**Supplementary Material:**

**Title:** Early childhood BMI trajectories in relation to pre-clinical cardiovascular measurements in adolescence

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**Table S1.** Covariate description

|  |  |  |
| --- | --- | --- |
| **Variable** | **Equipment/Tool Used** | **Protocol Followed** |
| Child’s age at cardiovascular measurement | -- | Calculated from birth date and date of measurement. |
| Child´s height at cardiovascular measurement (cm) | Stadiometer: Seca 214, d=1mm | Measured without shoes and the child standing upright and centrically with legs straight and weight evenly distributed on the floorboard of the stadiometer. The examiner took the height by going down face level with the child and child´s head maintained in the Frankfort Horizontal Plane. |
| Child Sex | Medical record | Taken from medical record file as male or female. |
| Gestational Weeks | Medical record | Taken from medical record file in weeks and days of gestation at birth. |
| Family socioeconomic status | Questionnaire | Based on occupation, using the Goldthorpe model as a reference. Social class was ranked according to the more privileged partner. Possible allocations were “low”, “middle”, “high”. |
| Maternal smoking status during pregnancy | Questionnaire | Mother asked about tobacco use at 12 weeks and 32 weeks. Possible response included: “yes” or “no”. |
| Maternal prepregnancy BMI | Questionnaire | Calculated using the standard formula (kg/m2) from two questions. “How much did you weigh before this pregnancy? (Kg)” and “Height in cm.” |
| Paternal BMI during pregnancy | Questionnaire | Calculated using the standard formula (kg/m2) from two questions asked to the mother. “How much does the father weigh (Kg)?” and “How tall is the father (cm).” |
| Parental Cardiovascular History | Questionnaire | Both mother and father asked about previous cardiovascular events, such as: “heart attack, angina, hemorrhage or stroke, arthrosclerosis in legs, high cholesterol, high blood sugar, and high blood pressure.” These factors were combined into a scored variable: “parents have 1+ diagnosis”, “one parent has 1+ diagnosis”, “neither parent has diagnosis”. |

|  |  |  |  |
| --- | --- | --- | --- |
|  | N missing | Original data set | Imputed data set |
|  | *percent or mean±sd* | *percent or mean±sd* |
| **Child Characteristics** |  |  |  |
| Sex (female) | 0 | 48.3% | - |
| Birth weight (g) | 0 | 3278.8±409.1 | - |
| Height at birth (cm) | 13 | 49.6±1.9 | - |
| Gestational age (weeks) | 0 | 39.8±1.3 | - |
| BMI trajectories from birth to 9 years | 0 |  |  |
| *Class 1: higher birth size – accelerated gain* |  | 9.8% | - |
| *Class 2: higher birth size – slower gain* |  | 27.0% | - |
| *Class 3: lower birth size – accelerated gain* |  | 13.7% | - |
| *Class 4: average birth size – slower gain (ref.)* |  | 35.0% | - |
| *Class 5: lower birth size – slower gain* |  | 14.5% | - |
| Agea | 0 | 11.0±0.6 | - |
| Weighta (kg) | 0 | 42.0±10.5 | - |
| Heighta (cm) | 0 | 146.1±8.0 | - |
| zBMIa | 0 | 0.70±1.24 | - |
| Systolic blood pressure (mmHg) | 0 | 101.6±9.9 | - |
| Diastolic blood pressure (mmHg) | 1 | 59.9±7.7 | - |
| Pulse wave velocity (PWV) (m/s) | 22 | 4.4±0.5 | - |
| Central retinal artery equivalent (CRAE) (μm) | 35 | 180.6±12.9 | - |
| Central retinal vein equivalent (CRVE) (μm) | 35 | 252.0±17.1 | - |
| **Family Characteristics** |  |  |  |
| Family SES (during pregnancy) | 60 |  |  |
| *High* |  | 35.4% | 36.1% |
| *Middle* |  | 30.5% | 30.3% |
| *Low* |  | 34.0% | 33.7% |
| Maternal BMI (prepregnancy) | 11 | 23.8±4.5 | 23.8±4.5 |
| Maternal smoking (during pregnancy) | 65 |  |  |
| *None* |  | 73.1% | 73.3% |
| *Until 1st trimester* |  | 14.4% | 14.2% |
| *Until 3rd trimester* |  | 12.5% | 12.5% |
| Paternal BMI (pregnancy 1st trimester) | 10 | 25.8±3.5 | 25.8±3.5 |
| Parental cardiovascular historyb | 4 |  |  |
| *Neither parent has diagnosis* |  | 47.2% | 47.2% |
| *1 parent has at least one diagnosis* |  | 42.7% | 42.6% |
| *Both parents have at least one diagnosis* |  | 10.1% | 10.2% |
| a Taken at the time of cardiovascular measurement.  b  Doctor diagnosis of cardiovascular disease (coronary heart disease, cerebrovascular disease, and peripheral vascular disease) or cardiovascular risk factors (hypercholesterolemia, hypertension, and diabetes). | | | |

**Table S2.** Characteristics of the study population (n=489)

**Table S3.** Pearson correlation coefficients between cardiovascular measurements

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Systolic Blood Pressure** | **Diastolic Blood Pressure** | **Pulse Wave Velocity** | **Central Retinal Artery Equivalent** | **Central Retinal Vein Equivalent** |
|  | Coefficient  (p-value) | Coefficient  (p-value) | Coefficient  (p-value) | Coefficient  (p-value) | Coefficient  (p-value) |
| **Systolic Blood Pressure** | 1.00 |  |  |  |  |
| **Diastolic Blood Pressure** | 0.66  (<0.01) | 1.00 |  |  |  |
| **Pulse Wave Velocity** | 0.36  (<0.01) | 0.43  (<0.01) | 1.00 |  |  |
| **Central Retinal Artery Equivalent** | -0.12  (0.01) | -0.05  (0.26) | -0.13  (0.01) | 1.00 |  |
| **Central Retinal Vein Equivalent** | -0.01  (0.82) | 0.08  (0.10) | -0.06  (0.25) | 0.57  (<0.01) | 1.00 |

**Figure S1:** Correlation graphs between cardiovascular measurements

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**Table S4.** Associations between covariates and cardiovascular measurements, using imputed data.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Covariate** | **Systolic Blood Pressure** | **Diastolic Blood Pressure** | **Pulse Wave Velocity** | **Central Retinal Artery Equivalent** | **Central Retinal Vein Equivalent** |
|  | *n=489* | *n=488* | *n=467* | *n=454* | *n=454* |
|  | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* |
| Age at cardiovascular measurement | 1.25 (-0.25, 2.75) | 0.26 (-0.99, 1.52) | -0.03 (-0.10, 0.04) | 0.84 (-1.13, 2.82) | -0.85 (-3.50, 1.80) |
| Sex male (vs female) | 1.96 (0.37, 3.55)\* | 0.11 (-1.23, 1.44) | 0.16 (0.09, 0.24)\* | -4.47 (-6.83, -2.11)\* | -4.11 (-7.28, -0.94)\* |
| Height at cardiovascular measurement | 0.43 (0.32, 0.55)\* | 0.17 (0.07, 0.26)\* | 0.02 (0.01, 0.02)\* | -- | -- |
| Gestational age at birth | -0.25 (-0.84, 0.35) | 0.08 (-0.42, 0.58) | -0.01 (-0.04, 0.02) | 0.96 (0.05, 1.86)\* | 0.19 (-1.02, 1.41) |
| Family SES middle (vs high) | 1.28 (-0.74, 3.30) | 0.90 (-0.82, 2.62) | 0.05 (-0.05, 0.15) | 0.03 (-2.99, 3.05) | 1.22 (-2.77, 5.21) |
| Family SES low (vs high) | 3.30 (1.28, 5.32)\* | 2.99 (1.27, 4.70)\* | 0.08 (-0.02, 0.18) | -0.57 (-3.58, 2.43) | 1.77 (-2.22, 5.75) |
| Smoking 1st trimester (vs none) | 0.54 (-1.88, 2.96) | 0.16 (-1.89, 2.21) | -0.05 (-0.17, 0.08) | -0.17 (-3.73, 3.38) | -0.84 (-5.45, 3.76) |
| Smoking 3rd trimester (vs none) | 2.51 (-0.11, 5.13)\* | 0.68 (-1.57, 2.92) | -0.01 (-0.13, 0.13) | -2.41 (-6.38, 1.57) | -0.26 (-5.55, 5.03) |
| Maternal prepregnancy BMI | 0.22 (0.03, 0.40)\* | 0.15 (-0.01, 0.30) | 0.01 (0.00, 0.02)\* | -0.07 (-0.34, 0.21) | 0.07 (-0.30, 0.44) |
| Paternal pregnancy BMI | 0.01 (-0.23, 0.25) | -0.05 (-0.25, 0.16) | -0.01 (-0.02, 0.00) | 0.20 (-0.17, 0.56) | 0.08 (-0.40, 0.57) |
| Parental CVD - 1 parent with 1+ diagnosis (vs no diagnosis) | -0.01 (1.71, 1.70) | 0.25 (-1.18, 1.68) | 0.09 (0.01, 0.18)\* | 1.72 (-0.82, 4.27) | 2.08 (-1.35, 5.50) |
| Parental CVD - both parents with 1+ diagnosis (vs no diagnosis) | 2.38 (-0.45, 5.21) | 1.82 (-0.55, 4.19) | 0.09 (-0.05, 0.23) | -2.34 (-6.55, 1.86) | -0.94 (-6.64, 4.76) |

Coefficients marked with \* are significant at p<0.05.

**Table S5.** Crude associations between BMI z-score trajectory class and cardiovascular measurements.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **BMI *z*-score trajectory** | **Systolic Blood Pressure** | **Diastolic Blood Pressure** | **Pulse Wave Velocity** | **Central Retinal Artery Equivalent** | **Central Retinal Vein Equivalent** |
|  | *n=489* | *n=488* | *n=467* | *n=454* | *n=454* |
|  | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* |
| Class 1:  higher birth size-accelerated BMI gain | 7.32 (4.37, 10.26)\* | 1.63 (-0.77, 4.03) | 0.14 (-0.01, 0.29) | -3.50 (-7.91, 0.90) | -1.64 (-7.47, 4.19) |
| Class 2:  higher birth size-slower BMI gain | 0.33 (-1.76, 2.41) | -0.55 (-2.26, 1.15) | -0.02 (-0.12, 0.08) | 1.89 (-1.19, 4.97) | -0.26 (-4.34, 3.82) |
| Class 3:  lower birth size-accelerated BMI gain | 9.30 (6.70, 11.90)\* | 4.71 (2.59, 6.83)\* | 0.26 (0.13, 0.39)\* | 0.29 (-3.49, 4.06) | 0.10 (-4.90, 5.10) |
| Class 4:  Average birth size- slower gain | Ref. | Ref. | Ref. | Ref. | Ref. |
| Class 5:  lower birth size-slower BMI gain | -1.14 (-3.68, 1.41) | -0.80 (-2.88, 1.27) | 0.07 (-0.05, 0.20) | 0.31 (-3.31, 3.92) | -1.56 (-6.36, 3.23) |

Coefficients marked with \* are significant at p<0.05.

**Table S6.** Adjusted associations between BMI z-score trajectory class and cardiovascular outcomes stratified by sex, *imputed*.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **BMI *z*-score trajectory** | **Systolic Blood Pressure** | **Diastolic Blood Pressure** | **Pulse Wave Velocity** | **Central Retinal Artery Equivalent** | **Central Retinal Vein Equivalent** |
|  | *Female; n=236*  *Male; n=253* | *Female; n=235*  *Male; n=253* | *Female; n=229*  *Male; n=238* | *Female; n=217*  *Male; n=237* | *Female; n=217*  *Male; n=237* |
|  | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* |
| Class 1: higher birth size-accelerated BMI gain  Female  Male | 7.08 (2.19, 11.97)\*  4.51 (0.62, 8.41)\* | -0.26 (-4.62, 4.09)  1.59 (-1.64, 4.83) | -0.22 (-0.46, 0.03)  0.16 (-0.04, 0.28) | 0.63 (-7.62, 8.87)  -4.69 (-10.34, 0.97) | 1.65 (-9.15, 12.44)  -3.77 (-11.58, 4.04) |
| Class 2: higher birth size-slower BMI gain  Female  Male | -1.66 (-4.26, 0.94)  1.69 (-1.42, 4.81) | -1.81 (-4.14, 0.52)  -0.22 (-2.80, 2.37) | -0.15 (0.28, -0.02)\*  0.12 (-0.04, 0.28) | 4.03 (-0.29, 8.35)  -1.33 (-5.85, 3.18) | 2.60 (-3.05, 8.26)  -5.92 (-12.16, 0.32) |
| Class 3: lower birth size-accelerated BMI gain  Female  Male | 5.65 (1.80, 9.51)\*  7.69 (4.07, 11.32)\* | 1.94 (-1.50, 5.38)  5.04 (2.03, 8.05)\* | -0.01 (-0.20, 0.18)  0.25 (0.07, 0.44)\* | 0.73 (-5.54, 7.01)  -0.53 (-5.51, 4.46) | 1.52 (-6.70, 9.74)  -2.52 (-9.42, 4.38) |
| Class 4: Average birth size- slower gain | Ref. | Ref. | Ref. | Ref. | Ref. |
| Class 5: lower birth size-slower BMI gain  Female  Male | -1.11, (-4.50, 2.29)  -2.05 (-5.53, 1.44) | -2.10 (-5.14, 0.94)  -0.37 (-3.26, 2.51) | 0.03 (-0.14, 0.19)  0.09 (-0.09, 0.28) | -0.08 (-5.53, 5.36)  1.04 (-3.81, 5.88) | -1.36 (-8.50, 5.77)  -1.96 (-8.67, 4.75) |

Coefficients marked with \* are significant at p<0.05.

Models using imputed data and adjusted for: child age at cardiovascular measurement, gestational age, family SES, maternal smoking (during pregnancy), maternal prepregnancy BMI, paternal BMI (during pregnancy), and parental cardiovascular history. Systolic blood pressure, diastolic blood pressure and pulse wave velocity were additionally adjusted for child´s height at cardiovascular measurement.

**Table S7.** Adjusted associations between BMI z-score trajectory class and systolic blood pressure, diastolic blood pressure and pulse wave velocity not adjusting for height, *imputed*.

|  |  |  |  |
| --- | --- | --- | --- |
| **BMI *z*-score trajectory** | **Systolic Blood Pressure** | **Diastolic Blood Pressure** | **Pulse Wave Velocity** |
|  | *n=489* | *n=488* | *n=467* |
|  | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* |
| Class 1:  higher birth size-accelerated BMI gain | 5.92 (2.88, 8.95)\* | 0.92 (-1.60, 3.45) | 0.06 (-0.09, 0.22) |
| Class 2:  higher birth size-slower BMI gain | -0.10 (-2.16, 1.95) | -0.95 (-2.66, 0.75) | -0.03 (-0.13, 0.08) |
| Class 3:  lower birth size-accelerated BMI gain | 8.38 (5.78, 10.97)\* | 4.27 (2.11, 6.43)\* | 0.21 (0.08, 0.34)\* |
| Class 4:  Average birth size- slower gain | Ref. | Ref. | Ref. |
| Class 5:  lower birth size-slower BMI gain | -1.26 (-3.75, 1.22) | -0.92 (-2.99, 1.15) | 0.05 (-0.08, 0.18) |

Coefficients marked with \* are significant at p<0.05.

Models using imputed data and adjusted for: child age at cardiovascular measurement, child sex, gestational age, family SES, maternal smoking (during pregnancy), maternal prepregnancy BMI, paternal BMI (during pregnancy), and parental cardiovascular history.

**Table S8.** Descriptive statistics for cardiovascular measures separated by those children with complete measurements and those with only partial.

|  |  |  |
| --- | --- | --- |
|  | **Complete Measurements** | **Partial Measurements** |
|  | mean (sd) *n* | mean (sd) *n* |
| Systolic Blood Pressurea | - | - |
| Diastolic Blood Pressureb | 59.9 (7.6) *486* | 60.5 (9.2) *2* |
| Pulse Wave Velocityc | 4.4 (0.4) *407* | 4.3 (0.5) *60* |
| Central Retinal Artery Equivalentd | 180.9 (12.7) *359* | 179.2 (13.6) *95* |
| Central Retinal Vein Equivalentd | 251.5 (16.8) *359* | 253.6 (17.9) *95* |
| a All children had two measures for systolic blood pressure.  b Two children had one usable measures for diastolic blood pressure.  c 60 children had less than three measures for pulse wave velocity.  d 95 children had only one usable measure or two measures with one being recorded as less than good quality. | | |

Coefficients marked with \* are significant at p<0.05.

**Table S9.** Adjusted associations between BMI z-score trajectory class and pulse wave velocity using only children with three measurements, and with CRAE and CRVE using only children with two good measurements, *imputed*.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **BMI *z*-score trajectory** | **Diastolic Blood Pressure** | **Pulse Wave Velocity** | **Central Retinal Artery Equivalent** | **Central Retinal Vein Equivalent** |
|  | *n=486* | *n=407* | *n=359* | *n=359* |
|  | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* |
| Class 1:  higher birth size-accelerated BMI gain | 0.47 (-2.07, 3.01) | 0.01 (-0.18, 0.15) | -2.43 (-7.70, 2.83) | 0.63 (-6.46, 7.71) |
| Class 2:  higher birth size-slower BMI gain | -1.08 (-2.79, 0.62) | -0.03 (-0.13, 0.08) | 2.37 (-0.99, 5.73) | 0.62 (-3.90, 5.15) |
| Class 3:  lower birth size-accelerated BMI gain | 3.59 (1.38, 5.80)\* | 0.15 (0.01, 0.29)\* | -0.25 (-4.49, 4.00) | 0.01 (-5.71, 5.71) |
| Class 4:  Average birth size- slower gain | Ref. | Ref. | Ref. | Ref. |
| Class 5:  lower birth size-slower BMI gain | -1.02 (-3.08, 1.04) | 0.02 (-0.11, 0.14) | 0.99 (-3.11, 5.09) | -0.53 (-6.05, 5.00) |

Coefficients marked with \* are significant at p<0.05.

Models using imputed data and adjusted for: child age at cardiovascular measurement, child sex, gestational age, family SES, maternal smoking (during pregnancy), maternal prepregnancy BMI, paternal BMI (during pregnancy), and parental cardiovascular history. Systolic blood pressure, diastolic blood pressure and pulse wave velocity were additionally adjusted for child´s height at cardiovascular measurement.

**Table S10.** Adjusted associations between BMI z-score trajectory class and cardiovascular outcomes, *complete case*.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **BMI *z*-score trajectory** | **Systolic Blood Pressure** | **Diastolic Blood Pressure** | **Pulse Wave Velocity** | **Central Retinal Artery Equivalent** | **Central Retinal Vein Equivalent** |
|  | *n=415* | *n=414* | *n=396* | *n=384* | *n=384* |
|  | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* |
| Class 1:  higher birth size-accelerated BMI gain | 5.21 (1.92, 8.51)\* | 1.05 (-1.77, 3.86) | 0.05 (-0.12, 0.22) | -2.01 (-7.04, 3.02) | -0.34 (-7.30, 6.63) |
| Class 2:  higher birth size-slower BMI gain | 0.09 (-2.11, 2.30) | -0.87 (-2.75, 1.01) | -0.03 (-0.14, 0.08) | 2.03 (-1.30, 5.36) | -0.44 (-5.06, 4.17) |
| Class 3:  lower birth size-accelerated BMI gain | 6.21 (3.39, 9.04)\* | 3.31 (0.90, 5.72)\* | 0.16 (0.01, 0.30)\* | 0.46 (-3.64, 4.56) | 0.20 (-5.49, 5.88) |
| Class 4:  Average birth size- slower gain | Ref. | Ref. | Ref. | Ref. | Ref. |
| Class 5:  lower birth size-slower BMI gain | -1.86 (-4.51, 0.80) | -0.84 (-3.11, 1.42) | 0.06 (-0.08, 0.19) | 0.66 (-3.22, 4.55) | -0.03 (-5.42, 5.35) |

Coefficients marked with \* are significant at p<0.05.

Models adjusted for: child age at cardiovascular measurement, child sex, gestational age, family SES, maternal smoking (during pregnancy), maternal prepregnancy BMI, paternal BMI (during pregnancy), and parental cardiovascular history. Systolic blood pressure, diastolic blood pressure and pulse wave velocity were additionally adjusted for child´s height at cardiovascular measurement.

**Table S11.** Adjusted associations between zBMI at 11 years and cardiovascular outcomes (cross-sectional), *imputed*.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Systolic Blood Pressure** | **Diastolic Blood Pressure** | **Pulse Wave Velocity** | **Central Retinal Artery Equivalent** | **Central Retinal Vein Equivalent** |
|  | *n=489* | *n=488* | *n=467* | *n=454* | *n=454* |
|  | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* | *β (95% CI)* |
| zBMI | 3.59 (2.92, 4.26)\* | 1.61 (1.00, 2.22)\* | 0.01 (-0.03, 0.04) | -0.52 (-1.57, 0.53) | 0.14 (-1.39, 1.42) |

Coefficients marked with \* are significant at p<0.05.

Models using imputed data and adjusted for: child age at cardiovascular measurement, child sex, gestational age, family SES, maternal smoking (during pregnancy), maternal prepregnancy BMI, paternal BMI (during pregnancy), and parental cardiovascular history.