.2 (1542)</td>
</tr>
<tr>
<td>Gestational age at birth (weeks)</td>
<td>40.3 (36.0-42.4)</td>
<td>40.3 (36.0-42.4)</td>
</tr>
<tr>
<td>Birth weight (grams)</td>
<td>3497 ± 549</td>
<td>3497 ± 550</td>
</tr>
</tbody>
</table>

*a* Values are mean ± SD when normally distributed or median (95% range) when not normally distributed for continuous variables and percentages (n) for categorical outcomes. The number of missings were 0.03% (n = 1) for maternal age, 0.4% (n = 14) for BMI at enrolment, 0.2% (n = 7) for parity, 0.6% (n = 19) for maternal education, 7.0% (n = 219) for smoking, 7.6% (n = 238) for alcohol use, 17.6% (n = 552) for folic acid supplementation use, 1.8% (n = 56) for pregnancy-induced hypertension, 5.2% (n = 164) for preeclampsia, 0.03% (n = 1) for season of conception, 13.9% (n = 435) for plasma fatty acids, 0.03% (n = 1) for child sex, 0.03% (n = 1) gestational age at birth and 0.2% (n = 5) for birth weight. AA: Arachidonic acid, DHA: Docosahexanoic acid, EPA: Eicosapentanoic acid, PI GF: Placental growth factor, sFlt-1: Soluble Flt-1. *b* Value corresponds to a daily energy intake of 2143 ± 508 kcal/day. *c* Absolute values of fish consumption.
Supplementary Table 3.1.2. Associations between weekly maternal fatty fish consumption and levels of angiogenic factors \(^a\)

<table>
<thead>
<tr>
<th>Fatty fish consumption (energy-adjusted g/week)</th>
<th>First Trimester</th>
<th></th>
<th>Second Trimester</th>
<th></th>
<th>Cord Blood</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Beta</td>
<td>95% CI</td>
<td>n</td>
<td>Beta</td>
<td>95% CI</td>
</tr>
<tr>
<td><strong>Ln-PIGF pg/mL (n=2515)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>222</td>
<td>Reference</td>
<td></td>
<td>256</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>1-34</td>
<td>1098</td>
<td>0.003</td>
<td>-0.065, 0.071</td>
<td>1242</td>
<td>0.010</td>
<td>-0.059, 0.078</td>
</tr>
<tr>
<td>35-69</td>
<td>720</td>
<td>-0.020</td>
<td>-0.089, 0.050</td>
<td>797</td>
<td>-0.024</td>
<td>-0.095, 0.046</td>
</tr>
<tr>
<td>&gt;70</td>
<td>475</td>
<td>0.002</td>
<td>-0.071, 0.076</td>
<td>550</td>
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<td><strong>Ln-sFlt-1 ng/mL (n=2513)</strong></td>
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<td></td>
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<tr>
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<td></td>
<td>256</td>
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<td>0.064</td>
<td>-0.023, 0.150</td>
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<tr>
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<td>797</td>
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<td>-0.089, 0.079</td>
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<td>-0.044, 0.143</td>
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<td>-0.048, 0.156</td>
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<td>-0.102, 0.094</td>
<td>797</td>
<td>0.060</td>
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<td>0.066</td>
<td>-0.045, 0.176</td>
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<tr>
<td><strong>P for trend</strong></td>
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</tbody>
</table>

Results from multivariable linear regression model, based on imputed data. P for trend was conducted by including fatty fish consumption categories in the multivariable linear regression model. + P < 0.05, * P < 0.01. **Abbreviations:** CI: confidence interval, n: number of participants, PIGF: placental growth factor, sFlt-1: soluble Flt-1. \(a\) Adjusted for total energy intake, maternal age, gestational age at measurement, BMI at enrolment, foetal sex, parity, maternal education, smoking, and season of conception.
**Supplementary Table 3.1.3.** Associations between weekly maternal lean fish consumption and levels of angiogenic factors

<table>
<thead>
<tr>
<th>Lean fish consumption (energy-adjusted g/week)</th>
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<th>Second Trimester</th>
<th></th>
<th>Cord Blood</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Beta</td>
<td>95% CI</td>
<td>n</td>
<td>Beta</td>
<td>95% CI</td>
</tr>
<tr>
<td><strong>Ln-PIGF pg/mL</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>657</td>
<td>Reference</td>
<td></td>
<td>744</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>1-34</td>
<td>932</td>
<td>-0.049†</td>
<td>-0.095, -0.004</td>
<td>1052</td>
<td>-0.054†</td>
<td>-0.100, -0.008</td>
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<td>613</td>
<td>-0.023</td>
<td>-0.073, 0.027</td>
<td>680</td>
<td>-0.002</td>
<td>-0.053, 0.049</td>
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<tr>
<td>&gt;70</td>
<td>313</td>
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<td>-0.066, 0.054</td>
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<td>-0.025</td>
<td>-0.085, 0.035</td>
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<tr>
<td><strong>P for trend</strong></td>
<td>0.94</td>
<td>0.90</td>
<td>0.64</td>
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<td></td>
<td></td>
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<tr>
<td><strong>Ln-sFlt-1 ng/mL</strong></td>
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<td></td>
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</tr>
<tr>
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<td>Reference</td>
<td></td>
<td>744</td>
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<td>-0.038, 0.078</td>
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<td>0.028</td>
<td>-0.030, 0.085</td>
<td>680</td>
<td>0.027</td>
<td>-0.037, 0.092</td>
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<tr>
<td>&gt;70</td>
<td>314</td>
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<td>-0.093, 0.044</td>
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<td><strong>Ln-sFlt-1/PIGF ratio</strong></td>
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<td>Reference</td>
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<td>744</td>
<td>Reference</td>
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<td>1-34</td>
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<td>0.023, 0.150</td>
<td>1052</td>
<td>0.074†</td>
<td>0.005, 0.143</td>
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<td>0.051</td>
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<td>680</td>
<td>0.030</td>
<td>-0.047, 0.106</td>
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<td>&gt;70</td>
<td>312</td>
<td>-0.020</td>
<td>-0.104, 0.064</td>
<td>368</td>
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<td>-0.099, 0.081</td>
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<td><strong>P for trend</strong></td>
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<td>0.76</td>
<td>0.24</td>
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</table>

Results from multivariable linear regression model, based on imputed data. P for trend was conducted by including lean fish consumption categories in the multivariable linear regression model. † P<0.05, * P < 0.01.

**Abbreviations:** CI: confidence interval, n: number of participants, PIGF: placental growth factor, sFlt-1: soluble Flt-1. † Adjusted for total energy intake, maternal age, gestational age at measurement, BMI at enrolment, foetal sex, parity, maternal education, smoking, and season of conception.
**Supplementary Table 3.1.4.** Associations between weekly maternal shellfish consumption and levels of angiogenic factors

<table>
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<tr>
<th>Shellfish consumption (energy-adjusted g/week)</th>
<th>First Trimester</th>
<th></th>
<th>Second Trimester</th>
<th></th>
<th>Cord Blood</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Beta</td>
<td>95% CI</td>
<td>n</td>
<td>Beta</td>
<td>95% CI</td>
</tr>
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<td>1569</td>
<td>Reference</td>
<td></td>
<td>1769</td>
<td>Reference</td>
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<td>1-13</td>
<td>462</td>
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<td>509</td>
<td>-0.002</td>
<td>-0.049, 0.045</td>
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<tr>
<td>&gt;14</td>
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<td>567</td>
<td>0.004</td>
<td>-0.041, 0.050</td>
</tr>
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<td>0.88</td>
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<td>0</td>
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<td>Reference</td>
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<tr>
<td>1-13</td>
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<td>-0.062, 0.056</td>
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<tr>
<td>&gt;14</td>
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<td>-0.055, 0.049</td>
<td>566</td>
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<td>-0.084, 0.032</td>
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<tr>
<td>1-13</td>
<td>457</td>
<td>-0.007</td>
<td>-0.071, 0.057</td>
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<td>0.42</td>
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Results from multivariable linear regression model, based on imputed data. P for trend was conducted by including shellfish consumption categories in the multivariable linear regression model. † P < 0.05, * P < 0.01.

**Abbreviations:** CI: confidence interval, n: number of participants, PlGF: placental growth factor, sFlt-1: soluble Flt-1. * Adjusted for total energy intake, maternal age, gestational age at measurement, BMI at enrolment, foetal sex, parity, maternal education, smoking, and season of conception.
Chapter 3.2

Circulating fatty acid patterns, gestational weight gain and hypertensive complications in pregnancy: The Generation R Study


* Contributed equally

Submitted for publication
Supplementary Figure 3.2.1. Selection of participants: the Generation R Study, Rotterdam, the Netherlands (2002 – 2006)

Women enrolled in the Generation R Study (n=9,778)

- n=1,115 women excluded due to enrolment after 25 weeks of gestation (n=216) or postnatal enrolment (n=899)

Women enrolled before 25 weeks of gestation (n=8,663)

- n=1,664 women excluded due to incomplete plasma fatty acid profiles (n=372) or no blood drawn (n=1,292)

Women with complete plasma fatty acid profiles (n=6,999)

- n=74 women excluded due to multiple pregnancy (n=73) or due to loss to follow up (n=1)

Women with singleton live births (n=6,925)

Women with measured gestational weight gain (n=6,567)

- n=358 women excluded due to missing gestational weight gain information between 20 and 30 weeks of gestation

Population for PCA

Abbreviation: PCA, principal component analysis
Supplementary Figure 3.2.2. Evaluation of non-linear associations of the ‘High n-3 PUFA’ pattern with gestational weight gain (n=6567)

Multivariable linear regression using natural cubic splines (df = 2) improved the fit of the model significantly for the association of the ‘High n-3 PUFA’ pattern with gestational weight gain (X²=15.8, P<0.001). Adjusted for fetal sex, gestational age at birth, gestational age at fatty acid measurement, other fatty acid patterns, maternal age, ethnicity, educational level, household income, pre-pregnancy BMI, parity, alcohol consumption during pregnancy, maternal smoking during pregnancy, and folic acid supplementation. SDS: standard deviation score.

Supplementary Figure 3.2.3. Evaluation of non-linear association of the ‘High n-6 PUFA’ pattern with gestational weight gain (n=6567)

Multivariable linear regression using natural cubic splines (df = 3) did not improve the fit of the model for the association of the ‘High n-6 PUFA’ pattern with weekly gestational weight gain (X²=2.3, P=0.32). Adjusted for gestational age at fatty acid measurement, other fatty acid patterns, maternal age, ethnicity, educational level, household income, pre-pregnancy BMI, parity, alcohol consumption during pregnancy, maternal smoking during pregnancy, folic acid supplementation and fetal sex. SDS: standard deviation score.
Supplementary Figure 3.2.4. Evaluation of non-linear association of the 'MUFA and SFA' pattern with gestational weight gain (n=6567)

Multivariable linear regression using natural cubic splines (df = 3) did not improve the fit of the model for the association of the 'MUFA and SFA' pattern with weekly gestational weight gain ($X^2=3.0$, $P=0.22$). Adjusted for gestational age at fatty acid measurement, other fatty acid patterns, maternal age, ethnicity, educational level, household income, pre-pregnancy BMI, parity, alcohol consumption during pregnancy, maternal smoking during pregnancy, folic acid supplementation and fetal sex. SDS: standard deviation score.
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<th>16:1n-7</th>
<th>18:1n-7</th>
<th>18:2n</th>
<th>20:2n</th>
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<td>P-value</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>22:5n-22:5n</td>
<td>1</td>
<td>-0.33</td>
<td>0.08</td>
<td>0.51</td>
<td>-0.15</td>
<td>0.55</td>
<td>0.51</td>
<td>0.28</td>
<td>0.16</td>
<td>0.16</td>
<td>0.18</td>
<td>0.64</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

**Supplementary Table 3.2.1:** Spearman correlations between individual plasma fatty acids (in percentage of total plasma fatty acids) (n=6999)
### Supplementary Table 3.2.2. Details of the multiple imputation process

<table>
<thead>
<tr>
<th><strong>Multiple imputation</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Software used</strong></td>
<td>IBM SPSS statistics version 21</td>
</tr>
<tr>
<td><strong>Imputation method and key settings</strong></td>
<td>Fully conditional specification (Markov chain Monte Carlo method); maximum iterations: 10</td>
</tr>
<tr>
<td><strong>No. of imputed data sets created</strong></td>
<td>10</td>
</tr>
<tr>
<td><strong>Variables included in the imputation procedure as both predictor variable as a variable to be imputed</strong></td>
<td>Age at enrolment, ethnicity, gravidity, parity, educational level at enrolment, marital status, household income at enrolment, gestational age at enrolment, pre-pregnancy BMI, alcohol consumption during pregnancy, smoking during pregnancy, folic acid supplementation during pregnancy, maternal stress during pregnancy, nausea during 1st trimester, vomiting during 1st trimester, gestational age at birth, birth weight, standardized birth weight (Niklasson) and fetal sex.</td>
</tr>
<tr>
<td><strong>Variables added as predictors (not used in the main analysis) of missing data to increase plausibility of missing at random assumption</strong></td>
<td>‘High n-6 PUFA’ pattern, ‘MUFA and SFA’ pattern, ‘High n-3 PUFA’ pattern, ethnicity father of the child, educational level 6 years after enrolment, paternal education at enrolment, paternal education 6 years after enrolment, household income 6 years after enrolment, pre-pregnancy weight, weight at enrolment, gestational age at 1st visit, weight at 1st visit, height at 1st visit, gestational age at 2nd visit, weight at 2nd visit, height at 2nd visit, gestational age at 3rd visit, weight at 3rd visit, height at 3rd visit, smoking during 1st trimester, smoking during 2nd trimester, smoking during 3rd trimester, alcohol consumption during 1st trimester, alcohol consumption during 2nd trimester, alcohol consumption during 3rd trimester, energy intake, combined 4 items of the Dutch Healthy Diet-index, serum folate levels &lt; 18 weeks of gestation, gestational weight gain between 1st and 2nd visit, gestational weight gain between 2nd and 3rd visit, weekly weight gain between 2nd and 3rd visit</td>
</tr>
<tr>
<td><strong>Treatment of not normally distributed variables</strong></td>
<td>Predictive mean matching</td>
</tr>
<tr>
<td><strong>Treatment of binary/categorical variables</strong></td>
<td>Logistic regression models</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>For the multiple imputation we included those mothers with complete plasma fatty acid profiles (n=6,999)</td>
</tr>
</tbody>
</table>
**Supplementary Table 3.2.3.** Differences between population of analysis and eligible women not included in the analysis (n=8663)

<table>
<thead>
<tr>
<th>Subject characteristics</th>
<th>Included (n=6567)</th>
<th>Excluded (n=2096)</th>
<th>P-value$^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>29.8 ± 5.2</td>
<td>29.3 ± 5.5</td>
<td>0.002</td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
<td>1 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Western</td>
<td>3716 (58.9)</td>
<td>1031 (54.6)</td>
<td></td>
</tr>
<tr>
<td>Non western</td>
<td>2598 (41.1)</td>
<td>858 (45.4)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>253 (3.9)</td>
<td>276 (9.9)</td>
<td></td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low and midlow</td>
<td>1571 (25.8)</td>
<td>557 (30.9)</td>
<td></td>
</tr>
<tr>
<td>Midhigh</td>
<td>3090 (50.7)</td>
<td>856 (47.4)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>1436 (23.6)</td>
<td>392 (21.7)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>470 (7.2)</td>
<td>291 (13.9)</td>
<td></td>
</tr>
<tr>
<td>Household income (Euro/month)</td>
<td></td>
<td></td>
<td>0.15</td>
</tr>
<tr>
<td>&lt; 2,200</td>
<td>2365 (45.1)</td>
<td>607 (47.3)</td>
<td></td>
</tr>
<tr>
<td>≥ 2,200</td>
<td>2880 (54.9)</td>
<td>675 (52.7)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>1322 (20.1)</td>
<td>814 (38.8)</td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td>0.005</td>
</tr>
<tr>
<td>0</td>
<td>3685 (56.6)</td>
<td>1079 (53.0)</td>
<td></td>
</tr>
<tr>
<td>≥1</td>
<td>2831 (43.4)</td>
<td>957 (47.0)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>51 (0.8)</td>
<td>60 (2.9)</td>
<td></td>
</tr>
<tr>
<td>Pre-pregnancy BMI (kg/m$^2$)</td>
<td></td>
<td></td>
<td>0.42</td>
</tr>
<tr>
<td></td>
<td>23.6 ± 4.3</td>
<td>23.7 ± 4.5</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>1172 (17.8)</td>
<td>504 (24.1)</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Never during pregnancy</td>
<td>2783 (48.2)</td>
<td>904 (52.8)</td>
<td></td>
</tr>
<tr>
<td>Until pregnancy was known</td>
<td>798 (13.8)</td>
<td>241 (14.1)</td>
<td></td>
</tr>
<tr>
<td>Continued throughout pregnancy</td>
<td>2191 (38.0)</td>
<td>566 (33.1)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>795 (12.1)</td>
<td>385 (18.4)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td>0.93</td>
</tr>
<tr>
<td>Never during pregnancy</td>
<td>4250 (72.6)</td>
<td>1259 (72.8)</td>
<td></td>
</tr>
<tr>
<td>Until pregnancy was known</td>
<td>517 (8.8)</td>
<td>148 (8.6)</td>
<td></td>
</tr>
<tr>
<td>Continued throughout pregnancy</td>
<td>1085 (18.5)</td>
<td>323 (18.7)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>715 (10.9)</td>
<td>366 (17.5)</td>
<td></td>
</tr>
<tr>
<td>Folic acid supplementation</td>
<td></td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>Started periconceptional</td>
<td>2011 (40.5)</td>
<td>552 (37.8)</td>
<td></td>
</tr>
<tr>
<td>Started first 10 weeks</td>
<td>1566 (31.5)</td>
<td>443 (30.3)</td>
<td></td>
</tr>
<tr>
<td>No supplementation</td>
<td>1391 (28.0)</td>
<td>467 (31.9)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>1599 (24.3)</td>
<td>634 (30.2)</td>
<td></td>
</tr>
<tr>
<td>Energy intake (kcal/day)</td>
<td>2041 ± 568</td>
<td>2028 ± 572</td>
<td>0.48</td>
</tr>
<tr>
<td>Missing</td>
<td>1582 (24.1)</td>
<td>759 (36.2)</td>
<td></td>
</tr>
<tr>
<td>DHD-index (maximum score: 40)</td>
<td>22.4 ± 5.7</td>
<td>22.1 ± 6.0</td>
<td>0.13</td>
</tr>
</tbody>
</table>

$^1$ Values represent n (%), mean ± SD, median (interquartile range).
$^2$ Differences between continuous variables tested using independent student t-test and between categorical variables were tested using Chi-square statistics. **Abbreviations:** BMI: body mass index; DHD-index: Dutch Healthy Diet-index; GWG: gestational weight gain.
**Supplementary Table 3.2.4.** Association of plasma fatty acid patterns with mid-pregnancy adequacy of gestational weight gain (n=6567)¹

<table>
<thead>
<tr>
<th>Mid-pregnancy adequacy of GWG</th>
<th>Inadequate GWG (n=1490)</th>
<th>Adequate GWG (n=1405)</th>
<th>Excessive GWG (n=3672)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma fatty acid patterns</td>
<td>Crude¹</td>
<td>Multivariable²</td>
<td>Crude¹</td>
</tr>
<tr>
<td>'High n-6 PUFA' (per SD)</td>
<td>0.80 (0.74, 0.86)*</td>
<td>0.78 (0.72, 0.85)*</td>
<td>1.00</td>
</tr>
<tr>
<td>'MUFA and SFA' (per SD)</td>
<td>0.99 (0.91, 1.06)</td>
<td>1.01 (0.93, 1.09)</td>
<td>1.00</td>
</tr>
<tr>
<td>'High n-3 PUFA' (per SD)</td>
<td>0.97 (0.90, 1.04)</td>
<td>1.03 (0.95, 1.11)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Results from multinomial logistic regression analyses. Odds ratios reflect difference in odds to have an inadequate or excess GWG as compared with adequate mid-pregnancy GWG. ¹ Adjusted for gestational age at measurements and other fatty acid patterns. ²Crude model additionally adjusted for maternal age, ethnicity, educational level, household income, pre-pregnancy BMI, parity, alcohol consumption during pregnancy, maternal smoking during pregnancy, folic acid supplementation and fetal sex. * Statistical significant result (P-value <0.05). **Abbreviations:** CI: confidence interval, GWG: gestational weight gain, MUFA: mono-unsaturated fatty acids, OR: odds ratio, PUFA: poly-unsaturated fatty acids, SD: standard deviation, SFA: saturated fatty acids

**Supplementary Table 3.2.5.** Association of plasma fatty patterns with mid-pregnancy gestational weight gain, stratified by pre-pregnancy BMI and ethnicity (n=6567)¹

<table>
<thead>
<tr>
<th>Gestational weight gain (g/week) between 20-30 weeks of gestation</th>
<th>Western (n=2986)</th>
<th>Non-Western (n=1810)</th>
<th>Western (n=876)</th>
<th>Non-Western (n=895)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt; 25 kg/m²</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma fatty acid patterns</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
</tr>
<tr>
<td>'High n-6 PUFA' (per SD)</td>
<td>28 (18, 38)*</td>
<td>40 (26, 53)*</td>
<td>60 (36, 83)*</td>
<td>75 (52, 98)*</td>
</tr>
<tr>
<td>'MUFA and SFA' (per SD)</td>
<td>-3 (-13, 8)</td>
<td>6 (-7, 20)</td>
<td>-16 (-40, 8)</td>
<td>-4 (-25, 16)</td>
</tr>
<tr>
<td>'High n-3 PUFA' (per SD)</td>
<td>-3 (-13, 8)</td>
<td>-12 (-25, 1)</td>
<td>-6 (-29, 17)</td>
<td>-23 (-43, -2)</td>
</tr>
</tbody>
</table>

Results from multivariable linear regression analyses. Beta-coefficients reflect the change in gestational weight gain (g/week) per standard deviation increase in plasma fatty acid pattern. ¹ Adjusted for gestational age at both measurements, other fatty acid patterns, maternal age, educational level, household income, pre-pregnancy BMI, parity, alcohol consumption during pregnancy, folic acid supplementation and fetal sex. * Statistical significant result (P-value <0.05). **Abbreviations:** BMI: body mass index, CI: confidence interval, MUFA: mono-unsaturated fatty acids, PUFA: poly-unsaturated fatty acids, SD: standard deviation, SFA: saturated fatty acids

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**Supplementary Table 3.2.6.** Association of plasma fatty patterns with pregnancy-induced hypertension, stratified by ethnicity (n=6224)

<table>
<thead>
<tr>
<th>Plasma fatty acid patterns</th>
<th>Pregnancy-induced hypertension (cases n=6224)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Western (cases n=167)</td>
</tr>
<tr>
<td>'High n-6 PUFA' (per SD)</td>
<td>1.09 (0.92, 1.31)</td>
</tr>
<tr>
<td>'MUFA and SFA' (per SD)</td>
<td>1.01 (0.85, 1.20)</td>
</tr>
<tr>
<td>'High n-3 PUFA' (per SD)</td>
<td>0.91 (0.76, 1.10)</td>
</tr>
</tbody>
</table>

Results from multivariable logistic regression. Odds ratios reflect the odds of having pregnancy-induced hypertension per SD higher score on that fatty acid pattern. Adjusted for gestational age at both measurements, maternal age, educational level, household income, prepregnancy BMI, parity, alcohol consumption during pregnancy, smoking during pregnancy, folic acid supplementation and fetal sex. *Statistical significant result (P-value <0.05).

**Abbreviations:** CI: confidence interval, MUFA: mono-unsaturated fatty acids, OR: odds ratio, PUFA: poly-unsaturated fatty acids, SD: standard deviation, SFA: saturated fatty acids

---

**Supplementary Table 3.2.7.** Association of plasma fatty acid patterns with mid-pregnancy gestational weight gain, when taking into account early-pregnancy gestational weight gain (n=5131)

<table>
<thead>
<tr>
<th>Plasma fatty acid patterns</th>
<th>GWG (g/week) between 20 – 30 weeks of gestation (n = 5131)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted¹</td>
</tr>
<tr>
<td>'High n-6 PUFA' (per SD)</td>
<td>40 (33, 48)*</td>
</tr>
<tr>
<td>'MUFA and SFA' (per SD)</td>
<td>0 (-8, 8)</td>
</tr>
<tr>
<td>'High n-3 PUFA' (per SD)</td>
<td>-10 (-18, -2)*</td>
</tr>
</tbody>
</table>

Results from multivariable linear regression analyses. Beta-coefficient reflects the change in gestational weight gain (g/week) per standard deviation increase in plasma fatty acid pattern. Adjusted for gestational age at measurements, other fatty acid patterns, maternal age, ethnicity, educational level, household income, prepregnancy BMI, parity, alcohol consumption during pregnancy, maternal smoking during pregnancy, folic acid supplementation, and fetal sex. *Statistical significant result (P-value <0.05).

**Abbreviations:** CI: confidence interval, MUFA: mono-unsaturated fatty acids, PUFA: poly-unsaturated fatty acids, SD: standard deviation, SFA: saturated fatty acids
Supplementary Table 3.2.8. Association of plasma fatty acid patterns with mid-pregnancy gestational weight gain in women with available fetal ultrasound measurements (n=6380)

<table>
<thead>
<tr>
<th>Plasma fatty acid patterns</th>
<th>GWG (g/week) between 20 – 30 weeks of gestation (n = 6380)</th>
<th>Crude (^1)</th>
<th>Multivariable (^2)</th>
<th>Model (^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>'High n-6 PUFA' (per SD)</td>
<td></td>
<td>42 (35, 49)*</td>
<td>42 (35, 49)*</td>
<td>41 (35, 48)*</td>
</tr>
<tr>
<td>'MUFA and SFA' (per SD)</td>
<td></td>
<td>-1 (-8, 6)</td>
<td>-2 (-9, 5)</td>
<td>-3 (-10, 4)</td>
</tr>
<tr>
<td>'High n-3 PUFA' (per SD)</td>
<td></td>
<td>-3 (-10, 4)</td>
<td>-3 (-16, -2)*</td>
<td>-9 (-16, -1)*</td>
</tr>
</tbody>
</table>

Results from multivariable linear regression analyses. Beta-coefficient reflects the change in gestational weight gain (g/week) per standard deviation increase in plasma fatty acid pattern. \(^1\) Adjusted for gestational age at measurements and other fatty acid patterns. \(^2\) Crude model additionally adjusted for maternal age, ethnicity, educational level, household income, pre-pregnancy BMI, parity, alcohol consumption during pregnancy, maternal smoking during pregnancy, folic acid supplementation, and foetal sex. \(^3\) Multivariable model, additionally adjusted for change in estimated fetal weight. \(^*\) Statistical significant result (P-value <0.05). **Abbreviations:** CI: confidence interval, MUFA: mono-unsaturated fatty acids, PUFA: poly-unsaturated fatty acids, SD: standard deviation, SFA: saturated fatty acids

Supplementary Table 3.2.9. Association of plasma fatty acid patterns with gestational weight gain between 20 and 39 weeks of gestation in women with available information on birthweight and placental weight (n=2478)

<table>
<thead>
<tr>
<th>Plasma fatty acid patterns</th>
<th>GWG (g/week) between 20 – 39 weeks of gestation (n = 2478)</th>
<th>Crude (^1)</th>
<th>Multivariable (^2)</th>
<th>Model (^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>'High n-6 PUFA' (per SD)</td>
<td></td>
<td>24 (-9, 57)</td>
<td>28 (-7, 62)</td>
<td>28 (-7, 62)</td>
</tr>
<tr>
<td>'MUFA and SFA' (per SD)</td>
<td></td>
<td>-15 (-49, 20)</td>
<td>-17 (-53, 18)</td>
<td>-16 (-52, 19)</td>
</tr>
<tr>
<td>'High n-3 PUFA' (per SD)</td>
<td></td>
<td>11 (-23, 45)</td>
<td>-4 (-40, 31)</td>
<td>-5 (-40, 31)</td>
</tr>
</tbody>
</table>

Results from multivariable linear regression analyses. Beta-coefficient reflects the change in gestational weight gain (g/week) per standard deviation increase in plasma fatty acid pattern. \(^1\) Adjusted for gestational age at measurements and other fatty acid patterns. \(^2\) Crude model additionally adjusted for maternal age, ethnicity, educational level, household income, pre-pregnancy BMI, parity, alcohol consumption during pregnancy, maternal smoking during pregnancy, folic acid supplementation, and foetal sex. \(^3\) Multivariable model additionally adjusted for birthweight and placental weight. All results were non-significant. **Abbreviations:** CI: confidence interval, MUFA: mono-unsaturated fatty acids, PUFA: poly-unsaturated fatty acids, SD: standard deviation, SFA: saturated fatty acids
Chapter 3.3

Maternal vitamin B12 in pregnancy and risk of preterm birth and low birth weight: A systematic review and individual participant data meta-analysis


Submitted for publication
**Supplementary Figure 3.3.1.** Forest plot presenting the association between B12-deficiency and the risk of low birth weight (left panel) and preterm birth (right panel)

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Low birth weight RR (95% CI)</th>
<th>Preterm birth RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baker</td>
<td>290</td>
<td>0.50 (0.19, 1.30)</td>
<td>1.74 (0.77, 3.91)</td>
</tr>
<tr>
<td>Bergen</td>
<td>5,577</td>
<td>1.10 (0.87, 1.40)</td>
<td>1.01 (0.79, 1.29)</td>
</tr>
<tr>
<td>Bhate</td>
<td>194</td>
<td>1.14 (0.67, 1.93)</td>
<td>0.56 (0.20, 1.54)</td>
</tr>
<tr>
<td>Chen</td>
<td>972</td>
<td>1.68 (0.98, 2.86)</td>
<td>1.69 (1.02, 2.79)</td>
</tr>
<tr>
<td>Dwarkanath</td>
<td>344</td>
<td>1.20 (0.83, 1.74)</td>
<td>0.99 (0.54, 1.81)</td>
</tr>
<tr>
<td>Kaymaz</td>
<td>103</td>
<td>5.05 (0.77, 33.01)</td>
<td>0.95 (0.25, 3.55)</td>
</tr>
<tr>
<td>Krishnaveni</td>
<td>654</td>
<td>1.22 (0.90, 1.67)</td>
<td>1.42 (0.89, 2.26)</td>
</tr>
<tr>
<td>Sukumar</td>
<td>196</td>
<td>1.80 (0.51, 6.34)</td>
<td>5.60 (0.71, 43.87)</td>
</tr>
<tr>
<td>Yajnik</td>
<td>700</td>
<td>1.07 (0.86, 1.34)</td>
<td>1.31 (0.87, 1.97)</td>
</tr>
<tr>
<td>Overall</td>
<td>9,030</td>
<td>1.15 (1.01, 1.31)</td>
<td>1.21 (0.99, 1.49)</td>
</tr>
</tbody>
</table>

Test for heterogeneity: $F = 5\%$  
$F = 20\%$

Meta-analysis of studies of the association between vitamin B12-deficiency and the risk of low birth weight (left panel) and preterm birth (right panel) after adjustment for maternal age, parity and body mass index or weight. Effect estimate expressed as risk ratio of the outcome comparing B12 deficient to non-deficient. CI, confidence interval; n, number pregnancies; RR, risk ratio.
Supplementary Figure 3.3.2. Funnel plot of studies evaluating the association between B12 and birth weight

Funnel plot of studies evaluating the association between vitamin B12 and birth weight after adjustment for maternal age, parity and body mass index or weight. Individual studies are represented by solid dots, and the pseudo-95% confidence interval by broken lines.
**Supplementary Figure 3.3.3.** Forest plot presenting the association between B12 and birth weight SD score

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Mean difference of birth weight in SD-scores (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baker</td>
<td>286</td>
<td>-0.11 (-0.22, 0.01)</td>
</tr>
<tr>
<td>Bergen</td>
<td>5,508</td>
<td>-0.01 (-0.04, 0.02)</td>
</tr>
<tr>
<td>Chen</td>
<td>965</td>
<td>-0.04 (-0.10, 0.03)</td>
</tr>
<tr>
<td>Dayaldasani</td>
<td>178</td>
<td>-0.01 (-0.14, 0.13)</td>
</tr>
<tr>
<td>Dwarkanath</td>
<td>340</td>
<td>0.12 (0.02, 0.21)</td>
</tr>
<tr>
<td>Krishnaveni</td>
<td>640</td>
<td>0.07 (0.00, 0.13)</td>
</tr>
<tr>
<td>Sukumar</td>
<td>195</td>
<td>0.07 (-0.05, 0.18)</td>
</tr>
<tr>
<td>Overall</td>
<td>8,112</td>
<td>0.01 (-0.03, 0.06)</td>
</tr>
</tbody>
</table>

Test for heterogeneity: $I^2 = 62\%$

Meta-analysis of studies of the association between vitamin B12 and birth weight standard deviation scores (i.e. accounting for length of gestation and sex) after adjustment for maternal age, parity and body mass index or weight. Effect estimate expressed as change in birth weight standard deviation score per one standard deviation increase of vitamin B12. CI, confidence interval; n, number pregnancies.
**Supplementary Figure 3.3.4.** Forest plot presenting the association between B12-deficiency and the risk of small-for-gestational-age birth

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baker</td>
<td>286</td>
<td>0.82 (0.40, 1.70)</td>
</tr>
<tr>
<td>Bergen</td>
<td>5,508</td>
<td>0.97 (0.80, 1.18)</td>
</tr>
<tr>
<td>Chen</td>
<td>965</td>
<td>1.03 (0.57, 1.86)</td>
</tr>
<tr>
<td>Dwarkanath</td>
<td>340</td>
<td>1.32 (0.95, 1.84)</td>
</tr>
<tr>
<td>Krishnaveni</td>
<td>640</td>
<td>1.07 (0.85, 1.35)</td>
</tr>
<tr>
<td>Sukumar</td>
<td>195</td>
<td>1.12 (0.42, 2.94)</td>
</tr>
<tr>
<td>Overall</td>
<td>7,934</td>
<td>1.05 (0.92, 1.19)</td>
</tr>
</tbody>
</table>

Test for heterogeneity: $I^2 = 0\%$

Meta-analysis of studies of the association between vitamin B12-deficiency and the risk of small-for-gestational-age birth after adjustment for maternal age, parity and body mass index or weight. Effect estimate expressed as risk ratio of small-for-gestational-age birth comparing B12-deficient to non-deficient. CI, confidence interval; n, number pregnancies; RR, risk ratio.
### Supplementary Table 3.3.1 Study characteristics of eligible studies not included in the meta-analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Country</th>
<th>Study years</th>
<th>B12 analysis method</th>
<th>Week of B12 measurement, range, median</th>
<th>Main objectives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karakantza 2008⁵⁶</td>
<td>392</td>
<td>Greece</td>
<td>2004-2006</td>
<td>NA</td>
<td>6-8</td>
<td>Studied three thrombophilic mutations in relation to pregnancy outcomes (including IUGR).</td>
</tr>
<tr>
<td>Lee 2014⁵⁸</td>
<td>T2: 83</td>
<td>USA</td>
<td>2006-2012</td>
<td>RIA</td>
<td>T2: 24.4 ± 2.2⁸ T3: 29.7 ± 1.8⁸</td>
<td>Studied changes in iron status in pregnant adolescents, and iron status in relation to hepcidin and inflammatory markers.</td>
</tr>
</tbody>
</table>

Studies are referred to according to their citation number in the text. **Abbreviations:** ECL, electroluminescence; IUGR, intrauterine growth restriction; n, number of pregnancies; NA, not available; RIA, radioimmunoassay; T2, 2nd trimester; T3, 3rd trimester. * Eligible studies were not included in the systematic review or the meta-analyses when individual participant data or results from requested reanalyses were not provided, appropriate data and results were not available in the original report, and when no association between B12 and birth weight or length of gestation was presented; a. mean ± SD.
## Supplementary Table 3.3.2 Risk of bias of studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baker 200918</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Bergen 201219</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Bhate 201232</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Chen 201520</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Dayaldasani 201433</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Dwarkanath 201321</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Furness 201332</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Halicioglu 201233</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Hay 201024</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Hogeveen 201024</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Kaymaz 201135</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Krishnaveni 201325</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Mamabolo 200626</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Relton 200527</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>?</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Sukumar 201128</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Takimoto 200729</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Wu 201330</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>?</td>
<td>1</td>
<td>1</td>
<td>?</td>
<td>3</td>
</tr>
<tr>
<td>Yajnik 200831</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
</tbody>
</table>

Each item was scored “1” (i.e. “yes”), “0” (i.e. “no”) or “?” (i.e. “uncertain”), where only the answer “1” scored 1 point. The following questions were evaluated: 1: Was B12 ascertained irrespective of the risk of low birth weight birth or preterm birth, and otherwise not prone to selection bias?; 2: Was the study controlled for maternal body mass index or weight either by matching or by statistical methods?; 3: Was the study controlled for previous low birth weight birth or preterm birth, or maternal age, parity, socioeconomic status, smoking habits, ethnicity, vegetarian status or B12 supplement use (at least two of these) either by matching or by statistical methods? In addition, because of potential over-adjustment, if a study adjusted for levels of folate, homocysteine or methylmalonic acid, they earned no point on this item (even if they had adjusted for two or more of the mentioned confounders); 4: Was the exposed cohort truly or somewhat representative of the average pregnant population in the community?; 5: Did the women with B12-deficiency receive the same follow-up and interventions as the non-deficient women?; 6: Was the outcome assessed by independent or blind assessment, or by secure records or record linkage?; 7: Was follow-up >80% or was any description provided for those lost to follow-up? Studies are referred to according to their citation number in the text.
### Supplementary Table 3.3.3 Pooled results from subgroup and sensitivity analyses of B12 SD score on birth weight

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Number of studies</th>
<th>Number of pregnancies</th>
<th>Birth weight (g) per 1 SD increase in B12 (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alternative models</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude</td>
<td>12</td>
<td>38,21,24,25,28,31-35</td>
<td>9,819</td>
</tr>
<tr>
<td>Adjusting for BMI or weight</td>
<td>9</td>
<td>18,21,25,28,33-35</td>
<td>8,505</td>
</tr>
<tr>
<td>Adjusting for maternal age, parity, and BMI or weight (&quot;main model&quot;)</td>
<td>12</td>
<td>18,21,25,28,29,31-35</td>
<td>9,406</td>
</tr>
<tr>
<td>Adjusting for maternal age, parity, BMI or weight, and smoking</td>
<td>10</td>
<td>18,20,25,28,31-35</td>
<td>8,420</td>
</tr>
<tr>
<td>Adjusting for maternal age, parity, BMI or weight, smoking and education (&quot;extended model&quot;)</td>
<td>4</td>
<td>18,19,25,34</td>
<td>5,948</td>
</tr>
<tr>
<td>Adjusted main model among those with data on smoking</td>
<td>10</td>
<td>18,20,25,28,31-35</td>
<td>8,420</td>
</tr>
<tr>
<td>Adjusted main model among those with data on the extended model</td>
<td>4</td>
<td>18,19,25,34</td>
<td>5,948</td>
</tr>
<tr>
<td>Adjusting for BMI among those with weight</td>
<td>4</td>
<td>18,20,25,33</td>
<td>7,416</td>
</tr>
<tr>
<td>Adjusting for weight among those with BMI</td>
<td>4</td>
<td>18,20,25,33</td>
<td>7,416</td>
</tr>
<tr>
<td><strong>Fixed effects model</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimester of B12 measurement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st trimester</td>
<td>4</td>
<td>18,21,25,28,33</td>
<td>1,461</td>
</tr>
<tr>
<td>2nd trimester</td>
<td>8</td>
<td>19,21,25,28,33-35</td>
<td>6,217</td>
</tr>
<tr>
<td>1st and 2nd trimester</td>
<td>10</td>
<td>19,21,25,28,31,33-35</td>
<td>8,325</td>
</tr>
<tr>
<td>3rd trimester</td>
<td>6</td>
<td>18,20,21,25,28,29</td>
<td>1,140</td>
</tr>
<tr>
<td>Measurement technique</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radioimmunoassay</td>
<td>2</td>
<td>18,28</td>
<td>459</td>
</tr>
<tr>
<td>Electroluminescence assay</td>
<td>7</td>
<td>19,21,28,29,33,35</td>
<td>7,256</td>
</tr>
<tr>
<td>Microbiologic assay</td>
<td>4</td>
<td>19,31,32,34</td>
<td>1,691</td>
</tr>
<tr>
<td>Country income category</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High income</td>
<td>7</td>
<td>18,20,28,29,33,34</td>
<td>7,411</td>
</tr>
<tr>
<td>Middle or low income</td>
<td>5</td>
<td>21,25,31,32,35</td>
<td>1,995</td>
</tr>
<tr>
<td>Maternal BMI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI &lt;25 kg/m²</td>
<td>6</td>
<td>19,20,25,28,33,35</td>
<td>4,728</td>
</tr>
<tr>
<td>BMI ≥25 kg/m²</td>
<td>6</td>
<td>19,20,25,28,33,35</td>
<td>2,945</td>
</tr>
</tbody>
</table>

Pooled results of the mean difference (95% CI) in birth weight (g) per 1 SD increase in maternal B12. All analyses are linear regression analyses with random effects, and adjusted for the main model (i.e. maternal age, BMI (weight if missing BMI), and parity (nulliparous yes/no)) unless otherwise specified. Studies included in the analyses are referred to according to their citation number in the text. BMI, body mass index; CI, confidence interval; SD, standard deviation. a BMI and weight (if missing BMI) as continuous covariates; b continuous covariate; c nulliparous (yes/no); d smoking during pregnancy (yes/no); e completed high school (yes/no); f Sukumar 2011 measured n=182 by radioimmunoassay and n=27 by electroluminescence assay.
### Supplementary Table 3.3.4. B12-deficiency and B12 tertiles in relation to birth weight

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Number of studies</th>
<th>Number of pregnancies</th>
<th>Number of exposed</th>
<th>Mean difference in birth weight (g) in exposed versus non-exposed (95% CI)</th>
<th>I²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B12-deficiency</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPD, crude</td>
<td>918-21,24,25,28,34,35</td>
<td>8,735</td>
<td>3,006</td>
<td>9.3 (-14.9, 33.5)</td>
<td>0</td>
</tr>
<tr>
<td>IPD, main model&lt;sup&gt;a&lt;/sup&gt;</td>
<td>818-21,25,28,34,35</td>
<td>8,279</td>
<td>2,846</td>
<td>-14.5 (-39.1, 10.2)</td>
<td>0</td>
</tr>
<tr>
<td>Aggregate, crude&lt;sup&gt;b&lt;/sup&gt;</td>
<td>421,30-32</td>
<td>1,323</td>
<td>695</td>
<td>63.8 (-32.6, 159.9)</td>
<td>69</td>
</tr>
<tr>
<td>Aggregate, main model&lt;sup&gt;a&lt;/sup&gt;</td>
<td>223,32</td>
<td>894</td>
<td>542</td>
<td>-1.36 (-53.5, 50.8)</td>
<td>0</td>
</tr>
<tr>
<td>IPD + aggregate, crude</td>
<td>1318-21,23,25,28,30-32,34,35</td>
<td>10,058</td>
<td>3,701</td>
<td>23.3 (-6.7, 53.4)</td>
<td>24</td>
</tr>
<tr>
<td>IPD + aggregate, main model&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1018-21,25,28,31,32,34,35</td>
<td>9,173</td>
<td>3,388</td>
<td>-14.0 (-36.3, 8.3)</td>
<td>0</td>
</tr>
<tr>
<td><strong>B12 tertiles&lt;sup&gt;c&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPD, crude</td>
<td>1018-21,24,25,28,33-35</td>
<td>5,942</td>
<td>3,179</td>
<td>18.9 (-15.8, 53.8)</td>
<td>8</td>
</tr>
<tr>
<td>IPD, main model&lt;sup&gt;a&lt;/sup&gt;</td>
<td>918-21,25,28,33-35</td>
<td>5,633</td>
<td>2,997</td>
<td>-16.6 (-54.5, 21.2)</td>
<td>11</td>
</tr>
</tbody>
</table>

Pooled results of the mean difference in birth weight (g) in exposed versus non-exposed pregnancies. All analyses are random effects models and crude, unless otherwise specified. Studies included in the analyses are referred to according to their citation number in the text. CI, confidence interval; IPD, individual participant data. <sup>a</sup> adjusted for maternal age, body mass index (weight if missing body mass index), and parity (nulliparous yes/no); <sup>b</sup> B12-deficiency defined as <148 pmol/L except for Halicioglu 2012<sup>21</sup> (<118 pmol/L); <sup>c</sup> lowest tertile (i.e. exposed) versus highest tertile.
### Supplementary Table 3.3.5 Pooled results from subgroup and sensitivity analyses of B12 SD score and the risk of preterm birth

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Number of studies</th>
<th>Number of pregnancies</th>
<th>Number of preterm births</th>
<th>Risk ratio of preterm birth per 1 SD increase in B12 (95% CI)</th>
<th>$i^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alternative models</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude</td>
<td>$^{18-21,24,25,28,31-33,35}$</td>
<td>11</td>
<td>9,747</td>
<td>643</td>
<td>0.90 (0.81, 1.00)</td>
</tr>
<tr>
<td>Adjusting for BMI or weight$^a$</td>
<td>$^{18-21,25,28,33,35}$</td>
<td>8</td>
<td>8,362</td>
<td>510</td>
<td>0.89 (0.81, 0.98)</td>
</tr>
<tr>
<td>Adjusting for maternal age,$^b$ parity,$^c$ and BMI or weight$^a$ (&quot;main model&quot;)</td>
<td>$^{18-21,25,28,31-33,35}$</td>
<td>10</td>
<td>9,291</td>
<td>615</td>
<td>0.89 (0.82, 0.97)</td>
</tr>
<tr>
<td>Adjusting for maternal age,$^b$ parity,$^c$ BMI or weight,$^a$ and smoking$^d$</td>
<td>$^{18-20,25,28,31-35}$</td>
<td>9</td>
<td>8,365</td>
<td>531</td>
<td>0.90 (0.82, 0.99)</td>
</tr>
<tr>
<td>Adjusting for maternal age,$^b$ parity,$^c$ BMI or weight,$^a$ smoking$^d$ and education$^e$ (&quot;extended model&quot;)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted main model among those with data on smoking</td>
<td>$^{18-20,25,28,31-33,35}$</td>
<td>9</td>
<td>8,365</td>
<td>531</td>
<td>0.89 (0.81, 0.98)</td>
</tr>
<tr>
<td>Adjusted main model among those with data on the extended model</td>
<td>$^{18-21,25,28,33}$</td>
<td>3</td>
<td>5,813</td>
<td>304</td>
<td>0.92 (0.82, 1.03)</td>
</tr>
<tr>
<td>Adjusting for BMI$^b$ among those with data on weight</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusting for weight$^b$ among those with data on BMI</td>
<td>$^{19-20,25,33}$</td>
<td>4</td>
<td>7,416</td>
<td>424</td>
<td>0.91 (0.82, 1.01)</td>
</tr>
<tr>
<td>Fixed effects model</td>
<td>$^{18-20,25,28,31-33,35}$</td>
<td>10</td>
<td>9,291</td>
<td>615</td>
<td>0.89 (0.82, 0.97)</td>
</tr>
<tr>
<td>Non-robust error variance</td>
<td>$^{18-21,25,28,31-33,35}$</td>
<td>10</td>
<td>9,291</td>
<td>615</td>
<td>0.90 (0.82, 0.99)</td>
</tr>
<tr>
<td>Logistic regression</td>
<td>$^{18-21,25,28,31-33,35}$</td>
<td>10</td>
<td>9,285</td>
<td>615</td>
<td>0.88 (0.80, 0.97$^f$)</td>
</tr>
<tr>
<td><strong>Trimester of B12 measurement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1$^{st}$ trimester</td>
<td>$^{18,21,33}$</td>
<td>3</td>
<td>1,453</td>
<td>107</td>
<td>1.01 (0.84, 1.20)</td>
</tr>
<tr>
<td>2$^{nd}$ trimester</td>
<td>$^{19-21,25,28,35}$</td>
<td>6</td>
<td>6,061</td>
<td>344</td>
<td>0.85 (0.67, 1.07)</td>
</tr>
<tr>
<td>1$^{st}$ and 2$^{nd}$ trimesters</td>
<td>$^{15-21,25,28,31,33,35}$</td>
<td>3</td>
<td>8,190</td>
<td>522</td>
<td>0.86 (0.71, 1.05)</td>
</tr>
<tr>
<td>3$^{rd}$ trimester</td>
<td>$^{18,20,21,25,28}$</td>
<td>5</td>
<td>1,058</td>
<td>86</td>
<td>0.86 (0.70, 1.06)</td>
</tr>
<tr>
<td><strong>Measurement technique</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radioimmunoassay</td>
<td>$^{18,28}$</td>
<td>2</td>
<td>459</td>
<td>29</td>
<td>0.60 (0.33, 1.07)</td>
</tr>
<tr>
<td>Electroluminescence assay</td>
<td>$^{19-21,33,35}$</td>
<td>3</td>
<td>7,178</td>
<td>418</td>
<td>0.93 (0.83, 1.04)</td>
</tr>
<tr>
<td>Microbiologic assay</td>
<td>$^{25,31,32}$</td>
<td>3</td>
<td>1,627</td>
<td>168</td>
<td>0.86 (0.73, 1.02$^f$)</td>
</tr>
<tr>
<td><strong>Country income category</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High income</td>
<td>$^{18-20,28,33}$</td>
<td>5</td>
<td>7,217</td>
<td>391</td>
<td>0.87 (0.74, 1.02)</td>
</tr>
<tr>
<td>Middle or low income</td>
<td>$^{21,25,31,32,35}$</td>
<td>5</td>
<td>2,074</td>
<td>224</td>
<td>0.88 (0.76, 1.02)</td>
</tr>
<tr>
<td><strong>Maternal BMI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI &lt;25 kg/m$^2$</td>
<td>$^{19-20,25,28,33,35}$</td>
<td>6</td>
<td>4,728</td>
<td>241</td>
<td>0.90 (0.81, 1.01)</td>
</tr>
<tr>
<td>BMI ≥25 kg/m$^2$</td>
<td>$^{19-20,25,28,33}$</td>
<td>5</td>
<td>2,913</td>
<td>200</td>
<td>0.81 (0.63, 1.05)</td>
</tr>
</tbody>
</table>

Pooled results of the risk ratio (95% CI) of preterm birth per 1 SD increase in maternal B12. All analyses are Poisson regression analyses with random effects, robust error variance and adjusted for the main model (maternal age, BMI (weight if missing BMI), and parity (nulliparous yes/no)) unless otherwise specified. Studies included in the analyses are referred to according to their citation number in the text. BMI, body mass index; CI, confidence interval; SD, standard deviation. $^a$ BMI and weight (if missing BMI) as continuous covariates; $^b$ continuous covariate; $^c$ nulliparous (yes/no); $^d$ smoking during pregnancy (yes/no); $^e$ completed high school (yes/no); $^f$ odds ratio.
### Supplementary Table 3.3.6 Level of B12 in small-for-gestational-age and non-small-for-gestational-age pregnancies

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Number of studies</th>
<th>Number of pregnancies</th>
<th>Number of SGA births</th>
<th>Mean difference in B12 (pmol/L) in SGA versus non-SGA (95% CI)</th>
<th>$I^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPD</td>
<td>5</td>
<td>8,561</td>
<td>882</td>
<td>3.3 (-3.4, 9.9)</td>
<td>0</td>
</tr>
<tr>
<td>Aggregate</td>
<td>2</td>
<td>303</td>
<td>87</td>
<td>-11.7 (-47.4, 24.1)</td>
<td>49</td>
</tr>
<tr>
<td>IPD + aggregate</td>
<td>10</td>
<td>8,864</td>
<td>969</td>
<td>2.4 (-3.9, 8.7)</td>
<td>0</td>
</tr>
</tbody>
</table>

Pooled results of the mean difference in maternal B12 (pmol/L) in SGA versus non-SGA pregnancies. All analyses are random effects models and crude. Studies included in the analyses are referred to according to their citation number in the text. CI, confidence interval; IPD, individual participant data; SGA, small-for-gestational-age. $^*$ SGA defined as birth weight <10th centile after taking sex and length of gestation into account, with the following exceptions: In Furness 2013, $^{22}$ SGA was defined as “serial tapering of growth in abdominal circumference and of estimated fetal weight below the 10th centile of population-based growth charts”, and in Mamabolo 2006, $^{26}$ SGA was defined as birth weight in the 1st tertile (mean 2,940 g).
Chapter 4.1

Protein intake during pregnancy and offspring body composition at 6 years: The Generation R Study


* Contributed equally

In revision (European Journal of Nutrition)
**Supplementary Figure 4.1.1.** Flow chart of the study population: the Generation R Study, Rotterdam, the Netherlands

- Dutch women enrolled during pregnancy *n* = 4,101
  - *n* = 542 women excluded who did not receive FFQ, did not return FFQ or had implausible dietary data
  - Women with eligible FFQ data *n* = 3,559
    - *n* = 80 women excluded due to no live birth (*n* = 24), multiple pregnancy (*n* = 53) or loss to follow-up (*n* = 3)
    - Women with singleton live birth *n* = 3,479
      - *n* = 785 mother-child pairs excluded due to missing body composition data at the age of 6 years
  - Eligible mother-child pairs for current study *n* = 2,694

Participation of the children in follow-up measurements at the age of 6 years

- *n* = 2,694

Data available on:
- Anthropometrics: *n* = 2,694
- Body composition: *n* = 2,624
Supplementary Figure 4.1.2. Bland-Altman plot validation of protein intake comparing FFQ and 24-hour dietary recall method (n=71)
| **Supplementary Table 4.1.1.** Details of the multiple imputation process\(^a\) | \*
| --- | ---
| **Software used** | IBM SPSS statistics version 21 |
| **Imputation method and key settings** | Fully conditional specification (Markov chain Monte Carlo method); maximum iterations: 10 |
| **No. of imputed data sets created** | 10 |
| **Variables included in the imputation procedure as both predictor variable as a variable to be imputed** | Age mother at enrolment; Gravidity at enrolment; Parity at enrolment; Maternal educational level at enrolment; Pre-pregnancy maternal BMI; Maternal BMI at intake; Maternal alcohol consumption during pregnancy; Maternal smoking during pregnancy; Maternal folic acid use during pregnancy; Measured gestational weight gain; Gestational weight gain based on self-reported pre-pregnancy weight; Age partner at enrolment; BMI partner; Educational level partner at enrolment; Household income at enrolment; Gender child; Birth weight; Gestational age at birth; Standardized birth weight (Niklasson); Breastfeeding practice at the age of 2 months; Age of the children at follow-up; Height of the children at follow-up; Screen time of the children at the age of 6 years; Participation in sports of the children at the age of 6 years. |
| **Variables added as predictors (not used in the main analyses) of missing data to increase plausibility of missing at random assumption** | Maternal energy-adjusted protein intake during pregnancy; Maternal energy intake during pregnancy; Maternal serum folate level <18 weeks of gestation; Breastfeeding practice (ever versus never); Maternal educational level 6 years after enrolment; Household income 6 years after enrolment; Total energy intake of the children at the age of 14 months; Weight of the children at DXA measurement; Android/gynoid fat mass ratio of the children at follow-up (measured by DXA); Total fat percentage of the children at follow-up (measured by DXA); Fat-free mass index of the children at follow-up (measured by DXA); Fat mass index of the children at follow-up (measured by DXA); BMI-for-age of the children between 10-13 months; BMI-for-age of the children between 13-17 months; BMI-for-age of the children between 17-23 months; BMI-for-age of the children between 23-35 months; BMI-for-age of the children between 35-44 months; BMI-for-age of the children between 44-56 months; BMI of the children at follow-up; Overweight status of the children at follow-up. |
| **Treatment of not normally distributed variables** | Predictive mean matching |
| **Treatment of binary/categorical variables** | Logistic regression models |
| **Population** | For the multiple imputation we included those mothers with a Dutch ancestry, available dietary information, and those who visited the research center with their children at the age of 6 years (n=2,777) |

\(^a\) The missing values of the covariate ‘hypertensive complications during pregnancy’ were not imputed as a result of lacking predictive variables.

**Abbreviations:** BMI: body mass index, DXA: dual-energy X-ray absorptiometry.

**References table 4.1.1.**

### Supplementary Table 4.1.2. Maternal and children's characteristics presented per quartile of energy-adjusted maternal protein intake (n=2694)α

<table>
<thead>
<tr>
<th>Maternal and children's characteristics presented per quartile of energy-adjusted maternal protein intake (n=2694)α</th>
<th>Quartile 1</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
<th>Quartile 4</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude values of protein intake (g/day)β</td>
<td>65 (16,110)</td>
<td>74 (38,115)</td>
<td>81 (49,120)</td>
<td>95 (55,145)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Energy-adjusted values of protein intakeβ</td>
<td>-12 (-43,-8)</td>
<td>-4 (-8,0)</td>
<td>3 (-0,7)</td>
<td>13 (7,41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maternal Characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational age at enrolment (weeks)</td>
<td>13.4 (12.2-15.8)</td>
<td>13.5 (12.4-15.7)</td>
<td>13.4 (12.2-15.2)</td>
<td>13.2 (12.2-15.4)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>30.8 ±4.5</td>
<td>31.6 ± 4.3</td>
<td>32.0 ± 3.9</td>
<td>32.2 ± 4.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maternal education (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low and midlow (%)</td>
<td>21.3</td>
<td>10.5</td>
<td>8.4</td>
<td>7.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Midhigh (%)</td>
<td>55.2</td>
<td>55.5</td>
<td>51.6</td>
<td>49.9</td>
<td></td>
</tr>
<tr>
<td>High (%)</td>
<td>23.5</td>
<td>34.1</td>
<td>40.0</td>
<td>42.7</td>
<td></td>
</tr>
<tr>
<td>Missing (%)</td>
<td>1.5</td>
<td>2.1</td>
<td>1.0</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Nulliparity (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing (%)</td>
<td>63.1</td>
<td>59.7</td>
<td>63.1</td>
<td>61.6</td>
<td>0.53</td>
</tr>
<tr>
<td>Body mass index at enrolment (kg/m²)</td>
<td>23.4 (21.2-26.2)</td>
<td>23.3 (21.3-25.8)</td>
<td>23.4 (21.9-25.8)</td>
<td>23.7 (22.1-26.2)</td>
<td>0.15</td>
</tr>
<tr>
<td>Missing (%)</td>
<td>0.6</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Gestational weight gain (g/week)</td>
<td>498 ±208</td>
<td>509 ± 188</td>
<td>495 ± 193</td>
<td>509 ± 197</td>
<td>0.50</td>
</tr>
<tr>
<td>Smoking during pregnancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never (%)</td>
<td>71.5</td>
<td>75.8</td>
<td>79.2</td>
<td>77.2</td>
<td>0.004</td>
</tr>
<tr>
<td>Until pregnancy was known (%)</td>
<td>10.1</td>
<td>9.0</td>
<td>8.5</td>
<td>10.5</td>
<td></td>
</tr>
<tr>
<td>Continued (%)</td>
<td>18.4</td>
<td>15.3</td>
<td>12.3</td>
<td>12.4</td>
<td></td>
</tr>
<tr>
<td>Missing (%)</td>
<td>7.3</td>
<td>10.5</td>
<td>5.8</td>
<td>7.6</td>
<td></td>
</tr>
<tr>
<td>Alcohol during pregnancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never (%)</td>
<td>42.1</td>
<td>29.9</td>
<td>26.9</td>
<td>26.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Until pregnancy was known (%)</td>
<td>16.8</td>
<td>16.9</td>
<td>16.3</td>
<td>17.0</td>
<td></td>
</tr>
<tr>
<td>Continued (%)</td>
<td>41.1</td>
<td>53.2</td>
<td>56.7</td>
<td>56.2</td>
<td></td>
</tr>
<tr>
<td>Missing (%)</td>
<td>8.2</td>
<td>11.3</td>
<td>6.4</td>
<td>8.0</td>
<td></td>
</tr>
<tr>
<td>Alcohol consumption (g/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Folic acid supplementation</td>
<td>No (%)</td>
<td>11.7</td>
<td>10.4</td>
<td>7.6</td>
<td>7.0</td>
</tr>
<tr>
<td>Started &lt; 10 wk of gestation (%)</td>
<td>88.3</td>
<td>89.6</td>
<td>92.4</td>
<td>93.0</td>
<td></td>
</tr>
<tr>
<td>Missing (%)</td>
<td>18.9</td>
<td>20.3</td>
<td>16.3</td>
<td>15.3</td>
<td></td>
</tr>
<tr>
<td>Energy intake (kcal/day)</td>
<td>2178 ±560</td>
<td>2104 ± 507</td>
<td>2128 ± 472</td>
<td>2200 ± 462</td>
<td>0.001</td>
</tr>
<tr>
<td>Protein intake (g/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total protein</td>
<td>66 ±16</td>
<td>74 ± 15</td>
<td>82 ± 14</td>
<td>96 ± 16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Animal protein</td>
<td>37 ±11</td>
<td>44 ± 10</td>
<td>51 ± 9</td>
<td>63 ± 11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vegetable protein</td>
<td>30 ±9</td>
<td>31 ± 9</td>
<td>31 ± 8</td>
<td>32 ± 9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Protein intake (E%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total protein</td>
<td>12 ±1</td>
<td>14 ± 1</td>
<td>16 ± 1</td>
<td>18 ± 2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Animal protein</td>
<td>7 ±1</td>
<td>8 ± 1</td>
<td>10 ± 1</td>
<td>12 ± 2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vegetable protein</td>
<td>5 ±1</td>
<td>6 ± 1</td>
<td>6 ± 1</td>
<td>6 ± 1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pregnancy outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertensive complications (%)</td>
<td>8.3</td>
<td>6.0</td>
<td>6.4</td>
<td>8.4</td>
<td>0.18</td>
</tr>
<tr>
<td>Missing (%)</td>
<td>3.9</td>
<td>2.8</td>
<td>2.7</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>Gender, boy (%)</td>
<td>50.5</td>
<td>51.6</td>
<td>47.9</td>
<td>50.4</td>
<td>0.58</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>3473 ±536</td>
<td>3500 ± 537</td>
<td>3509 ± 553</td>
<td>3530 ±536</td>
<td>0.27</td>
</tr>
<tr>
<td>Gestational weight gain (g/week)</td>
<td>0.4</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Weight gain (g/week)</td>
<td>39.9 ±1.7</td>
<td>40.0 ± 1.8</td>
<td>40.0 ± 1.7</td>
<td>40.1 ±1.5</td>
<td>0.11</td>
</tr>
<tr>
<td>Preterm birth (%)</td>
<td>4.8</td>
<td>4.6</td>
<td>4.6</td>
<td>2.8</td>
<td>0.24</td>
</tr>
<tr>
<td>Breastfeeding at 2 months (%)</td>
<td>60.7</td>
<td>70.1</td>
<td>73.1</td>
<td>74.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dietary intake of the children aged 13 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy intake (kcal/day)</td>
<td>1326 ±365</td>
<td>1273 ± 335</td>
<td>1310 ± 340</td>
<td>1293 ± 326</td>
<td>0.15</td>
</tr>
<tr>
<td>Protein intake (g/day)</td>
<td>41 ± 12</td>
<td>40 ± 11</td>
<td>42 ± 11</td>
<td>43 ± 11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Protein intake (E%)</td>
<td>12 ± 2</td>
<td>13 ± 2</td>
<td>13 ± 2</td>
<td>14 ± 2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
### Supplementary Table 4.1.2. (continued) Maternal and children’s characteristics presented per quartile of energy-adjusted maternal protein intake (n=2694)\(^a\)

<table>
<thead>
<tr>
<th>Children's characteristics aged 6 years</th>
<th>Quartile 1</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
<th>Quartile 4</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=673</td>
<td>n=674</td>
<td>n=674</td>
<td>n=673</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>6.1 ±0.5</td>
<td>6.1 ± 0.4</td>
<td>6.1 ± 0.5</td>
<td>6.1 ± 0.4</td>
<td>0.39</td>
</tr>
<tr>
<td>Playing sports (%)</td>
<td>48.1</td>
<td>48.1</td>
<td>50.6</td>
<td>52.9</td>
<td>0.26</td>
</tr>
<tr>
<td>Missing (%)</td>
<td>6.7</td>
<td>8.2</td>
<td>5.3</td>
<td>5.1</td>
<td></td>
</tr>
<tr>
<td>≥ 2h/day screen time (%)</td>
<td>25.8</td>
<td>19.9</td>
<td>17.7</td>
<td>16.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Missing (%)</td>
<td>16.3</td>
<td>18.0</td>
<td>13.1</td>
<td>13.4</td>
<td></td>
</tr>
<tr>
<td>Height of the children (cm)</td>
<td>120 ±6</td>
<td>119 ± 6</td>
<td>119 ± 6</td>
<td>120 ± 6</td>
<td>0.41</td>
</tr>
<tr>
<td>Overweight/obese (%)</td>
<td>13.0</td>
<td>9.7</td>
<td>11.1</td>
<td>11.5</td>
<td>0.30</td>
</tr>
<tr>
<td>Missing (%)</td>
<td>0.3</td>
<td>0.1</td>
<td>0.0</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
<td>15.6 (14.9-16.6)</td>
<td>15.6 (14.9-16.6)</td>
<td>15.7 (15.0-16.6)</td>
<td>15.7 (15.0-16.6)</td>
<td>0.75</td>
</tr>
<tr>
<td>Fat mass index (kg/m(^2))</td>
<td>3.6 (3.2-4.3)</td>
<td>3.5 (3.0-4.3)</td>
<td>3.6 (3.2-4.3)</td>
<td>3.5 (3.1-4.1)</td>
<td>0.12</td>
</tr>
<tr>
<td>Missing (%)</td>
<td>2.8</td>
<td>2.7</td>
<td>1.9</td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>Fat-free mass index (kg/m(^2))</td>
<td>11.8 ± 0.8</td>
<td>11.9 ± 0.8</td>
<td>11.9 ± 0.8</td>
<td>12.0 ± 0.8</td>
<td>0.03</td>
</tr>
<tr>
<td>Missing (%)</td>
<td>2.8</td>
<td>2.7</td>
<td>1.9</td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>Total fat percentage (%)</td>
<td>23.7 (21.0-27.0)</td>
<td>23.2 (20.0-26.6)</td>
<td>23.5 (20.8-26.8)</td>
<td>23.1 (20.3-26.2)</td>
<td>0.02</td>
</tr>
<tr>
<td>Missing (%)</td>
<td>2.8</td>
<td>2.7</td>
<td>1.9</td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>Android/gynoid fat mass ratio</td>
<td>0.24 (0.21-0.27)</td>
<td>0.24 (0.20-0.27)</td>
<td>0.24 (0.21-0.27)</td>
<td>0.24 (0.21-0.27)</td>
<td>0.21</td>
</tr>
<tr>
<td>Missing (%)</td>
<td>2.8</td>
<td>2.7</td>
<td>1.9</td>
<td>3.0</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) The values represent for continuous measures mean ± SD or median (interquartile range), and for dichotomous values the percentage of participants per category are presented. The missing values are also presented in percentages. The p-values were calculated using Analysis of Variance (ANOVA). \(^b\) Results for protein intake are presented as median and total range. \(^c\) Weekly gestational weight gain (g/week) between enrolment around 13 weeks of pregnancy and early-third trimester (around 30 weeks). **Abbreviations:** CI: confidence interval, E%: energy percent.
**Supplementary Table 4.1.3.** Association of maternal protein intake during pregnancy with childhood body composition at the age of 6 years, in non-imputed data

<table>
<thead>
<tr>
<th>Childhood body mass index (SDS)</th>
<th>Fat-free mass index (SDS)</th>
<th>Fat mass index (SDS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Model 2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Model 1&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>n=2694</td>
<td>n=1611</td>
<td>n=2624</td>
</tr>
<tr>
<td><strong>Total protein intake&lt;sup&gt;c&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>-0.03 (-0.14, 0.07)</td>
<td>-0.00 (-0.14, 0.14)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>-0.00 (-0.11, 0.11)</td>
<td>0.07 (-0.07, 0.21)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>0.02 (-0.08, 0.13)</td>
<td>0.06 (-0.08, 0.21)</td>
</tr>
<tr>
<td><strong>p for trend</strong></td>
<td>0.56</td>
<td>0.25</td>
</tr>
<tr>
<td><strong>Animal protein intake&lt;sup&gt;c&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>0.03 (-0.07, 0.14)</td>
<td>0.07 (-0.07, 0.20)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>0.04 (-0.07, 0.14)</td>
<td>0.08 (-0.07, 0.22)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>0.07 (-0.04, 0.18)</td>
<td>0.15 (-0.00, 0.29)</td>
</tr>
<tr>
<td><strong>p for trend</strong></td>
<td>0.23</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Vegetable protein intake&lt;sup&gt;c&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>-0.07 (-0.18, 0.04)</td>
<td>-0.06 (-0.20, 0.08)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>-0.03 (-0.13, 0.08)</td>
<td>0.01 (-0.14, 0.15)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>-0.03 (-0.14, 0.08)</td>
<td>0.05 (-0.10, 0.20)</td>
</tr>
<tr>
<td><strong>p for trend</strong></td>
<td>0.75</td>
<td>0.30</td>
</tr>
</tbody>
</table>

Results from multivariable linear regression analyses in non-imputed data. The regression coefficients (95% CI) reflect the difference in age- and sex-specific SDS of childhood body mass index, fat-free mass index and fat mass index relative to the first quartile of energy-adjusted protein intake. Trend tests were conducted by using the quartiles of protein intake as a continuous variable in the model. <sup>a</sup> **Model 1**: Vegetable and animal protein intake were additionally adjusted for each other. <sup>b</sup> **Model 2**: **Model 1** further adjusted for maternal age, educational level, smoking and alcohol use and folic acid supplementation during pregnancy, energy and carbohydrate intake during pregnancy, gestational age at birth, breastfeeding 2 months postpartum and screen time of the children at 6 years of age. <sup>c</sup> Energy-adjusted protein intake using the nutritional residual method. **Abbreviations**: CI: confidence interval, SDS: standard deviation score.
**Supplementary Table 4.1.4.** Association between protein intake during pregnancy and childhood total fat percentage and android/gynoid fat mass ratio at the age of 6 years

<table>
<thead>
<tr>
<th>Total fat percentage (SDS)</th>
<th>Android/gynoid fat mass ratio (SDS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=2,624</td>
<td>n=2,624</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Model 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Model 2&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Model 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Model 2&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total protein intake&lt;sup&gt;c&lt;/sup&gt;</strong></td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>-0.13 (-0.22, -0.03)</td>
<td>-0.05 (-0.15, 0.04)</td>
<td>-0.10 (-0.20, 0.01)</td>
<td>-0.03 (-0.14, 0.08)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>-0.09 (-0.18, 0.01)</td>
<td>0.03 (-0.07, 0.13)</td>
<td>-0.02 (-0.13, 0.09)</td>
<td>0.07 (-0.04, 0.18)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>-0.15 (-0.24, -0.05)</td>
<td>-0.01 (-0.12, 0.09)</td>
<td>-0.08 (-0.19, 0.03)</td>
<td>0.02 (-0.10, 0.14)</td>
</tr>
<tr>
<td><strong>p for trend</strong></td>
<td>0.009</td>
<td>0.77</td>
<td>0.36</td>
<td>0.35</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Animal protein intake&lt;sup&gt;c&lt;/sup&gt;</th>
<th>β (95% CI)</th>
<th>β (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>-0.01 (-0.10, 0.09)</td>
<td>0.05 (-0.05, 0.14)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>-0.04 (-0.13, 0.06)</td>
<td>0.06 (-0.04, 0.15)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>-0.08 (-0.18, 0.01)</td>
<td>0.04 (-0.06, 0.15)</td>
</tr>
<tr>
<td><strong>p for trend</strong></td>
<td>0.08</td>
<td>0.45</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vegetable protein intake&lt;sup&gt;c&lt;/sup&gt;</th>
<th>β (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quartile 1</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>-0.12 (-0.22, -0.03)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>-0.12 (-0.22, -0.03)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>-0.23 (-0.32, -0.13)</td>
</tr>
<tr>
<td><strong>p for trend</strong></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Results from multivariable linear regression analyses, based on imputed data. The regression coefficients (95% CI) reflect the difference in age- and sex-specific SDS of total fat percentage and android/gynoid fat mass ratio of the child relative to the first quartile of energy-adjusted protein intake. Trend tests were conducted by using the quartiles of protein intake as a continuous variable in the model.  
<sup>a</sup> Model 1: Adjusted for height of the child aged 6 years. The vegetable and animal protein intake were additionally adjusted for each other.  
<sup>b</sup> Model 2: Model 1 additionally adjusted for maternal age, educational level, smoking and alcohol use and folic acid supplementation during pregnancy, energy and carbohydrate intake during pregnancy, gestational age at birth, breastfeeding 2 months postpartum and screen time of the children at 6 years of age.  
<sup>c</sup> Energy-adjusted protein intake using the nutritional residual method.  
**Abbreviations:** CI: confidence interval. SDS: standard deviation score.
**Supplementary Table 4.1.5.** Association between protein intake during pregnancy and childhood BMI and fat-free mass index at the age of 6 years, stratified by maternal overweight status at enrollment

<table>
<thead>
<tr>
<th></th>
<th>Childhood Body Mass Index (SDS)</th>
<th>Childhood Fat-Free Mass Index (SDS)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Maternal BMI &lt;25 kg/m²</td>
<td>Maternal BMI ≥25 kg/m²</td>
</tr>
<tr>
<td>n = 2694</td>
<td>n = 2624</td>
<td>n = 2617</td>
</tr>
<tr>
<td>Total protein intake⁹</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>0.01 (-0.11, 0.13)</td>
<td>0.05 (-0.17, 0.26)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>0.03 (-0.10, 0.15)</td>
<td>0.17 (-0.05, 0.39)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>0.03 (-0.11, 0.16)</td>
<td><strong>0.28 (0.05, 0.51)</strong></td>
</tr>
<tr>
<td>p for trend</td>
<td>0.67</td>
<td><strong>0.01</strong></td>
</tr>
<tr>
<td>Animal protein intake⁹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td><strong>0.12 (0.01, 0.24)</strong></td>
<td>-0.05 (-0.27, 0.17)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>0.06 (-0.06, 0.19)</td>
<td>0.14 (-0.08, 0.36)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>0.10 (-0.03, 0.24)</td>
<td>0.21 (-0.03, 0.45)</td>
</tr>
<tr>
<td>p for trend</td>
<td>0.28</td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td>Vegetable protein intake⁹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>0.08 (-0.04, 0.20)</td>
<td>-0.08 (-0.29, 0.13)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>0.08 (-0.04, 0.21)</td>
<td>0.16 (-0.06, 0.37)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>0.08 (-0.05, 0.22)</td>
<td>0.19 (-0.04, 0.42)</td>
</tr>
<tr>
<td>p for trend</td>
<td>0.27</td>
<td><strong>0.04</strong></td>
</tr>
</tbody>
</table>

⁹ Results from multivariable linear regression analyses, based on imputed data. The regression coefficients (95% CI) reflect the difference in age- and sex-specific SDS of childhood body mass index and fat-free mass index relative to the first quartile of energy-adjusted protein intake. Trend tests were conducted by using the quartiles of protein intake as a continuous variable in the model. The analyses were adjusted for maternal age, educational level, smoking and alcohol use and folic acid supplementation during pregnancy, energy and carbohydrate intake during pregnancy, gestational age at birth, breastfeeding 2 months postpartum and screen time of the children at 6 years of age. Vegetable and animal protein intake were additionally adjusted for each other. ⁹ Energy-adjusted protein intake using the nutritional residual method. **Abbreviations:** CI: confidence interval, SDS: standard deviation score.
### Supplementary Table 4.1.6. Association between protein intake during pregnancy and childhood fat-free mass index at the age of 6 years, in the population with available protein intake of the children at 14 months of age (n=1558)

<table>
<thead>
<tr>
<th>Total protein intake d</th>
<th>Model 1 a</th>
<th>Model 2 b</th>
<th>Model 2 c</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fat-free mass index (SDS) n=1558</strong></td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>0.04 (-0.09, 0.17)</td>
<td>0.02 (-0.11, 0.15)</td>
<td>0.02 (-0.11, 0.15)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>0.12 (-0.01, 0.24)</td>
<td>0.11 (-0.03, 0.24)</td>
<td>0.10 (-0.04, 0.23)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td><strong>0.14 (0.02, 0.27)</strong></td>
<td>0.14 (-0.01, 0.28)</td>
<td>0.11 (-0.03, 0.26)</td>
</tr>
<tr>
<td><strong>p for trend</strong></td>
<td><strong>0.01</strong></td>
<td><strong>0.03</strong></td>
<td><strong>0.06</strong></td>
</tr>
<tr>
<td>Animal protein intake d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>0.06 (-0.06, 0.19)</td>
<td>0.07 (-0.06, 0.20)</td>
<td>0.06 (-0.07, 0.19)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>0.09 (-0.03, 0.22)</td>
<td>0.10 (-0.03, 0.23)</td>
<td>0.09 (-0.05, 0.22)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td><strong>0.17 (0.04, 0.31)</strong></td>
<td><strong>0.20 (0.06, 0.34)</strong></td>
<td><strong>0.18 (0.03, 0.32)</strong></td>
</tr>
<tr>
<td><strong>p for trend</strong></td>
<td><strong>0.009</strong></td>
<td><strong>0.007</strong></td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td>Vegetable protein intake d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>-0.05 (-0.18, 0.08)</td>
<td>-0.05 (-0.19, 0.08)</td>
<td>-0.06 (-0.19, 0.08)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>0.04 (-0.09, 0.17)</td>
<td>0.04 (-0.10, 0.18)</td>
<td>0.03 (-0.11, 0.17)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td><strong>0.17 (0.03, 0.31)</strong></td>
<td><strong>0.16 (0.01, 0.30)</strong></td>
<td><strong>0.15 (0.00, 0.30)</strong></td>
</tr>
<tr>
<td><strong>p for trend</strong></td>
<td><strong>0.003</strong></td>
<td><strong>0.009</strong></td>
<td><strong>0.01</strong></td>
</tr>
</tbody>
</table>

Results from multivariable linear regression analyses, based on imputed data. The regression coefficients (95% CI) reflect the difference in age- and sex-specific SDS of the fat-free mass index of the child relative to the first quartile of energy-adjusted protein intake. Trend tests were conducted by using the quartiles of protein intake as a continuous variable in the model.  

- Model 1: The vegetable and animal protein intake were additionally adjusted for each other.  
- Model 2: Model 1 additionally adjusted for maternal age, educational level, smoking and alcohol use during pregnancy, folic acid supplementation, energy and carbohydrate intake during pregnancy, gestational age at birth, breastfeeding 2 months postpartum and screen time of the children at 6 years of age.  
- Model 2*: Model 2 additionally adjusted for protein intake of the children at 14 months of age.  
- Energy-adjusted protein intake using the nutritional residual method.  

**Abbreviations:** CI: confidence interval, SDS: standard deviation score.
Supplementary Table 4.1.7. Association between protein intake during pregnancy and childhood lean mass index at the age of 6 years (n=2624)

<table>
<thead>
<tr>
<th>Lean mass index (SDS)</th>
<th>Model 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Model 2&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=2624</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
</tr>
<tr>
<td>Total protein intake&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>0.10 (0.00, 0.20)</td>
<td>0.10 (-0.00, 0.20)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>0.12 (0.02, 0.21)</td>
<td>0.11 (0.01, 0.22)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>0.17 (0.07, 0.27)</td>
<td>0.16 (0.05, 0.27)</td>
</tr>
<tr>
<td>p for trend</td>
<td>0.001</td>
<td>0.005</td>
</tr>
<tr>
<td>Animal protein intake&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>0.09 (-0.01, 0.19)</td>
<td>0.10 (0.00, 0.21)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>0.10 (0.00, 0.20)</td>
<td>0.11 (0.01, 0.22)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>0.18 (0.07, 0.28)</td>
<td>0.19 (0.08, 0.31)</td>
</tr>
<tr>
<td>p for trend</td>
<td>0.001</td>
<td>0.002</td>
</tr>
<tr>
<td>Vegetable protein intake&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>0.05 (-0.05, 0.15)</td>
<td>0.06 (-0.04, 0.16)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>0.14 (0.04, 0.24)</td>
<td>0.15 (0.04, 0.25)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>0.22 (0.12, 0.32)</td>
<td>0.22 (0.11, 0.33)</td>
</tr>
<tr>
<td>p for trend</td>
<td>0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Results from multivariable linear regression analyses, based on imputed data. The regression coefficients (95% CI) reflect the difference in age- and sex-specific SDS of lean mass index of the child relative to the first quartile of energy-adjusted protein intake. Trend tests were conducted by using the quartiles of protein intake as a continuous variable in the model. <sup>a</sup> Model 1: The vegetable and animal protein intake were additionally adjusted for each other. <sup>b</sup> Model 2: Model 1 further adjusted for maternal age, maternal educational level, maternal smoking and alcohol use during pregnancy, folic acid supplementation, maternal energy and carbohydrate intake, gestational age at birth, gender of the child, breastfeeding practice 2 months postpartum, and screen time of the children at 6 years of age; <sup>c</sup> Energy-adjusted protein intake using the nutritional residual method. Abbreviations: CI: confidence interval. SDS: standard deviation score.
**Supplementary Table 4.1.8.** Association between protein intake during pregnancy and childhood fat-free mass index at the age of 6 years in mothers without hypertensive complications in pregnancy, preterm child birth, or those who gave birth to a new-born with a birth weight outside ±2 SD (n=2242)

<table>
<thead>
<tr>
<th></th>
<th>Fat-free mass index (SDS)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Model 1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Model 2&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Total protein intake&lt;sup&gt;c&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 1</td>
<td>reference</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>0.11 (0.06, 0.17)</td>
<td>0.11 (0.00, 0.22)</td>
<td></td>
</tr>
<tr>
<td>Quartile 3</td>
<td>0.11 (0.05, 0.16)</td>
<td>0.11 (-0.00, 0.22)</td>
<td></td>
</tr>
<tr>
<td>Quartile 4</td>
<td>0.20 (0.14, 0.25)</td>
<td>0.20 (0.08, 0.32)</td>
<td></td>
</tr>
<tr>
<td><strong>p for trend</strong></td>
<td></td>
<td>0.001</td>
<td>0.002</td>
</tr>
</tbody>
</table>

| **Animal protein intake<sup>c</sup>** |                           |      |      |
| Quartile 1                     | reference                 | reference | reference |
| Quartile 2                     | 0.08 (0.03, 0.13)         | 0.10 (-0.01, 0.21) |
| Quartile 3                     | 0.11 (0.05, 0.17)         | 0.13 (0.01, 0.24) |
| Quartile 4                     | 0.17 (0.12, 0.23)         | 0.19 (0.07, 0.32) |
| **p for trend**                |                           | 0.002 | 0.002 |

| **Vegetable protein intake<sup>c</sup>** |                           |      |      |
| Quartile 1                     | reference                 | reference | reference |
| Quartile 2                     | 0.06 (0.01, 0.12)         | 0.07 (-0.04, 0.18) |
| Quartile 3                     | 0.14 (0.09, 0.20)         | 0.16 (0.04, 0.27) |
| Quartile 4                     | 0.25 (0.19, 0.30)         | 0.25 (0.13, 0.37) |
| **p for trend**                |                           | <0.001 | <0.001 |

Results from multivariable linear regression analyses, based on imputed data. The regression coefficients (95% CI) reflect the difference in age- and gender-specific SDS of the fat-free mass index of the child relative to the first quartile of energy-adjusted protein intake. Trend tests were conducted by using the quartiles of protein intake as a continuous variable in the model. <sup>a</sup> Model 1: The vegetable and animal protein intake were additionally adjusted for each other. <sup>b</sup> Model 2: Model 1 further adjusted for maternal age, maternal educational level, maternal smoking and alcohol use during pregnancy, folic acid supplementation, maternal energy and carbohydrate intake during pregnancy, gestational age at birth, gender of the child, breastfeeding practice 2 months postpartum, and screen time of the children at 6 years of age; <sup>c</sup> Energy-adjusted protein intake using the nutritional residual method. **Abbreviations:** CI: confidence interval, SDS: standard deviation score.
Chapter 4.2

Maternal dietary patterns during pregnancy and offspring cardiometabolic health at age 6 years: The Generation R Study

Elisabeth T.M. Leermakers, Myrte J. Tielemans, Marion van den Broek, Vincent W.V. Jaddoe, Oscar H. Franco, Jessica C. Kiefte-de Jong

Clinical nutrition, 2016 jan [Epub ahead of print]
**Supplementary Table 4.2.1.** Comparison of a selection of the subject characteristics of the study population (n=2695, unimputed data) and the excluded mothers and children (n=1402, unimputed data): The Generation R Study Cohort, Rotterdam, The Netherlands

<table>
<thead>
<tr>
<th>Maternal characteristics</th>
<th>Participants in analysis (n=2695)</th>
<th>Participants not in analysis (n=1402)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31.7 ± 4.2</td>
<td>30.5 ± 5.1</td>
</tr>
<tr>
<td>Pre-pregnancy BMI (kg/m²)</td>
<td>23.3 ± 3.9</td>
<td>23.1 ± 4.0</td>
</tr>
<tr>
<td>Gestational age at enrolment (weeks)</td>
<td>13.4 (9.9; 22.8)</td>
<td>13.5 (9.5-27.8)</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary or secondary</td>
<td>1019 (37.8%)</td>
<td>697 (50.7%)</td>
</tr>
<tr>
<td>Higher</td>
<td>1640 (61.7%)</td>
<td>679 (49.3%)</td>
</tr>
<tr>
<td>Missing</td>
<td>36 (1.3%)</td>
<td>26 (1.9%)</td>
</tr>
<tr>
<td>Household income</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2200 (Euros/month)</td>
<td>591 (23.8%)</td>
<td>360 (33.1%)</td>
</tr>
<tr>
<td>&gt;2200 (Euros/month)</td>
<td>1893 (76.2%)</td>
<td>728 (51.9%)</td>
</tr>
<tr>
<td>Missing</td>
<td>211 (7.8%)</td>
<td>314 (22.4%)</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1665 (61.9%)</td>
<td>769 (55.2%)</td>
</tr>
<tr>
<td>≥1</td>
<td>1026 (38.1%)</td>
<td>623 (44.8%)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (0.1%)</td>
<td>10 (0.1%)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never during pregnancy</td>
<td>1,886 (75.9%)</td>
<td>875 (67.3%)</td>
</tr>
<tr>
<td>Until pregnancy was known</td>
<td>236 (9.5%)</td>
<td>113 (8.7%)</td>
</tr>
<tr>
<td>Continued throughout pregnancy</td>
<td>363 (14.6%)</td>
<td>313 (24.1%)</td>
</tr>
<tr>
<td>Missing</td>
<td>210 (7.8%)</td>
<td>101 (7.2%)</td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never during pregnancy</td>
<td>776 (28.8%)</td>
<td>525 (40.7%)</td>
</tr>
<tr>
<td>Until pregnancy was known</td>
<td>413 (15.3%)</td>
<td>208 (16.1%)</td>
</tr>
<tr>
<td>Continued throughout pregnancy</td>
<td>1,278 (51.8%)</td>
<td>558 (43.2%)</td>
</tr>
<tr>
<td>Missing</td>
<td>228 (8.5%)</td>
<td>111 (8.5%)</td>
</tr>
<tr>
<td>Folic acid use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>203 (9.2%)</td>
<td>192 (13.7%)</td>
</tr>
<tr>
<td>Start first 10 weeks</td>
<td>734 (33.1%)</td>
<td>380 (33.7%)</td>
</tr>
<tr>
<td>Start periconceptional</td>
<td>1,281 (57.8%)</td>
<td>555 (49.2%)</td>
</tr>
<tr>
<td>Missing</td>
<td>477 (17.7%)</td>
<td>275 (19.6%)</td>
</tr>
<tr>
<td>Total energy intake, FFQ (kcal/day)</td>
<td>2153 ± 503</td>
<td>2125 ± 539</td>
</tr>
<tr>
<td>Stress during pregnancy, global severity index</td>
<td>0.12 (0.00-0.77)</td>
<td>0.12 (0.00-0.77)</td>
</tr>
</tbody>
</table>

*Values represent n (%), mean ± SD, or median (95% range). BMI: body mass index. FFQ: food-frequency questionnaire. Missing values for continuous variables for the population in the analysis were 373 (14%) for pre-pregnancy BMI and 284 (11%) for stress during pregnancy. Missing values for continuous variables in the population not in the analysis were 214 (15%), 538 (38%) for total energy intake and 322 (23%) for stress during pregnancy.