

Supplementary Table S1: Spearman's rank correlation coefficients between DNAm z-score at LINE-1 CpG sites:

| | LINE-1 site 1 | LINE-1 site 2 | LINE-1 site 3 | LINE-1 site 4 |
|---------------|----------------|----------------|----------------|----------------|
| LINE-1 site 1 | | 0.69 (<0.0001) | 0.57 (<0.0001) | 0.31 (<0.0001) |
| LINE-1 site 2 | 0.69 (<0.0001) | | 0.79 (<0.0001) | 0.55 (<0.0001) |
| LINE-1 site 3 | 0.57(<0.0001) | 0.79 (<0.0001) | | 0.59 (<0.0001) |

Values presented are Spearman's rank correlation coefficients (*p*)

Supplementary Table S2: Spearman's rank correlation coefficients between DNAm z-score at *11β-HSD-2* CpG sites:

| | <i>11β-HSD-2</i> site 1 | <i>11β-HSD-2</i> site 2 | <i>11β-HSD-2</i> site 3 | <i>11β-HSD-2</i> site 4 | <i>11β-HSD-2</i> site 5 |
|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| <i>11β-HSD-2</i> site 1 | | 0.29 (<0.0001) | 0.69 (<0.0001) | -0.37 (<0.0001) | 0.16 (0.0131) |
| <i>11β-HSD-2</i> site 2 | 0.29 (<0.0001) | | 0.41 (<0.0001) | -0.08 (0.2556) | -0.03 (0.6497) |
| <i>11β-HSD-2</i> site 3 | 0.69 (<0.0001) | 0.41 (<0.0001) | | -0.27 (<0.0001) | 0.10 (0.1265) |
| <i>11β-HSD-2</i> site 4 | -0.37 (<0.0001) | -0.08 (0.2556) | -0.27 (<0.0001) | | -0.20 (0.0022) |

Values presented are Spearman's rank correlation coefficients (*p*)

Supplementary Table S3: Spearman's rank correlation coefficients between DNAm z-score at *H19* CpG sites:

| | <i>H19</i> site 1 | <i>H19</i> site 2 | <i>H19</i> site 3 | <i>H19</i> site 4 |
|-------------------|-------------------|-------------------|-------------------|-------------------|
| <i>H19</i> site 1 | | 0.26 (<0.0001) | 0.44 (<0.0001) | 0.94 (<0.0001) |
| <i>H19</i> site 2 | 0.26 (<0.0001) | | 0.84 (<0.0001) | 0.17 (<0.0001) |
| <i>H19</i> site 3 | 0.44 (<0.0001) | 0.84 (<0.0001) | | 0.37 (<0.0001) |

Values presented are Spearman's rank correlation coefficients (*p*)

Supplementary Table S4: Spearman's rank correlation coefficients between DNAm z-score at *PPAR-α* CpG sites:

| | |
|----------------------|----------------------|
| | <i>PPAR-α</i> site 2 |
| <i>PPAR-α</i> site 1 | 0.47 (<0.0001) |

Values presented are Spearman's rank correlation coefficients (*p*)

Supplementary Table S5: Associations between DNAm z-score at LINE- 1 and Repeated Measures of Cardiometabolic Risk Factors using Mixed-effects Models Adjusting for Pubertal Onset ($n=242$):

| | LINE-1 z-score at site 1 | | LINE-1 score at site 2 | | LINE-1 score at site 3 | | LINE-1 score at site 4 | |
|---|--------------------------|---------|------------------------|---------|------------------------|---------|------------------------|---------|
| | Estimate (SE) | P-value | Estimate (SE) | P-value | Estimate (SE) | P-value | Estimate (SE) | P-value |
| Waist circumference (cm) | | | | | | | | |
| (Total number of observations=441; of which 43 (17.77%) subjects had one measurement, and 199 (82.23%) subjects had two measurements) | | | | | | | | |
| Model 1 | -0.5960 (1.0435) | 0.5684 | 1.1418 (1.4217) | 0.4227 | -0.4783 (1.1510) | 0.6781 | 0.2997 (0.9013) | 0.7398 |
| Model 2 | 0.6325 (1.0098) | 0.5317 | 1.0269 (1.3678) | 0.4535 | -1.9266 (1.1252) | 0.0881 | 0.3154 (0.8699) | 0.7172 |
| Systolic blood pressure (mmHg) | | | | | | | | |
| (Total number of observations=441; of which 43 (17.77%) subjects had one measurement, and 199 (82.23%) subjects had two measurements) | | | | | | | | |
| Model 1 | -0.4560 (0.8541) | 0.5939 | -0.1855 (1.1698) | 0.8741 | 0.1632 (0.9435) | 0.8628 | 0.9703 (0.7361) | 0.1887 |
| Model 2 | -0.6264 (0.8602) | 0.4672 | 0.2907 (1.1720) | 0.8043 | -0.3020 (0.9613) | 0.7537 | 0.8606 (0.7375) | 0.2444 |
| Diastolic blood pressure (mmHg) | | | | | | | | |
| (Total number of observations=441; of which 43 (17.77%) subjects had one measurement, and 199 (82.23%) subjects had two measurements) | | | | | | | | |
| Model 1 | -0.5185 (0.5769) | 0.3697 | 0.1316 (0.7927) | 0.8682 | 0.2271 (0.6379) | 0.7221 | 0.3619 (0.4966) | 0.4669 |
| Model 2 | -0.4927 (0.5769) | 0.3940 | 0.1524 (0.7887) | 0.8469 | -0.09831 (0.6458) | 0.8791 | 0.3551 (0.4932) | 0.4723 |
| Log transformed fasting glucose (mg/dL) | | | | | | | | |
| (Total number of observations=438; of which 46 (19.01%) subjects had one measurement, and 196 (80.99%) subjects had two measurements) | | | | | | | | |
| Model 1 | -0.01570 (0.007838) | 0.0463 | 0.02427 (0.01086) | 0.0263 | -0.00357 (0.008708) | 0.6825 | -0.00361 (0.006726) | 0.5917 |
| Model 2 | -0.02747 (0.008217) | 0.0010* | 0.02862 (0.01124) | 0.0115 | 0.008495 (0.009213) | 0.3575 | -0.00145 (0.007023) | 0.8362 |
| Log transformed high-density lipoprotein cholesterol (mg/dL) | | | | | | | | |
| (Total number of observations=438; of which 46 (19.01%) subjects had one measurement, and 196 (80.99%) subjects had two measurements) | | | | | | | | |
| Model 1 | 0.02078 (0.01893) | 0.2733 | -0.02664 (0.02610) | 0.3083 | 0.01023 (0.02099) | 0.6265 | -0.01677 (0.01627) | 0.3039 |
| Model 2 | -0.00710 (0.02059) | 0.7305 | -0.02295 (0.02796) | 0.4127 | 0.04707 (0.02299) | 0.0417 | -0.00636 (0.01771) | 0.7197 |
| Log transformed triglycerides (mg/dL) | | | | | | | | |
| (Total number of observations=438; of which 46 (19.01%) subjects had one measurement, and 196 (80.99%) subjects had two measurements) | | | | | | | | |
| Model 1 | -0.05170 (0.04055) | 0.2035 | -0.03424 (0.05541) | 0.5372 | 0.05445 (0.04481) | 0.2255 | -0.00392 (0.03498) | 0.9109 |
| Model 2 | -0.02828 (0.03955) | 0.4752 | -0.04454 (0.05388) | 0.4093 | 0.05366 (0.04424) | 0.2263 | 0.009718 (0.03392) | 0.7747 |

- Long interspersed nuclear elements (LINE-1)
- Model 1 includes LINE-1 z-score at CpG site 1, 2, 3, and 4 as fixed effects, and compound symmetry matrix structure to model the covariance structure of the repeated measurements for each outcome
- Model 2 is additionally adjusted for the following fixed effects: age, sex, duration of breastfeeding, and pubertal onset

* $p < 0.008$

Supplementary Table S6: Associations between DNAm z-score at *11β-HSD-2* and Repeated Measures of Cardiometabolic Risk

Factors using Mixed-effects Models Adjusting for Pubertal Onset (*n*=229):

| | <i>11β-HSD-2</i> score at site 1 | | <i>11β-HSD-2</i> score at site 2 | | <i>11β-HSD-2</i> score at site 3 | | <i>11β-HSD-2</i> score at site 4 | | <i>11β-HSD-2</i> score at site 5 | |
|---|----------------------------------|---------|----------------------------------|---------|----------------------------------|---------|----------------------------------|---------|----------------------------------|---------|
| | Estimate (SE) | P-value | Estimate (SE) | P-value | Estimate (SE) | P-value | Estimate (SE) | P-value | Estimate (SE) | P-value |
| Waist circumference (cm) | | | | | | | | | | |
| (Total number of observations=415; of which 43 (18.78%) subjects had one measurement, and 186 (81.22%) subjects had two measurements) | | | | | | | | | | |
| Model 1 | -0.3822 (1.0424) | 0.7142 | -0.08657 (0.7980) | 0.9137 | 0.2635 (0.9701) | 0.7862 | 0.5264 (0.7690) | 0.4943 | 0.2132 (0.7252) | 0.7690 |
| Model 2 | -1.1584 (1.0033) | 0.2494 | 0.2359 (0.7715) | 0.7601 | 0.6570 (0.9358) | 0.4833 | 0.5122 (0.7455) | 0.4928 | -0.1516 (0.6976) | 0.8281 |
| Systolic blood pressure (mmHg) | | | | | | | | | | |
| (Total number of observations=415; of which 43(18.78%) subjects had one measurement, and 186 (81.22%) subjects had two measurements) | | | | | | | | | | |
| Model 1 | -1.6096 (0.8326) | 0.0545 | -0.7568 (0.6372) | 0.2362 | 1.2770 (0.7754) | 0.1010 | 0.3766 (0.6161) | 0.5416 | -0.4901 (0.5780) | 0.3974 |
| Model 2 | -1.6853 (0.8414) | 0.0464 | -0.6070 (0.6463) | 0.3487 | 1.6432 (0.7850) | 0.0375 | -0.2687 (0.6286) | 0.6695 | -0.4886 (0.5828) | 0.4027 |
| Diastolic blood pressure (mmHg) | | | | | | | | | | |
| (Total number of observations=415; of which 43 (18.78%) subjects had one measurement, and 186 (81.22%) subjects had two measurements) | | | | | | | | | | |
| Model 1 | -0.9251 (0.5519) | 0.0951 | -0.8601 (0.4222) | 0.0428 | 0.3540 (0.5143) | 0.4920 | 0.4535 (0.4092) | 0.2690 | -0.01360 (0.3827) | 0.9717 |
| Model 2 | -1.0194 (0.5506) | 0.0654 | -0.8295 (0.4225) | 0.0509 | 0.6060 (0.5139) | 0.2395 | 0.07628 (0.4130) | 0.8537 | -0.05509 (0.3803) | 0.8850 |
| Log transformed fasting glucose(mg/dL) | | | | | | | | | | |
| (Total number of observations=412; of which 46 (20.09%) subjects had one measurement, and 183 (79.91%) subjects had two measurements) | | | | | | | | | | |
| Model 1 | -0.00076 (0.007513) | 0.9193 | 0.001955 (0.005764) | 0.7348 | 0.006329 (0.006998) | 0.3668 | -0.01869 (0.005586) | 0.0010* | 0.002692 (0.005216) | 0.6064 |
| Model 2 | 0.007693 (0.007835) | 0.3273 | -0.00143 (0.006025) | 0.8121 | 0.004141 (0.007304) | 0.5713 | -0.02250 (0.005876) | 0.0002* | 0.006799 (0.005426) | 0.2116 |
| Log transformed high-density lipoprotein cholesterol (mg/dL) | | | | | | | | | | |
| (Total number of observations=412; of which 46 (20.09%) subjects had one measurement, and 183 (79.91%) subjects had two measurements) | | | | | | | | | | |
| Model 1 | 0.002550 (0.01874) | 0.8919 | -0.00550 (0.01438) | 0.7026 | -0.00829 (0.01745) | 0.6351 | -0.01132 (0.01390) | 0.4161 | 0.005434 (0.01303) | 0.6770 |
| Model 2 | 0.02022 (0.02000) | 0.3132 | -0.01804 (0.01539) | 0.2423 | -0.01149 (0.01865) | 0.5386 | -0.02960 (0.01489) | 0.0481 | 0.01555 (0.01390) | 0.2645 |
| Log transformed triglycerides (mg/dL) | | | | | | | | | | |
| (Total number of observations=412; of which 46 (20.09%) subjects had one measurement, and 183 (79.91%) subjects had two measurements) | | | | | | | | | | |

| | | | | | | | | | | |
|----------------|----------------------|--------|----------------------|--------|--------------------|--------|----------------------|--------|--------------------|--------|
| Model 1 | 0.02425 (0.04126) | 0.5572 | 0.03580 (0.03163) | 0.2588 | 0.004623 (0.03838) | 0.9042 | 0.01794 (0.03047) | 0.5566 | -0.00972 (0.02872) | 0.7354 |
| Model 2 | 0.01567 (0.04011) | 0.6964 | 0.03023 (0.03086) | 0.3282 | 0.008336 (0.03740) | 0.8238 | 0.02187 (0.02995) | 0.4660 | -0.01640 (0.02784) | 0.5564 |

- 11 β -hydroxysteroid dehydrogenase type 2 (*11 β -HSD-2*)
- Model 1 includes *11 β -HSD-2* z-scores for CpG sites 1, 2, 3, 4, and 5 as fixed effects and compound symmetry matrix structure to model the covariance structure of the repeated measurements for each outcome
- Model 2 is additionally adjusted for the following fixed effects: age, sex, and pubertal onset

* $p < 0.008$

Supplementary Table S7: Associations between DNAm z-score at *H19* and Repeated Measures of Cardiometabolic Risk Factors using Mixed-effects Models ($n=245$):

| | <i>H19</i> score at site 1 | | <i>H19</i> score at site 2 | | <i>H19</i> score at site 3 | | <i>H19</i> score at site 4 | |
|---|----------------------------|---------|----------------------------|---------|----------------------------|---------|----------------------------|---------|
| | Estimate (SE) | P-value | Estimate (SE) | P-value | Estimate (SE) | P-value | Estimate (SE) | P-value |
| Waist circumference (cm) | | | | | | | | |
| (Total number of observations=446; of which 44 (17.96%) subjects had one measurement, and 201 (82.04%) subjects had two measurements) | | | | | | | | |
| Model 1 | -2.0199 (2.3712) | 0.3951 | 0.4201 (0.9290) | 0.6515 | -0.1023 (1.0516) | 0.9226 | 1.7246 (2.3175) | 0.4575 |
| Model 2 | -0.4958 (2.2859) | 0.8285 | 0.07485 (0.9050) | 0.9342 | -0.01468 (1.0179) | 0.9885 | 1.0578 (2.2350) | 0.6364 |
| Systolic blood pressure (mmHg) | | | | | | | | |
| (Total number of observations=446; of which 44 (17.96%) subjects had one measurement, and 201 (82.04%) subjects had two measurements) | | | | | | | | |
| Model 1 | 2.9254 (1.9347) | 0.1318 | 0.5769 (0.7460) | 0.4402 | -0.3888 (0.8519) | 0.6485 | -2.0551 (1.8928) | 0.2786 |
| Model 2 | 2.1289 (2.0092) | 0.2905 | 0.6308 (0.7785) | 0.4188 | -0.3848 (0.8852) | 0.6643 | -1.4683 (1.9667) | 0.4561 |
| Diastolic blood pressure (mmHg) | | | | | | | | |
| (Total number of observations=446; of which 44 (17.96%) subjects had one measurement, and 201 (82.04%) subjects had two measurements) | | | | | | | | |
| Model 1 | 1.9218 (1.3080) | 0.1430 | 0.07059 (0.5004) | 0.8880 | -0.1770 (0.5740) | 0.7580 | -1.1655 (1.2803) | 0.3635 |
| Model 2 | 1.7656 (1.3295) | 0.1855 | 0.07927 (0.5086) | 0.8763 | -0.1730 (0.5822) | 0.7667 | -1.0460 (1.3026) | 0.4228 |
| Log transformed fasting glucose(mg/dL) | | | | | | | | |
| (Total number of observations=443; of which 47 (19.18%) subjects had one measurement, and 198 (80.82%) subjects had two measurements) | | | | | | | | |
| Model 1 | -0.00046 (0.01808) | 0.9796 | 0.002770 (0.006771) | 0.6829 | 0.004283 (0.007883) | 0.5875 | -0.00728 (0.01773) | 0.6816 |
| Model 2 | -0.01426 (0.01900) | 0.4536 | 0.006626 (0.007262) | 0.3627 | 0.001784 (0.008333) | 0.8307 | -0.00365 (0.01861) | 0.8448 |
| Log transformed high-density lipoprotein cholesterol (mg/dL) | | | | | | | | |
| (Total number of observations=443; of which 47 (19.18%) subjects had one measurement, and 198 (80.82%) subjects had two measurements) | | | | | | | | |
| Model 1 | 0.08297 (0.04325) | 0.0562 | -0.00522 (0.01640) | 0.7507 | -0.00854 (0.01895) | 0.6527 | -0.09188 (0.04237) | 0.0311 |
| Model 2 | 0.04381 (0.04758) | 0.3582 | 0.009569 (0.01869) | 0.6091 | -0.01912 (0.02112) | 0.3663 | -0.08270 (0.04654) | 0.0769 |
| Log transformed triglycerides (mg/dL) | | | | | | | | |
| (Total number of observations=443; of which 47 (19.18%) subjects had one measurement, and 198 (80.82%) subjects had two measurements) | | | | | | | | |
| Model 1 | -0.09145 (0.09240) | 0.3233 | 0.03856 (0.03589) | 0.2838 | -0.02407 (0.04087) | 0.5566 | 0.1266 (0.09037) | 0.1626 |
| Model 2 | -0.04746 (0.08976) | 0.5975 | 0.03792 (0.03481) | 0.2772 | -0.02790 (0.03962) | 0.4820 | 0.09088 (0.08786) | 0.3020 |

- Model 1 includes *H19* z-scores for CpG site 1, 2, 3, and 4 as fixed effects, and compound symmetry matrix structure to model the covariance structure of the repeated measurements for each outcome

- Model 2 is additionally adjusted for the following fixed effects: age and sex

* $p < 0.008$

Supplementary Table S8: Associations between DNAm z-score at *H19* and Repeated Measures of Cardiometabolic Risk Factors using Mixed-effects Models after Removing Outlier DNAm Value ($n=244$):

| | <i>H19</i> score at site 1 | | <i>H19</i> score at site 2 | | <i>H19</i> score at site 3 | | <i>H19</i> score at site 4 | |
|---|----------------------------|---------|----------------------------|---------|----------------------------|---------|----------------------------|---------|
| | Estimate (SE) | P-value | Estimate (SE) | P-value | Estimate (SE) | P-value | Estimate (SE) | P-value |
| Waist circumference (cm) | | | | | | | | |
| (Total number of observations=444; of which 44 (18.03%) subjects had one measurement, and 200 (81.97%) subjects had two measurements) | | | | | | | | |
| Model 1 | -1.9711 (2.3738) | 0.4072 | 1.7287 (1.9031) | 0.3646 | -0.9859 (1.5380) | 0.5221 | 1.8050 (2.3215) | 0.4376 |
| Model 2 | -0.4707 (2.2913) | 0.8374 | 0.5902 (1.8478) | 0.7497 | -0.3633 (1.4905) | 0.8076 | 1.0906 (2.2422) | 0.6271 |
| Systolic blood pressure (mmHg) | | | | | | | | |
| (Total number of observations=444; of which 44 (18.03%) subjects had one measurement, and 200 (81.97%) subjects had two measurements) | | | | | | | | |
| Model 1 | 2.9096 (1.9392) | 0.1348 | 0.1319 (1.5394) | 0.9318 | -0.08892 (1.2463) | 0.9432 | -2.0820 (1.8985) | 0.2739 |
| Model 2 | 2.1309 2.0126 | 0.2909 | 0.5685 (1.6014) | 0.7230 | -0.3428 (1.2944) | 0.7914 | -1.4729 (1.9721) | 0.4559 |
| Diastolic blood pressure (mmHg) | | | | | | | | |
| (Total number of observations=444; of which 44 (18.03%) subjects had one measurement, and 200 (81.97%) subjects had two measurements) | | | | | | | | |
| Model 1 | 1.9019 (1.3105) | 0.1480 | -0.5299 (1.0351) | 0.6092 | 0.2280 (0.8388) | 0.7860 | -1.2025 (1.2836) | 0.3498 |
| Model 2 | 1.7543 (1.3311) | 0.1889 | -0.4459 (1.0506) | 0.6717 | 0.1809 (0.8503) | 0.8317 | -1.0820 (1.3054) | 0.4081 |
| Log transformed fasting glucose(mg/dL) | | | | | | | | |
| (Total number of observations=441; of which 47 (19.26%) subjects had one measurement, and 197 (80.74%) subjects had two measurements) | | | | | | | | |
| Model 1 | -0.00042 (0.01812) | 0.9813 | 0.004047 (0.01413) | 0.7749 | 0.003419 (0.01151) | 0.7667 | -0.00720 (0.01778) | 0.6859 |
| Model 2 | -0.01405 (0.01903) | 0.4610 | 0.01456 (0.01502) | 0.3333 | -0.00357 (0.01217) | 0.7696 | -0.00310 (0.01866) | 0.8684 |
| Log transformed high-density lipoprotein cholesterol (mg/dL) | | | | | | | | |
| (Total number of observations=441; of which 47 (19.26%) subjects had one measurement, and 197 (80.74%) subjects had two measurements) | | | | | | | | |
| Model 1 | 0.08260 (0.04335) | 0.0579 | -0.01677 (0.03406) | 0.6229 | -0.00074 (0.02769) | 0.9788 | -0.09260 (0.04249) | 0.0303 |
| Model 2 | 0.04405 (0.04770) | 0.3568 | 0.01789 (0.03828) | 0.6407 | -0.02474 (0.03092) | 0.4245 | -0.08213 (0.04670) | 0.0799 |
| Log transformed triglycerides (mg/dL) | | | | | | | | |
| (Total number of observations=441; of which 47 (19.26%) subjects had one measurement, and 197 (80.74%) subjects had two measurements) | | | | | | | | |
| Model 1 | -0.08894 (0.09237) | 0.3365 | 0.1086 (0.07369) | 0.1420 | -0.07136 (0.05967) | 0.2329 | 0.1309 (0.09040) | 0.1488 |
| Model 2 | -0.04632 (0.08982) | 0.6066 | 0.08574 (0.07154) | 0.2319 | -0.06016 (0.05788) | 0.2997 | 0.09421 (0.08801) | 0.2854 |

- Model 1 includes *H19* z-scores for CpG site 1, 2, 3, and 4 as fixed effects, and compound symmetry matrix structure to model the covariance structure of the repeated measurements for each outcome
 - Model 2 is additionally adjusted for the following fixed effects: age and sex
- * $p < 0.008$

Supplementary Table S9: Associations between DNAm z-score at *H19* and Repeated Measures of Cardiometabolic Risk Factors using Mixed-effects Models Adjusting for Pubertal Onset ($n=245$):

| | <i>H19</i> score at site 1 | | <i>H19</i> score at site 2 | | <i>H19</i> score at site 3 | | <i>H19</i> score at site 4 | |
|---|----------------------------|---------|----------------------------|---------|----------------------------|---------|----------------------------|---------|
| | Estimate (SE) | P-value | Estimate (SE) | P-value | Estimate (SE) | P-value | Estimate (SE) | P-value |
| Waist circumference (cm) | | | | | | | | |
| (Total number of observations=446; of which 44 (17.96%) subjects had one measurement, and 201 (82.04%) subjects had two measurements) | | | | | | | | |
| Model 1 | -2.0199 (2.3712) | 0.3951 | 0.4201 (0.9290) | 0.6515 | -0.1023 (1.0516) | 0.9226 | 1.7246 (2.3175) | 0.4575 |
| Model 2 | -0.4601 (2.2842) | 0.8405 | 0.1017 (0.9050) | 0.9106 | 0.02333 (1.0184) | 0.9817 | 1.0305 (2.2331) | 0.6449 |
| Systolic blood pressure (mmHg) | | | | | | | | |
| (Total number of observations=446; of which 44 (17.96%) subjects had one measurement, and 201 (82.04%) subjects had two measurements) | | | | | | | | |
| Model 1 | 2.9254 (1.9347) | 0.1318 | 0.5769 (0.7460) | 0.4402 | -0.3888 (0.8519) | 0.6485 | -2.0551 (1.8928) | 0.2786 |
| Model 2 | 2.2231 (1.9256) | 0.2495 | 0.8875 (0.7469) | 0.2360 | -0.1066 (0.8494) | 0.9003 | -1.6144 (1.8851) | 0.3926 |
| Diastolic blood pressure (mmHg) | | | | | | | | |
| (Total number of observations=446; of which 44 (17.96%) subjects had one measurement, and 201 (82.04%) subjects had two measurements) | | | | | | | | |
| Model 1 | 1.9218 (1.3080) | 0.1430 | 0.07059 (0.5004) | 0.8880 | -0.1770 (0.5740) | 0.7580 | -1.1655 (1.2803) | 0.3635 |
| Model 2 | 1.7623 (1.2916) | 0.1737 | 0.2580 (0.4953) | 0.6030 | -0.01024 (0.5665) | 0.9856 | -1.1167 (1.2655) | 0.3784 |
| Log transformed fasting glucose(mg/dL) | | | | | | | | |
| (Total number of observations=443; of which 47 (19.18%) subjects had one measurement, and 198 (80.82%) subjects had two measurements) | | | | | | | | |
| Model 1 | -0.00046 (0.01808) | 0.9796 | 0.002770 (0.006771) | 0.6829 | 0.004283 (0.007883) | 0.5875 | -0.00728 (0.01773) | 0.6816 |
| Model 2 | -0.01454 (0.01894) | 0.4434 | 0.008114 (0.007262) | 0.2652 | 0.003016 (0.008321) | 0.7174 | -0.00410 (0.01855) | 0.8254 |
| Log transformed high-density lipoprotein cholesterol (mg/dL) | | | | | | | | |
| (Total number of observations=443; of which 47 (19.18%) subjects had one measurement, and 198 (80.82%) subjects had two measurements) | | | | | | | | |
| Model 1 | 0.08297 (0.04325) | 0.0562 | -0.00522 (0.01640) | 0.7507 | -0.00854 (0.01895) | 0.6527 | -0.09188 (0.04237) | 0.0311 |
| Model 2 | 0.04758 (0.04618) | 0.3039 | 0.01380 (0.01815) | 0.4478 | -0.01387 (0.02052) | 0.4996 | -0.08614 (0.04517) | 0.0577 |
| Log transformed triglycerides (mg/dL) | | | | | | | | |
| (Total number of observations=443; of which 47 (19.18%) subjects had one measurement, and 198 (80.82%) subjects had two measurements) | | | | | | | | |
| Model 1 | -0.09145 (0.09240) | 0.3233 | 0.03856 (0.03589) | 0.2838 | -0.02407 (0.04087) | 0.5566 | 0.1266 (0.09037) | 0.1626 |
| Model 2 | -0.04758 (0.08978) | 0.5966 | 0.03750 (0.03488) | 0.2834 | -0.02833 (0.03968) | 0.4760 | 0.09109 (0.08788) | 0.3010 |

- Model 1 includes *H19* z-scores for CpG site 1, 2, 3, and 4 as fixed effects, and compound symmetry matrix structure to model the covariance structure of the repeated measurements for each outcome

- Model 2 is additionally adjusted for the following fixed effects: age, sex, and pubertal onset

* $p < 0.008$

Supplementary Table S10: Cross-sectional Associations between DNAm z-score at *PPAR-α* and Cardiometabolic Risk Factors using Linear Regression Adjusting for Pubertal Onset ($n=345$):

| | <i>PPAR-α</i> score at site 1 | | <i>PPAR-α</i> score at site 2 | |
|--|-------------------------------|---------|-------------------------------|---------|
| | Estimate (SE) | P-value | Estimate (SE) | P-value |
| Waist circumference (cm) (N= 345) | | | | |
| Model 1 | 0.71915 (0.71474) | 0.3150 | -1.70941 (0.65445) | 0.0094 |
| Model 2 | 1.01378 (0.70496) | 0.1513 | -1.69631 (0.64590) | 0.0090 |
| Systolic blood pressure (mmHg) (N= 345) | | | | |
| Model 1 | 0.58582 (0.60305) | 0.3320 | -1.02922 (0.55218) | 0.0632 |
| Model 2 | 0.50301 (0.58038) | 0.3867 | -0.67188 (0.53176) | 0.2073 |
| Diastolic blood pressure (mmHg) (N= 345) | | | | |
| Model 1 | 0.58530 (0.42242) | 0.1668 | -0.57466 (0.38679) | 0.1383 |
| Model 2 | 0.59009 (0.40685) | 0.1479 | -0.34991 (0.37276) | 0.3486 |
| Log transformed fasting glucose (mg/dL) (N=310) | | | | |
| Model 1 | 0.00598 (0.00614) | 0.3305 | 0.00016627 (0.00600) | 0.9779 |
| Model 2 | 0.00293 (0.00609) | 0.6309 | 0.00134 (0.00595) | 0.8216 |
| Log transformed high-density lipoprotein cholesterol (mg/dL) (N= 310) | | | | |
| Model 1 | -0.00813 (0.01303) | 0.5329 | 0.01206 (0.01273) | 0.3445 |
| Model 2 | -0.00404 (0.01310) | 0.7577 | 0.00824 (0.01281) | 0.5205 |
| Log transformed triglycerides (mg/dL) (N= 310) | | | | |
| Model 1 | 0.01232 (0.03058) | 0.6873 | 0.00118 (0.02989) | 0.9684 |
| Model 2 | 0.02099 (0.03062) | 0.4936 | -0.01145 (0.02995) | 0.7026 |

- Peroxisome proliferator-activated receptor alpha (*PPAR-α*).
- Model 1 includes *PPAR-α* z-scores for CpG site 1 and 2
- Model 2 is additionally adjusted for age, sex, and pubertal onset

* $p < 0.008$

Supplementary Table S11: Primer Sequences and Details of CpG Sites Assessed ¹:

| Gene or Element Name | # of CpG Sites Assessed | Loci of CpG Sites ^a | Primer Sequences | | | Locus of Amplified Region |
|----------------------|-------------------------|---|--------------------------------|----------------------------------|-------------------------|------------------------------|
| | | | Forward | Reverse ^b | Sequencing | |
| LINE-1 | 4 | Various ^c | TTGAGTTAGGTGTGG GATATAGTT | CAAAAAATCAAAAAAT TCCCTTTCC | AGGTGTGGAT ATAGT | Various ³ |
| <i>11β-HSD-2</i> | 5 | chr16: 67430541, 67430543, 67430562, 67430564, and 67430580 | TTAAGTTTTGGAAGG AAAGGGAAAGA | ACATCCCCATACCCTTT ACTAATC | AGTTTTTGTTT TAGGTAGG | chr16: 67430512- 67430745 |
| <i>H19</i> | 4 | chr11: 2003031, 2003029, 2003027, and 2003024 | TTTGTTGATTTTATTA AGGGAG | CTATAAATAAACCCCA ACCAAAC | GTGTGGAATT AGAAGT | chr11: 2002966- 2003111 |
| <i>PPAR-α</i> | 2 | chr22: 46149160 and 46149179 | GGAGGTTTTTATGAG GATGTAGTT | ACACATATTAACCAAC AATAACTATCAT | GGATGTGGTT GTTTG | chr22: 46149046- 46149244 |

Notes:

a. Loci are based off genome build GRCh38/hg38

b. All reverse primers for pyrosequencing are 5'biotinylated.

c. A consensus sequence found in all LINE-1s (located throughout the genome) is amplified and sequenced here. The specific sequence is as follows: 5'-

CTCGTG GTGCGCCGTTTCTTAAGCCG

Long interspersed nuclear elements (LINE-1); 11β-hydroxysteroid dehydrogenase type 2 (*11β-HSD-2*); Peroxisome proliferator-activated receptor alpha (*PPAR-α*).

Supplementary Table S12: Average DNAm z-score at LINE-1¹ and Confounders Selection:

| | Average DNAm z-score at LINE-1 | | | | P-value |
|--|--------------------------------|---------------------|----------------------|----------------------|---------|
| | Q 1 <i>n</i> = 59 | Q 2 <i>n</i> =61 | Q 3 <i>n</i> = 61 | Q 4 <i>n</i> = 61 | |
| Maternal Characteristics (at time of child’s birth) | | | | | |
| Years of education, % | | | | | 0.1872 |
| < 12 years | 55.93 | 47.54 | 37.70 | 55.74 | |
| 12 years | 25.42 | 40.98 | 45.90 | 34.43 | |
| > 12 years | 18.64 | 11.48 | 16.39 | 9.84 | |
| Age at childbirth, (years) | 26.83 | 27.07 | 25.93 | 27.39 | 0.5188 |
| Parity, % | | | | | 0.1721 |
| 1 | 33.90 | 31.15 | 47.54 | 36.07 | |
| 2 | 33.90 | 44.26 | 36.07 | 29.51 | |
| ≥ 3 | 32.20 | 24.59 | 16.39 | 34.43 | |
| Marital Status, % | | | | | 0.1149 |
| Married | 59.32 | 72.13 | 73.77 | 78.69 | |
| Others (includes free union, single, separated, or divorced) | 40.68 | 27.87 | 26.23 | 21.31 | |
| Enrollment in calcium supplementation study, % | | | | | 0.4494 |
| Not enrolled | 59.32 | 57.38 | 70.49 | 60.66 | |
| Enrolled during pregnancy | 40.68 | 42.62 | 29.51 | 39.34 | |
| Child Characteristics (at birth) | | | | | |
| Female, % | 70.00 | 52.46 | 52.46 | 39.34 | 0.0092* |
| Gestation age, (weeks) | 38.81 | 38.82 | 38.97 | 38.75 | 0.9037 |
| Mode of delivery, % | | | | | 0.3939 |
| Vaginal delivery | 50.85 | 55.74 | 55.74 | 66.10 | |
| C Section | 49.15 | 44.26 | 44.26 | 33.90 | |
| Birth weight, (kg) | 3.15 | 3.13 | 3.20 | 3.13 | 0.8137 |
| Breastfeeding duration, (weeks) | 6.41 | 8.23 | 9.57 | 8.44 | 0.0171* |
| Child Characteristics (at follow-up visits) | | | | | |
| Age, (years) | 9.65 | 10.32 | 10.73 | 10.63 | 0.0003* |
| Metabolic equivalents, (METs/week) | 31.24 | 29.92 | 32.39 | 31.58 | 0.9341 |
| Pubertal onset, % | 25.00 | 44.26 | 57.38 | 42.62 | 0.0044* |
| Total caloric intake, (kcal/day) | 2617.89 | 2778.31 | 2576.08 | 2578.95 | 0.3748 |

¹ Average DNAm at LINE-1 was computed as the average LINE-1 z-score at CpG site 1, 2, 3, and 4.

Means or percentages are presented for continuous or categorical variables, respectively.

Long interspersed nuclear elements (LINE-1)

* $p < 0.05$

Supplementary Table S13: Average DNAm z-score at *11β-HSD-2*¹ and Confounders Selection:

| | Average DNAm z-score at <i>11β-HSD-2</i> | | | | P-value |
|--|--|----------------------|----------------------|----------------------|---------|
| | Q 1 <i>n</i> = 61 | Q 2 <i>n</i> = 62 | Q 3 <i>n</i> = 62 | Q 4 <i>n</i> = 61 | |
| Maternal Characteristics (at time of child’s birth) | | | | | |
| Years of education, % | | | | | 0.3280 |
| < 12 years | 55.74 | 48.39 | 46.77 | 45.90 | |
| 12 years | 32.79 | 45.16 | 33.87 | 34.43 | |
| > 12 years | 11.48 | 6.45 | 17.74 | 19.67 | |
| Age at childbirth, (years) | 26.62 | 26.97 | 27.16 | 26.67 | 0.9460 |
| Parity, % | | | | | 0.6075 |
| 1 | 34.43 | 38.71 | 29.03 | 44.26 | |
| 2 | 40.98 | 32.26 | 41.94 | 29.51 | |
| ≥ 3 | 24.59 | 29.03 | 27.42 | 26.23 | |
| Marital Status, % | | | | | 0.5323 |
| Married | 72.13 | 64.52 | 72.58 | 75.41 | |
| Others (includes free union, single, separated, or divorced) | 27.87 | 35.48 | 25.81 | 24.59 | |
| Enrollment in calcium supplementation study, % | | | | | 0.6592 |
| Not enrolled | 57.38 | 66.13 | 62.90 | 60.66 | |
| Enrolled during pregnancy | 42.62 | 33.87 | 35.48 | 39.34 | |
| Child Characteristics (at birth) | | | | | |
| Female, % | 50.82 | 56.45 | 51.61 | 54.10 | 0.9223 |
| Gestation age, (weeks) | 38.83 | 39.13 | 38.52 | 38.90 | 0.1080 |
| Mode of delivery, % | | | | | 0.8987 |
| Vaginal delivery | 52.46 | 61.29 | 59.68 | 54.10 | |
| C Section | 45.90 | 38.71 | 38.71 | 44.26 | |
| Birth weight, (kg) | 3.16 | 3.15 | 3.11 | 3.18 | 0.8933 |
| Breastfeeding duration, (weeks) | 8.13 | 7.40 | 8.46 | 8.61 | 0.7751 |
| Child Characteristics (at follow-up visits) | | | | | |
| Age, (years) | 9.90 | 10.64 | 10.50 | 10.30 | 0.0466* |
| Metabolic equivalents, (METs/week) | 29.31 | 29.89 | 34.25 | 32.04 | 0.5216 |
| Pubertal onset, % | 36.07 | 48.39 | 45.16 | 37.70 | 0.4510 |
| Total caloric intake, (kcal/day) | 2811.31 | 2640.92 | 2514.23 | 2580.73 | 0.1279 |

¹ Average DNAm at *11β-HSD-2* was computed as the average *11β-HSD-2* z-score at CpG site 1, 2, 3, 4 and 5.

Means or percentages are presented for continuous or categorical variables, respectively.

11β-hydroxysteroid dehydrogenase type 2 (*11β-HSD-2*)

* $p < 0.05$

Supplementary Table S14: Average DNAm z-score at *H19*¹ and Confounders Selection:

| | Average DNAm z-score at <i>H19</i> | | | | P-value |
|--|------------------------------------|----------------------|----------------------|----------------------|---------|
| | Q 1 <i>n</i> = 61 | Q 2 <i>n</i> = 61 | Q 3 <i>n</i> = 62 | Q 4 <i>n</i> = 61 | |
| Maternal Characteristics (at time of child's birth) | | | | | |
| Years of education, % | | | | | 0.8105 |
| < 12 years | 47.54 | 44.26 | 51.61 | 52.46 | |
| 12 years | 37.70 | 42.62 | 35.48 | 31.15 | |
| > 12 years | 14.75 | 13.11 | 11.29 | 16.39 | |
| Age at childbirth, (years) | 26.48 | 26.69 | 26.98 | 27.07 | 0.9340 |
| Parity, % | | | | | 0.0663 |
| 1 | 49.18 | 31.15 | 32.26 | 34.43 | |
| 2 | 27.87 | 42.62 | 27.42 | 45.90 | |
| ≥ 3 | 22.95 | 26.23 | 38.71 | 19.67 | |
| Marital Status, % | | | | | 0.1071 |
| Married | 75.41 | 80.33 | 69.35 | 59.02 | |
| Others (includes free union, single, separated, or divorced) | 24.59 | 19.67 | 29.03 | 40.98 | |
| Enrollment in calcium supplementation study, % | | | | | 0.7226 |
| Not enrolled | 63.93 | 65.57 | 58.06 | 60.66 | |
| Enrolled during pregnancy | 36.07 | 34.43 | 40.32 | 39.34 | |
| Child Characteristics (at birth) | | | | | |
| Female, % | 49.18 | 52.46 | 50.00 | 60.66 | 0.5675 |
| Gestation age, (weeks) | 38.82 | 38.71 | 38.89 | 38.95 | 0.6168 |
| Mode of delivery, % | | | | | 0.6757 |
| Vaginal delivery | 62.30 | 59.02 | 58.06 | 47.54 | |
| C Section | 36.07 | 40.98 | 40.32 | 50.82 | |
| Birth weight, (kg) | 3.20 | 3.13 | 3.10 | 3.18 | 0.5830 |
| Breastfeeding duration, (weeks) | 9.43 | 8.38 | 6.89 | 8.03 | 0.0799 |
| Child Characteristics (at follow-up visits) | | | | | |
| Age, (years) | 10.59 | 10.65 | 10.28 | 9.86 | 0.0140* |
| Metabolic equivalents, (METs/week) | 34.89 | 28.64 | 32.34 | 29.74 | 0.2589 |
| Pubertal onset, % | 47.54 | 40.98 | 48.39 | 31.15 | 0.1886 |
| Total caloric intake, (kcal/day) | 2581.31 | 2483.39 | 2709.46 | 2770.89 | 0.2434 |

¹ Average DNAm at *H19* was computed as the average *H19* z-score at CpG site 1, 2, 3, and 4.

Means or percentages are presented for continuous or categorical variables, respectively

* $p < 0.05$

Supplementary Table S15: Average DNAm z-score at *PPAR-α*¹ and Confounders Selection:

| | Average DNAm z-score at <i>PPAR-α</i> | | | | |
|--|---------------------------------------|----------------------|----------------------|----------------------|---------|
| | Q 1 <i>n</i> = 89 | Q 2 <i>n</i> = 89 | Q 3 <i>n</i> = 91 | Q 4 <i>n</i> = 89 | P-value |
| Maternal Characteristics (at time of child’s birth) | | | | | |
| Years of education, % | | | | | |
| < 12 years | 43.82 | 58.43 | 49.45 | 53.93 | 0.0766 |
| 12 years | 40.45 | 29.21 | 42.86 | 26.97 | |
| > 12 years | 15.73 | 12.36 | 6.59 | 19.10 | |
| Age at childbirth, (years) | 26.38 | 27.04 | 26.36 | 25.93 | 0.5899 |
| Parity, % | | | | | |
| 1 | 44.94 | 37.08 | 40.66 | 32.58 | 0.1289 |
| 2 | 34.83 | 28.09 | 35.16 | 46.07 | |
| ≥ 3 | 20.22 | 34.83 | 23.08 | 21.35 | |
| Marital Status, % | | | | | |
| Married | 76.40 | 78.65 | 70.33 | 65.17 | 0.2510 |
| Others (includes free union, single, separated, or divorced) | 23.60 | 21.35 | 28.57 | 34.83 | |
| Enrollment in calcium supplementation study, % | | | | | |
| Not enrolled | 76.40 | 67.42 | 65.93 | 64.04 | 0.3655 |
| Enrolled during pregnancy | 23.60 | 32.58 | 32.97 | 35.96 | |
| Child Characteristics (at birth) | | | | | |
| Female, % | 51.69 | 44.94 | 52.75 | 57.30 | 0.4259 |
| Gestation age, (weeks) | 38.78 | 38.70 | 39.03 | 38.62 | 0.3877 |
| Mode of delivery, % | | | | | |
| Vaginal delivery | 58.43 | 49.44 | 61.54 | 65.17 | 0.3060 |
| C Section | 40.45 | 50.56 | 37.36 | 34.83 | |
| Birth weight, (kg) | 3.09 | 3.16 | 3.18 | 3.18 | 0.6758 |
| Breastfeeding duration, (weeks) | 8.20 | 9.12 | 7.41 | 7.75 | 0.1482 |
| Child Characteristics (at follow-up visits) | | | | | |
| Age, (years) | 14.49 | 14.39 | 13.84 | 13.73 | 0.0318* |
| Metabolic equivalents, (METs/week) | 60.98 | 65.32 | 54.85 | 61.38 | 0.1592 |
| Pubertal onset, % | 92.13 | 94.38 | 92.31 | 92.13 | 0.9824 |
| Total caloric intake, (kcal/day) | 2423.71 | 2562.43 | 2144.12 | 2315.97 | 0.1417 |

¹ Average DNAm at *PPAR-α* was computed as the average *PPAR-α* z-score at CpG site 1, and 2.

Means or percentages are presented for continuous or categorical variables, respectively.

Peroxisome proliferator-activated receptor alpha (*PPAR-α*)

* $p < 0.05$

References

1. Wu, Y.; Goodrich, J.M.; Dolinoy, D.C.; Sanchez, B.N.; Ruiz-Narvaez, E.A.; Banker, M.; Cantoral, A.; Mercado-Garcia, A.; Tellez-Rojo, M.M.; Peterson, K.E. Accelerometer-measured Physical Activity, Reproductive Hormones, and DNA Methylation. *Med. Sci. Sports Exerc.* **2020**, *52*, 598-607, doi:10.1249/MSS.0000000000002175.