**Lutein intake at the age of 1 year and cardiometabolic health at the age of 6 years: The Generation R Study**

*Shortened title: child lutein intake and cardiometabolic health*

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***Supplementary material***

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**Table S1:** Details of the multiple imputation modeling

|  |  |
| --- | --- |
|  | Multiple imputation procedure |
| Software used | SPSS 21.0 for Windows |
| Imputation method  | Fully conditional specification (Markov chain Monte Carlo method) |
| Maximum iterations | 10 |
| Imputed datasets created | 10 |
| Exposures and outcomes (not imputed, used in model as predictor) | Lutein intake, Height, weight, body mass index, fat mass index, fat free mass index, body fat percentage, android/gynoid ratio, systolic blood pressure, diastolic blood pressure, insulin, triglycerides, HDL-cholesterol, cardiometabolic risk factor score, mean arterial pressure, c-peptide, total cholesterol, LDL cholesterol, pulse wave velocity |
| Covariates (imputed) | Maternal and paternal age, maternal and paternal BMI, household income, maternal education, parity, smoking, alcohol and folic acid supplement use during pregancny, child gender, birthweight, gestational age at birth, breastfeeding, timing of introduction of solids, hospitalization in the first year of life, allergy to cow’s milk, total energy intake, diet quality score, television watching at 2 years of age and playing sports at 6 years of age.  |
| Additional predictors  | Television watching at age 4 and 5 years, computer time at age 5, playing outside at age 4 and 5, active transport to school at age 5, maternal pre-pregnancy weight, maternal weight at child’s visit to research center, educational level partner, educational level of mother and partner, family income, and mothers marital status at child’s visit to research center |
| Treatment of non- normally distributed variables | Predictive mean matching |
| Treatment of binary/categorical variables | Logistic regression models |

*Number of missings for the variables imputed can be found in supplementary table S2.*

**Table S2** Basic characteristics before and after multiple imputation

|  |  |  |  |
| --- | --- | --- | --- |
|  | **N** | **Original data** | **Imputed data** |
| **Child characteristics** |  |  |  |
| Gender (% girls) | 2044 | 50.7 (1,036) | *No missings* |
| Gestational age at birth (weeks) | 2042 | 40.3 (35.9 – 42.3) | 40.3 (35.9 – 42.3) |
| Birth weight (grams) | 2043 | 3498 (566) | 3498 (566) |
| Time of introduction of solid foods | 2037 |  |  |
| 0-3 months |  | 4.2 (86) | 4.2 (86) |
| 3-6 months |  | 55.8 (1,136) | 55.7 (1,139) |
| After 6 months |  | 40.0 (815) | 40.0 (818) |
| Breastfed | 1846 |  |  |
| Never |  | 9.8 (181) | 10.1 (207) |
| Partially in the first 4 months |  | 60.2 (1,112) | 60.0 (1,225) |
| Exclusively for at least 4 months |  | 30.0 (553) | 30.0 (612) |
| Age at dietary assessment (months) | 2044 | 12.9 (12.2 – 19.2) | *No missings* |
| Total energy intake (kcal/day) | 2044 | 1267 (736 – 2077)  | *No missings* |
| Total lutein intake (mcg/day) | 2044 | 1317 (87 – 6069)  | *No missings* |
| Total dietary fiber intake (g/day) | 2044 | 14.7 (7.6 – 24.4) | *No missings* |
| Total fat intake (g/day) | 2044 | 38.5 (18.6 – 78.1) | *No missings* |
| Total beta-carotene intake (mcg/day) | 2044 | 1351 (158 – 4886) | *No missings* |
| Age at visit to research center (months) | 2044 | 71 (68 – 78)  | *No missings* |
| BMI (kg/m2) | 2044 | 15.7 (13.6 – 19.0) | *Not imputed* |
| FMI (kg/m2) | 1964 | 3.5 (2.4 – 6.3) | *Not imputed* |
| FFMI (kg/m2) | 1964 | 11.9 (10.4 – 13.6) | *Not imputed* |
| Android/gynoid fat ratio  | 1964 | 0.23 (0.15 – 0.37) | *Not imputed* |
| Total body fat percentage (%) | 1964 | 0.23 (0.16 – 0.34) | *Not imputed* |
| Insulin (pmol/l) | 1383 | 114 (18 – 392) | *Not imputed* |
| C-peptide (nmol/l) | 1381 | 0.98 (0.33 – 2.15) | *Not imputed* |
| Total cholesterol (mmol/l) | 1386 | 4.2 (3.0 – 5.6) | *Not imputed* |
| HDL-cholesterol (mmol/l) | 1389 | 1.3 (0.8 – 2.1) | *Not imputed* |
| LDL-cholesterol (mmol/l) | 1386 | 2.3 (1.4 – 3.6) | *Not imputed* |
| Triglycerides (mmol/l) | 1386 | 1.0 (0.4 – 2.4)  | *Not imputed* |
| Systolic blood pressure (mmHg) | 1968 | 101 (88 – 119) | *Not imputed* |
| Diastolic blood pressure (mmHg) | 1968 | 60 ( 47 – 73)  | *Not imputed* |
| Mean arterial pressure (mmHg) | 1968 | 74 (62 – 87) | *Not imputed* |
| Pulse wave velocity (m/s) | 1704 | 5.4 (4.1 – 7.5) | *Not imputed* |
| **Maternal characteristics** |  |  |  |
| Maternal age (years) | 2044 | 32.0 (4.1) | *No missings* |
| Maternal BMI at intake (kg/m2) | 1866 | 24.2 (4.0) | 24.2 (4.0) |
| Educational level | 2022 |  |  |
| Lower |  | 33.8 (683) | 34.1 (697) |
| Higher |  | 66.2 (1,339) | 65.9 (1,347) |
| Net household income | 1787 |  |  |
| <2200 Euros per month  |  | 20.3 (419) | 20.8 (426) |
| >2200 Euros per month |  | 79.7 (1,424) | 79.2 (1,618) |
| Folic acid use | 1539 |  |  |
| Never  |  | 7.2 (111) | 7.4 (151) |
| Periconceptionally |  | 63.4 (975) | 29.7 (607) |
| Started in first 10 weeks |  | 29.4 (453) | 62.9 (1,286) |
| Smoking in pregnancy | 1856 |  |  |
| Never smoked during pregnancy |  | 79.3 (1,472) | 79.3 (1621) |
| Smoked until pregnancy was known |  | 10.3 (191) | 10.3 (212) |
| Continued smoking in pregnancy |  | 10.4 (193) | (212) |

*Values are means (n), median (95% range) or valid percentages (n). Due to rounding, numbers may nog completely add up.*

**Table S3:** Crude associations of lutein and beta-carotene intake at 13 months with body composition at age 61

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| --- |
| **Table A. Associations of lutein (adjusted for beta-carotene)** |
|  | **Height****n=2044***SD change (95% CI)* | **Weight****n=2044***SD change (95% CI)* | **BMI****n=2044***SD change (95% CI)* | **FMI****n=1964***SD change (95% CI)* | **FFMI****n=1964***SD change (95% CI)* | **AG ratio****n=1964***SD change (95% CI)* | **Body fat%****n=1964***SD change (95% CI)* |
| Q1 Low intake | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* |
| Q2  | 0.09(-0.03; 0.20) | 0.09(-0.00; 0.18) | 0.08(-0.01; 0.17) | 0.03(-0.05; 0.12) | 0.08(-0.04; 0.19) | 0.03(-0.07; 0.13) | 0.01(-0.09; 0.11) |
| Q3 | 0.09(-0.03; 0.20) | 0.09(-0.00; 0.19) | 0.08 (-0.01; 0.17) | 0.04 (-0.05; 0.13) | 0.09(-0.02; 0.20) | -0.04(-0.14; 0.07) | 0.01(-0.09; 0.11) |
| Q4 High intake | 0.02 (-0.1; 0.13) | 0.08(-0.01; 0.18) | **0.12****(0.02; 0.21)\*** | 0.04(-0.05; 0.13) | **0.12****(0.01; 0.23)\*** | -0.00(-0.11; 0.10) | 0.01(-0.08; 0.11) |
| *Continuous (per SD)* | *0.01(-0.03; 0.05)* | *0.03**(-0.00; 0.07)* | ***0.04******(0.01; 0.07)\**** | *0.03**(-0.00; 0.06)* | *0.03**(-0.01; 0.07)* | *0.00**(-0.04; 0.04)* | *0.02**(-0.02; 0.05)* |
| **Table B. Associations of lutein (unadjusted for beta-carotene)**  |
|  | **Height****n=2044***SD change (95% CI)* | **Weight****n=2044***SD change (95% CI)* | **BMI****n=2044***SD change (95% CI)* | **FMI****n=1964***SD change (95% CI)* | **FFMI****n=1964***SD change (95% CI)* | **AG ratio****n=1964***SD change (95% CI)* | **Body fat%****n=1964***SD change (95% CI)* |
| Q1 Low intake | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* |
| Q2  | -0.02(-0.14; 0.1) | 0.03(-0.07; 0.12) | 0.06(-0.04; 0.15) | 0.05(-0.04; 0.14) | 0.02(-0.09; 0.14) | 0.09(-0.01; 0.20) | 0.04(-0.06; 0.14) |
| Q3 | 0.01(-0.11; 0.12) | 0.07(-0.03; 0.16) | **0.10****(0.00; 0.19)\*** | 0.04 (-0.05; 0.13) | 0.09(-0.02; 0.20) | 0.02(-0.08; 0.12) | 0.02(-0.08; 0.12) |
| Q4 High intake | -0.02(-0.14; 0.10) | **0.12(0.02; 0.21)\*** | **0.19****(0.10; 0.28)\*\*** | **0.09****(0.00; 0.18)\*** | **0.16****(0.05; 0.27)\*\*** | 0.02(-0.09; 0.13) | 0.06(-0.04; 0.16) |
| *Continuous (per SD)* | *0.00**(-0.04; 0.04)* | ***0.05(0.02; 0.09)\*\**** | ***0.08******(0.05; 0.11)\*\**** | ***0.05******(0.01; 0.08)\*\**** | ***0.07******(0.03; 0.11)\*\**** | *0.01**(-0.03; 0.05)* | *0.03**(-0.00; 0.07)* |
| **Table C. Associations of beta-carotene** |
|  | **Height****n=2044***SD change (95% CI)* | **Weight****n=2044***SD change (95% CI)* | **BMI****n=2044***SD change (95% CI)* | **FMI****n=1964***SD change (95% CI)* | **FFMI****n=1964***SD change (95% CI)* | **AG ratio****n=1964***SD change (95% CI)* | **Body fat%****n=1964***SD change (95% CI)* |
| Q1 Low intake | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* |
| Q2  | -0.03(-0.14; 0.08) | 0.04(-0.05; 0.14) | 0.08(-0.01; 0.18) | 0.06(-0.03; 0.15) | 0.05(-0.06; 0.16) | 0.07(-0.03; 0.17) | 0.05(-0.05; 0.15) |
| Q3 | -0.03(-0.15; 0.08) | 0.05(-0.04; 0.15) | 0.10 (0.00; 0.10) | 0.08 (-0.01; 0.17) | 0.06(-0.05; 0.17) | 0.04(-0.06; 0.14) | 0.07(-0.03; 0.16) |
| Q4 High intake | 0.02(-0.10; 0.13) | **0.14(0.04; 0.23)\*\*** | **0.20****(0.10; 0.29)\*\*** | 0.09(-0.00; 0.18) | **0.19****(0.08; 0.30)\*\*** | 0.01(-0.10; 0.11) | 0.05(-0.05; 0.14) |
| *Continuous (per SD)* | *0.00**(-0.04; 0.04)* | ***0.05(0.02; 0.08)\*\**** | *0.07**(0.04; 0.10)* | ***0.04******(0.01; 0.07)\**** | ***0.06******(0.02; 0.10)\*\**** | *0.01**(-0.02; 0.05)* | *0.03**(-0.01; 0.06)* |

*AG = android/gynoid, BMI = body mass index, FMI = fat mass index, FFMI = fat free mass index*

*1Values are linear regression coefficients (95% confidence interval) and reflect the difference in outcome (age and gender specific SD scores) for mid-low, mid-high and high intake, as compared to low intake of energy and beta carotene adjusted lutein intake.*

*\*P<0.05, \*\*P<0.01*

*Continuous model reflects the difference in outcome (age and gender specific SD scores) per SD increase of energy and beta carotene adjusted lutein intake.
Models are adjusted for age at dietary assessment.*

**Table S4:** Crude associations of lutein and beta-carotene intake at 13 months with cardiometabolic health at age 61

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| --- |
| **Table A. Associations of lutein (adjusted for beta-carotene)** |
|  | **Systolic blood pressure****n=1969***SD change (95% CI)* | **Diastolic blood pressure****n=1969***SD change (95% CI)* |  **HDL cholesterol****n=1390***SD change (95% CI)* | **Triglycerides****n=1387** *SD change (95% CI)* | **Insulin****n=1383***SD change (95% CI)* | **Cardiometabolic risk factor score****n=1305***SD change (95% CI)* |
| Q1 Low intake | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* |
| Q2  | -0.03(-0.15; 0.10) | -0.06(-0.18; 0.05) | -0.06(-0.20; 0.10) | -0.08(-0.22; 0.07) | -0.06(-0.20; 0.09) | -0.02(-0.16; 0.13) |
| Q3 | 0.12(-0.00; 0.24) | 0.04(-0.07; 0.16) | 0.06(-0.09; 0.20) | -0.24(-0.39; -0.09) | -0.08(-0.23; 0.06) | -0.11(-0.25; 0.04) |
| Q4 High intake | -0.00(-0.12; 0.12) | -0.04(-0.15; 0.08) | 0.04(-0.11; 0.19) | -0.02(-0.17; 0.13) | -0.03(-0.18; 0.12) | -0.09(-0.24; 0.05) |
| *Continuous (per SD)* | *0.00**(-0.04; 0.04)* | *-0.01**(-0.05; 0.04)* | *0.02**(-0.03; 0.08)* | *-0.04**(-0.09; 0.02)* | *-0.02**(-0.07; 0.03)* | *-0.04**(-0.10; 0.01)* |
| **Table B. Associations of lutein (unadjusted for beta-carotene)** |
|  | **Systolic blood pressure****n=1969***SD change (95% CI)* | **Diastolic blood pressure****n=1969***SD change (95% CI)* |  **HDL cholesterol****n=1390***SD change (95% CI)* | **Triglycerides****n=1387** *SD change (95% CI)* | **Insulin****n=1383***SD change (95% CI)* | **Cardiometabolic risk factor score****n=1305***SD change (95% CI)* |
| Q1 Low intake | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* |
| Q2  | -0.01(-0.13; 0.11) | -0.05(-0.17; 0.07) | 0.04(-0.11; 0.19) | -0.15(-0.30; 0.01) | -0.17(-0.31; 0.02) | -0.17(-0.31; 0.03) |
| Q3 | 0.04(-0.08; 0.16) | 0.02(-0.10; 0.14) | 0.00(-0.14; 0.15) | -0.01(-0.16; 0.14) | -0.02(-0.17; 0.13) | -0.05(-0.19; 0.10) |
| Q4 High intake | -0.01(-0.14; 0.10) | -0.05(-0.17; 0.07) | 0.14(-0.01; 0.28) | **-0.20****(-0.35;-0.05)\*** | -0.08(-0.22; 0.07) | **-0.21****(-0.36; -0.07)\*\*** |
| *Continuous (per SD)* | *0.00**(-0.04; 0.04)* | *-0.01**(-0.05; 0.03)* | ***0.06******(0.01; 0.12)\**** | ***-0.09******(-0.14;-0.04)\*\**** | *-0.02(-0.07; 0.03)* | ***-0.08******(-0.13; -0.03)\*\**** |
| **Table C. Associations of beta-carotene** |
|  | **Systolic blood pressure****n=1969***SD change (95% CI)* | **Diastolic blood pressure****n=1969***SD change (95% CI)* |  **HDL cholesterol****n=1390***SD change (95% CI)* | **Triglycerides****n=1387** *SD change (95% CI)* | **Insulin****n=1383***SD change (95% CI)* | **Cardiometabolic risk factor score****n=1305***SD change (95% CI)* |
| Q1 Low intake | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* | *Reference* |
| Q2  | 0.01(-0.11; 0.13) | -0.05(-0.17; 0.07) | -0.03(-0.18; 0.12) | -0.05(-0.20; 0.10) | -0.12(-0.27; 0.02) | -0.06(-0.20; 0.09) |
| Q3 | -0.03(-0.16; 0.09) | -0.09(-0.21; 0.03) | -0.07(-0.22; 0.08) | 0.04(-0.11; 0.19) | 0.03(-0.12; 0.18) | -0.00(-0.15; 0.14) |
| Q4 High intake | -0.01(-0.14; 0.11) | -0.07(-0.19; 0.05) | 0.06(-0.09; 0.21) | **-0.18****(-0.33;-0.03)\*** | -0.04(-0.18; 0.11) | -0.14(-0.28; 0.00) |
| *Continuous (per SD)* | *-0.01**(-0.05; 0.04)* | *-0.03**(-0.07; 0.02)* | *0.04**(-0.01; 0.09)* | ***-0.07******(-0.12;-0.02)\*\**** | *-0.01**(-0.06; 0.04)* | ***-0.06(-0.11; -0.01)\**** |

*1Values are linear regression coefficients (95% confidence interval) and reflect the difference in outcome (age and gender specific SD scores) for mid-low, mid-high and high intake, as compared to low intake of energy and beta carotene adjusted lutein intake.*

*\*P<0.05, \*\*P<0.01*

*Continuous model reflects the difference in outcome (age and gender specific SD scores) per SD increase of energy and beta carotene adjusted lutein intake.
Crude models are adjusted for age at dietary assessment.*