**Table 3–Source Data 1. Association between lifestyle factors and identified CpGs.**

CpG = cytosine-phosphoguanine site. Linear regression was fitted by including all 5 lifestyle factors simultaneously in the same model, with methylation values as dependent variables, and age, sex, study area, fasting time, education level, marital status and batch as covariates.

| CpGs | Smoking | | |  | Alcohol consumption | | |  | Physical activity | | |  | Diet score | | |  | Body mass index | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Effect  size | Standard error | P |  | Effect  size | Standard error | P |  | Effect  size | Standard error | P |  | Effect  size | Standard error | P |  | Effect  size | Standard error | P |
| cg01545454 | 3.31E-05 | 2.31E-05 | 0.153 |  | 3.34E-06 | 1.05E-05 | 0.750 |  | -8.42E-06 | 1.61E-05 | 0.602 |  | -2.78E-04 | 3.51E-04 | 0.429 |  | -4.31E-05 | 6.46E-05 | 0.505 |
| cg02386575 | 4.54E-05 | 5.66E-05 | 0.423 |  | 2.64E-05 | 2.57E-05 | 0.303 |  | 2.52E-05 | 3.95E-05 | 0.525 |  | 5.74E-04 | 8.60E-04 | 0.505 |  | 1.51E-04 | 1.58E-04 | 0.341 |
| cg02591826 | -7.58E-06 | 1.81E-05 | 0.675 |  | -9.22E-06 | 8.19E-06 | 0.261 |  | 4.05E-06 | 1.26E-05 | 0.749 |  | -2.85E-04 | 2.74E-04 | 0.299 |  | 8.38E-06 | 5.05E-05 | 0.868 |
| cg05681643 | -8.02E-05 | 6.04E-05 | 0.184 |  | 2.07E-05 | 2.74E-05 | 0.450 |  | 2.61E-05 | 4.22E-05 | 0.536 |  | 4.07E-04 | 9.17E-04 | 0.657 |  | 1.04E-04 | 1.69E-04 | 0.536 |
| cg05740632 | -4.86E-05 | 4.53E-05 | 0.284 |  | 1.84E-05 | 2.05E-05 | 0.370 |  | 3.43E-06 | 3.17E-05 | 0.914 |  | 1.37E-03 | 6.88E-04 | 0.047 |  | -5.72E-06 | 1.27E-04 | 0.964 |
| cg06358566 | 1.74E-05 | 3.06E-05 | 0.569 |  | 7.88E-06 | 1.39E-05 | 0.570 |  | -2.11E-05 | 2.14E-05 | 0.325 |  | -4.92E-05 | 4.65E-04 | 0.916 |  | -5.66E-05 | 8.54E-05 | 0.508 |
| cg07219103 | 2.70E-05 | 2.71E-05 | 0.319 |  | 1.63E-06 | 1.23E-05 | 0.895 |  | -7.37E-06 | 1.89E-05 | 0.697 |  | -5.42E-04 | 4.12E-04 | 0.189 |  | -2.88E-05 | 7.58E-05 | 0.704 |
| cg07560408 | -3.11E-05 | 5.97E-05 | 0.603 |  | 3.41E-06 | 2.70E-05 | 0.900 |  | -1.66E-05 | 4.17E-05 | 0.691 |  | 3.03E-06 | 9.07E-04 | 0.997 |  | -6.31E-05 | 1.67E-04 | 0.705 |
| cg08106661 | 1.50E-04 | 4.67E-05 | 0.001 |  | -2.03E-05 | 2.12E-05 | 0.337 |  | 2.32E-07 | 3.26E-05 | 0.994 |  | 2.21E-04 | 7.09E-04 | 0.756 |  | -5.47E-05 | 1.30E-04 | 0.675 |
| cg08484100 | -3.04E-05 | 7.53E-05 | 0.686 |  | -1.65E-05 | 3.41E-05 | 0.629 |  | 7.68E-05 | 5.26E-05 | 0.145 |  | 1.03E-03 | 1.14E-03 | 0.367 |  | 4.17E-04 | 2.10E-04 | 0.048 |
| cg10400937 | 4.46E-05 | 2.31E-05 | 0.054 |  | -5.80E-06 | 1.05E-05 | 0.580 |  | -3.26E-06 | 1.61E-05 | 0.840 |  | 1.59E-04 | 3.51E-04 | 0.651 |  | -5.23E-05 | 6.46E-05 | 0.418 |
| cg10643850 | -1.32E-04 | 8.33E-05 | 0.114 |  | -3.42E-05 | 3.77E-05 | 0.365 |  | -3.33E-06 | 5.81E-05 | 0.954 |  | 2.57E-03 | 1.26E-03 | 0.042 |  | 4.29E-05 | 2.33E-04 | 0.854 |
| cg11630610 | -3.94E-05 | 6.61E-05 | 0.552 |  | 1.00E-05 | 2.99E-05 | 0.738 |  | 4.41E-05 | 4.62E-05 | 0.340 |  | 4.95E-04 | 1.00E-03 | 0.622 |  | 1.63E-04 | 1.85E-04 | 0.379 |
| cg11754670 | 4.51E-05 | 2.94E-05 | 0.125 |  | 1.27E-05 | 1.33E-05 | 0.341 |  | -8.44E-06 | 2.05E-05 | 0.681 |  | -2.49E-04 | 4.47E-04 | 0.578 |  | -1.25E-04 | 8.22E-05 | 0.129 |
| cg13311494 | -1.62E-05 | 5.51E-05 | 0.769 |  | -1.15E-05 | 2.50E-05 | 0.645 |  | -2.66E-06 | 3.85E-05 | 0.945 |  | 8.87E-04 | 8.36E-04 | 0.289 |  | -1.12E-05 | 1.54E-04 | 0.942 |
| cg15833447 | -2.97E-06 | 6.82E-05 | 0.965 |  | 2.84E-05 | 3.09E-05 | 0.358 |  | 2.47E-06 | 4.76E-05 | 0.959 |  | 1.88E-03 | 1.04E-03 | 0.069 |  | 1.70E-04 | 1.91E-04 | 0.374 |
| cg16639138 | 1.80E-05 | 2.16E-05 | 0.406 |  | -4.35E-06 | 9.79E-06 | 0.657 |  | 1.50E-05 | 1.51E-05 | 0.322 |  | 1.48E-04 | 3.28E-04 | 0.653 |  | -4.85E-05 | 6.04E-05 | 0.422 |
| cg19583211 | 7.21E-05 | 5.37E-05 | 0.180 |  | 4.78E-06 | 2.43E-05 | 0.844 |  | -2.07E-05 | 3.75E-05 | 0.581 |  | -2.72E-04 | 8.16E-04 | 0.739 |  | -5.16E-06 | 1.50E-04 | 0.973 |
| cg20302171 | -4.17E-05 | 5.99E-05 | 0.487 |  | -2.04E-05 | 2.71E-05 | 0.453 |  | 8.16E-05 | 4.18E-05 | 0.051 |  | -5.39E-04 | 9.10E-04 | 0.554 |  | 3.90E-04 | 1.67E-04 | 0.020 |
| cg20562821 | -1.27E-04 | 7.02E-05 | 0.070 |  | -4.15E-05 | 3.18E-05 | 0.193 |  | -3.84E-05 | 4.90E-05 | 0.434 |  | 1.02E-03 | 1.07E-03 | 0.339 |  | 2.86E-05 | 1.96E-04 | 0.884 |
| cg21210537 | -1.54E-04 | 8.37E-05 | 0.067 |  | -7.31E-06 | 3.79E-05 | 0.847 |  | -9.10E-05 | 5.85E-05 | 0.120 |  | 3.60E-03 | 1.27E-03 | 0.005 |  | 1.76E-04 | 2.34E-04 | 0.452 |
| cg22794712 | -9.99E-06 | 6.83E-05 | 0.884 |  | 3.06E-05 | 3.09E-05 | 0.323 |  | -2.77E-05 | 4.77E-05 | 0.562 |  | 1.04E-03 | 1.04E-03 | 0.316 |  | 7.82E-05 | 1.91E-04 | 0.682 |
| cg24792179 | -8.69E-05 | 6.19E-05 | 0.161 |  | -7.09E-06 | 2.80E-05 | 0.800 |  | -1.69E-05 | 4.32E-05 | 0.695 |  | 8.73E-04 | 9.40E-04 | 0.353 |  | -1.14E-05 | 1.73E-04 | 0.947 |
| cg26334131 | -3.26E-05 | 8.21E-05 | 0.691 |  | 9.59E-06 | 3.72E-05 | 0.797 |  | 5.00E-05 | 5.74E-05 | 0.383 |  | 1.45E-04 | 1.25E-03 | 0.908 |  | 1.08E-04 | 2.29E-04 | 0.638 |
| cg23398826 | 4.58E-06 | 2.77E-05 | 0.869 |  | -8.73E-06 | 1.25E-05 | 0.487 |  | -2.74E-05 | 1.93E-05 | 0.156 |  | -1.79E-05 | 4.20E-04 | 0.966 |  | -1.44E-05 | 7.73E-05 | 0.852 |

**Table 4–Source Data 1. Association between quartile methylation level of identified CpGs and systolic blood pressure (mmHg).**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Quartile 2 | | Quartile 3 | | Quartile 4 | | P for trend  (adjusted for batch) | P for trend (adjusted for SVs) |  | Mediation effect | |
| CpGs | Effect size (se) | P | Effect size | P | Effect size | P |  | Proportion mediated, % | P |
| cg23398826 | -1.825 (2.079) | 0.380 | -3.918 (2.096) | 0.062 | -6.410 (2.118) | 0.003 | <0.001 | 0.009 |  | 7.65 | 0.003 |
| cg13311494 | -0.831 (2.087) | 0.691 | -1.981 (2.072) | 0.339 | -6.580 (2.122) | 0.002 | 0.020 | 0.013 |  | 15.61 | 0.031 |
| cg08106661 | 0.219 (2.140) | 0.918 | -1.100 (2.266) | 0.628 | -3.349 (2.404) | 0.164 | 0.151 | 0.634 |  | - | - |
| cg19583211 | 2.305 (2.107) | 0.274 | 4.571 (2.122) | 0.031 | 3.003 (2.125) | 0.158 | 0.176 | 0.275 |  | - | - |
| cg16639138 | 3.847 (2.073) | 0.064 | 3.811 (2.084) | 0.068 | 3.739 (2.092) | 0.074 | 0.130 | 0.034 |  | - | - |
| cg15833447 | 2.427 (2.096) | 0.247 | 1.993 (2.136) | 0.351 | 0.340 (2.165) | 0.875 | 0.336 | 0.388 |  | - | - |
| cg26334131 | 2.102 (2.118) | 0.321 | 2.932 (2.117) | 0.166 | 1.172 (2.144) | 0.585 | 0.361 | 0.617 |  | - | - |
| cg08484100 | 2.230 (2.086) | 0.285 | 1.163 (2.124) | 0.584 | 2.924 (2.145) | 0.173 | 0.687 | 0.993 |  | - | - |
| cg10643850 | -0.989 (2.116) | 0.640 | -3.207 (2.119) | 0.130 | -0.076 (2.156) | 0.972 | 0.336 | 0.346 |  | - | - |
| cg02386575 | -0.383 (2.080) | 0.854 | 2.455 (2.085) | 0.239 | 0.603 (2.106) | 0.775 | 0.564 | 0.479 |  | - | - |
| cg22794712 | -1.039 (2.110) | 0.623 | -0.306 (2.156) | 0.887 | -2.997 (2.200) | 0.173 | 0.342 | 0.857 |  | - | - |
| cg06358566 | 0.231 (2.088) | 0.912 | 0.912 (2.111) | 0.666 | -1.183 (2.136) | 0.580 | 0.538 | 0.772 |  | - | - |
| cg21210537 | 2.537 (2.133) | 0.235 | 2.328 (2.203) | 0.291 | 1.803 (2.280) | 0.429 | 0.578 | 0.042 |  | - | - |
| cg05681643 | 0.109 (2.082) | 0.958 | 1.617 (2.102) | 0.442 | 1.124 (2.182) | 0.607 | 0.571 | 0.558 |  | - | - |
| cg24792179 | -0.323 (2.109) | 0.878 | 1.585 (2.131) | 0.457 | 3.024 (2.183) | 0.166 | 0.453 | 0.638 |  | - | - |
| cg01545454 | -0.976 (2.094) | 0.641 | 0.159 (2.124) | 0.940 | -0.189 (2.124) | 0.929 | 0.596 | 0.244 |  | - | - |
| cg07560408 | -0.666 (2.121) | 0.753 | 0.483 (2.113) | 0.819 | 0.188 (2.150) | 0.930 | 0.481 | 0.984 |  | - | - |
| cg20302171 | -1.829 (2.095) | 0.383 | -0.342 (2.096) | 0.870 | -0.659 (2.146) | 0.759 | 0.905 | 0.654 |  | - | - |
| cg11754670 | 1.706 (2.117) | 0.421 | 2.328 (2.148) | 0.279 | 0.362 (2.168) | 0.868 | 0.949 | 0.182 |  | - | - |
| cg07219103 | 1.293 (2.107) | 0.540 | -0.044 (2.151) | 0.984 | 1.815 (2.234) | 0.417 | 0.603 | 0.248 |  | - | - |
| cg02591826 | -2.627 (2.081) | 0.207 | 0.069 (2.104) | 0.974 | -2.415 (2.148) | 0.261 | 0.673 | 0.571 |  | - | - |
| cg05740632 | -2.065 (2.099) | 0.326 | 1.208 (2.126) | 0.570 | -1.129 (2.142) | 0.598 | 0.744 | 0.312 |  | - | - |
| cg10400937 | 0.564 (2.078) | 0.786 | -0.390 (2.111) | 0.853 | 1.950 (2.129) | 0.360 | 0.607 | 0.881 |  | - | - |
| cg11630610 | 2.511 (2.123) | 0.237 | 0.576 (2.099) | 0.784 | 0.729 (2.122) | 0.731 | 0.648 | 0.889 |  | - | - |
| cg20562821 | -2.440 (2.123) | 0.251 | 2.679 (2.179) | 0.219 | -1.509 (2.203) | 0.494 | 0.950 | 0.566 |  | - | - |

CpG = cytosine-phosphoguanine site; SE = standard error; SV = surrogate variable.

Effect size is for the comparison with quartile 1. Systolic blood pressure added 15 mmHg if participants reported usage of blood pressure lowering medications. Multivariable model was adjusted for: age, sex, education level, marital status, smoking, drinking, physical activity, diet score, body mass index, fasting time, study area, and batch or SVs. Mediation analysis was performed for significant CpGs (P for trend < 0.05) only.

**Table 4–Source Data 2. Association between quartile methylation level of identified CpGs and diastolic blood pressure (mmHg).**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Quartile 2 | | Quartile 3 | | Quartile 4 | | P for trend  (adjusted for batch) | P for trend (adjusted for SVs) |  | Mediation effect | |
| CpGs | Effect size (se) | P | Effect size | P | Effect size | P |  | Proportion mediated, % | P |
| cg23398826 | -1.205 (1.196) | 0.314 | -2.206 (1.205) | 0.068 | -3.574 (1.218) | 0.003 | <0.001 | 0.006 |  | 6.39 | 0.006 |
| cg13311494 | -1.354 (1.201) | 0.260 | -2.371 (1.192) | 0.047 | -3.650 (1.221) | 0.003 | 0.029 | 0.047 |  | 12.38 | 0.045 |
| cg16639138 | 3.036 (1.190) | 0.011 | 2.920 (1.196) | 0.015 | 2.558 (1.200) | 0.033 | 0.109 | 0.054 |  | - | - |
| cg22794712 | -1.109 (1.212) | 0.360 | -0.387 (1.238) | 0.755 | -2.221 (1.264) | 0.079 | 0.135 | 0.264 |  | - | - |
| cg26334131 | 1.160 (1.218) | 0.341 | 1.413 (1.217) | 0.246 | 1.490 (1.233) | 0.227 | 0.263 | 0.781 |  | - | - |
| cg11630610 | 1.158 (1.218) | 0.342 | -1.356 (1.205) | 0.261 | -0.601 (1.218) | 0.622 | 0.169 | 0.385 |  | - | - |
| cg05681643 | 0.133 (1.196) | 0.912 | 0.327 (1.208) | 0.786 | 1.487 (1.254) | 0.236 | 0.314 | 0.094 |  | - | - |
| cg08106661 | -0.497 (1.231) | 0.687 | -0.644 (1.304) | 0.622 | -1.468 (1.383) | 0.289 | 0.319 | 0.913 |  | - | - |
| cg20562821 | -1.341 (1.221) | 0.272 | 1.462 (1.253) | 0.244 | -0.014 (1.267) | 0.991 | 0.313 | 0.353 |  | - | - |
| cg19583211 | 0.375 (1.211) | 0.757 | 2.581 (1.219) | 0.035 | 1.343 (1.221) | 0.272 | 0.296 | 0.268 |  | - | - |
| cg11754670 | 1.191 (1.217) | 0.328 | 1.034 (1.235) | 0.403 | 0.268 (1.246) | 0.830 | 0.542 | 0.863 |  | - | - |
| cg08484100 | 0.885 (1.200) | 0.461 | 0.471 (1.222) | 0.700 | 1.432 (1.234) | 0.246 | 0.611 | 0.637 |  | - | - |
| cg24792179 | 0.111 (1.213) | 0.927 | 1.137 (1.226) | 0.354 | 1.386 (1.256) | 0.270 | 0.373 | 0.299 |  | - | - |
| cg02591826 | -3.096 (1.190) | 0.009 | 0.544 (1.203) | 0.651 | -2.201 (1.229) | 0.074 | 0.365 | 0.136 |  | - | - |
| cg15833447 | -0.281 (1.206) | 0.816 | -0.410 (1.229) | 0.739 | -0.081 (1.246) | 0.948 | 0.580 | 0.941 |  | - | - |
| cg10400937 | 1.189 (1.192) | 0.319 | -0.226 (1.211) | 0.852 | 2.327 (1.221) | 0.057 | 0.376 | 0.503 |  | - | - |
| cg21210537 | 1.040 (1.226) | 0.397 | 0.997 (1.267) | 0.432 | 0.651 (1.311) | 0.620 | 0.654 | 0.185 |  | - | - |
| cg06358566 | 0.136 (1.201) | 0.910 | -0.388 (1.214) | 0.750 | -0.078 (1.228) | 0.949 | 0.802 | 0.928 |  | - | - |
| cg07219103 | 0.789 (1.211) | 0.515 | 0.130 (1.236) | 0.917 | 0.941 (1.284) | 0.464 | 0.635 | 0.250 |  | - | - |
| cg20302171 | -0.575 (1.204) | 0.633 | 0.320 (1.205) | 0.790 | -0.698 (1.233) | 0.572 | 0.883 | 0.741 |  | - | - |
| cg10643850 | 0.493 (1.218) | 0.686 | 0.004 (1.220) | 0.998 | 0.243 (1.241) | 0.845 | 0.766 | 0.674 |  | - | - |
| cg01545454 | 0.797 (1.204) | 0.508 | 0.389 (1.221) | 0.750 | 0.855 (1.221) | 0.484 | 0.939 | 0.217 |  | - | - |
| cg02386575 | -0.855 (1.197) | 0.475 | -0.223 (1.200) | 0.853 | -0.153 (1.212) | 0.899 | 0.999 | 0.523 |  | - | - |
| cg05740632 | -0.266 (1.208) | 0.826 | -0.373 (1.224) | 0.761 | -0.184 (1.233) | 0.882 | 0.882 | 0.773 |  | - | - |
| cg07560408 | 0.011 (1.218) | 0.993 | 0.746 (1.214) | 0.539 | -0.821 (1.235) | 0.506 | 0.995 | 0.446 |  | - | - |

CpG = cytosine-phosphoguanine site; SE = standard error; SV = surrogate variable.

Effect size is for the comparison with quartile 1. Diastolic blood pressure added 10 mmHg if participants reported usage of blood pressure lowering medications. Multivariable model was adjusted for: age, sex, education level, marital status, smoking, drinking, physical activity, diet score, body mass index, fasting time, study area, and batch or SVs. Mediation analysis was performed for significant CpGs (P for trend < 0.05) only.

**Table 4–Source Data 3. Association between quartile methylation level of identified CpGs and total cholesterol (mmol/L).**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Quartile 2 | | Quartile 3 | | Quartile 4 | | P for trend  (adjusted for batch) | P for trend (adjusted for SVs) |  | Mediation effect | |
| CpGs | Effect size (se) | P | Effect size | P | Effect size | P |  | Proportion mediated, % | P |
| cg26334131 | 0.016 (0.087) | 0.853 | 0.090 (0.087) | 0.302 | 0.197 (0.089) | 0.026 | 0.003 | 0.003 |  | -31.62 | 0.168 |
| cg05740632 | 0.080 (0.087) | 0.355 | 0.137 (0.088) | 0.118 | 0.163 (0.089) | 0.066 | 0.013 | 0.033 |  | -3.21 | 0.126 |
| cg21210537 | 0.146 (0.088) | 0.097 | 0.182 (0.091) | 0.045 | 0.175 (0.094) | 0.064 | 0.027 | 0.095 |  | -8.19 | 0.197 |
| cg19583211 | 0.058 (0.087) | 0.504 | -0.068 (0.088) | 0.436 | -0.064 (0.088) | 0.466 | 0.047 | 0.058 |  | 2.73 | 0.270 |
| cg20302171 | 0.097 (0.087) | 0.264 | 0.110 (0.087) | 0.204 | 0.153 (0.089) | 0.085 | 0.051 | 0.313 |  | - | - |
| cg08106661 | -0.007 (0.088) | 0.94 | -0.186 (0.094) | 0.047 | -0.147 (0.099) | 0.139 | 0.095 | 0.268 |  | - | - |
| cg08484100 | 0.016 (0.086) | 0.854 | 0.078 (0.088) | 0.374 | 0.056 (0.089) | 0.531 | 0.265 | 0.722 |  | - | - |
| cg13311494 | 0.115 (0.087) | 0.183 | 0.001 (0.086) | 0.992 | -0.119 (0.088) | 0.178 | 0.150 | 0.020 |  | - | - |
| cg11630610 | 0.047 (0.088) | 0.591 | 0.095 (0.087) | 0.275 | 0.032 (0.088) | 0.717 | 0.209 | 0.485 |  | - | - |
| cg05681643 | -0.005 (0.086) | 0.949 | 0.080 (0.087) | 0.355 | 0.104 (0.090) | 0.251 | 0.196 | 0.617 |  | - | - |
| cg20562821 | 0.160 (0.088) | 0.069 | 0.100 (0.090) | 0.269 | 0.102 (0.091) | 0.264 | 0.192 | 0.921 |  | - | - |
| cg24792179 | 0.037 (0.087) | 0.675 | 0.039 (0.088) | 0.661 | 0.052 (0.090) | 0.568 | 0.236 | 0.843 |  | - | - |
| cg10643850 | -0.009 (0.088) | 0.915 | -0.046 (0.088) | 0.602 | 0.070 (0.089) | 0.432 | 0.269 | 0.900 |  | - | - |
| cg22794712 | 0.066 (0.087) | 0.448 | 0.042 (0.089) | 0.639 | -0.087 (0.091) | 0.338 | 0.217 | 0.150 |  | - | - |
| cg06358566 | 0.064 (0.086) | 0.461 | 0.049 (0.087) | 0.571 | -0.087 (0.088) | 0.322 | 0.333 | 0.914 |  | - | - |
| cg02591826 | -0.096 (0.086) | 0.266 | -0.101 (0.087) | 0.244 | -0.091 (0.089) | 0.304 | 0.294 | 0.550 |  | - | - |
| cg11754670 | 0.088 (0.088) | 0.317 | 0.062 (0.089) | 0.484 | 0.026 (0.090) | 0.774 | 0.489 | 0.425 |  | - | - |
| cg07560408 | -0.021 (0.088) | 0.815 | 0.031 (0.087) | 0.725 | 0.040 (0.089) | 0.653 | 0.331 | 0.495 |  | - | - |
| cg07219103 | 0.137 (0.087) | 0.116 | 0.155 (0.089) | 0.081 | 0.003 (0.092) | 0.972 | 0.440 | 0.231 |  | - | - |
| cg02386575 | 0.025 (0.086) | 0.770 | -0.072 (0.086) | 0.407 | 0.005 (0.087) | 0.954 | 0.633 | 0.444 |  | - | - |
| cg10400937 | -0.007 (0.086) | 0.934 | -0.031 (0.087) | 0.726 | -0.037 (0.088) | 0.674 | 0.673 | 0.909 |  | - | - |
| cg16639138 | 0.043 (0.086) | 0.618 | 0.072 (0.086) | 0.407 | -0.005 (0.087) | 0.951 | 0.490 | 0.196 |  | - | - |
| cg23398826 | -0.126 (0.086) | 0.146 | -0.032 (0.087) | 0.713 | -0.119 (0.088) | 0.176 | 0.646 | 0.769 |  | - | - |
| cg15833447 | -0.183 (0.087) | 0.035 | -0.109 (0.088) | 0.217 | -0.176 (0.089) | 0.049 | 0.514 | 0.023 |  | - | - |
| cg01545454 | -0.067 (0.087) | 0.438 | -0.100 (0.088) | 0.255 | -0.081 (0.088) | 0.357 | 0.797 | 0.280 |  | - | - |

CpG = cytosine-phosphoguanine site; SE = standard error; SV = surrogate variable.

Effect size is for the comparison with quartile 1. Multivariable model was adjusted for: age, sex, education level, marital status, smoking, drinking, physical activity, diet score, body mass index, fasting time, study area, and batch or SVs. Mediation analysis was performed for significant CpGs (P for trend < 0.05) only.

**Table 4–Source Data 4. Association between quartile methylation level of identified CpGs and cholesterol in low-density lipoprotein (mmol/L).**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Quartile 2 | | Quartile 3 | | Quartile 4 | | P for trend  (adjusted for batch) | P for trend (adjusted for SVs) |  | Mediation effect | |
| CpGs | Effect size (se) | P | Effect size | P | Effect size | P |  | Proportion mediated, % | P |
| cg26334131 | 0.015 (0.062) | 0.815 | 0.072 (0.062) | 0.245 | 0.110 (0.063) | 0.079 | 0.007 | 0.012 |  | -32.14 | 0.135 |
| cg20302171 | 0.056 (0.061) | 0.363 | 0.059 (0.061) | 0.338 | 0.107 (0.063) | 0.090 | 0.029 | 0.223 |  | -10.48 | 0.161 |
| cg05740632 | 0.058 (0.061) | 0.342 | 0.094 (0.062) | 0.132 | 0.109 (0.063) | 0.083 | 0.019 | 0.045 |  | -3.38 | 0.110 |
| cg19583211 | 0.016 (0.062) | 0.794 | -0.043 (0.062) | 0.485 | -0.078 (0.062) | 0.208 | 0.020 | 0.044 |  | 3.60 | 0.210 |
| cg13311494 | 0.096 (0.061) | 0.115 | -0.016 (0.061) | 0.794 | -0.117 (0.062) | 0.060 | 0.027 | 0.001 |  | 3.70 | 0.208 |
| cg21210537 | 0.119 (0.062) | 0.057 | 0.132 (0.064) | 0.040 | 0.126 (0.067) | 0.059 | 0.044 | 0.259 |  | -8.55 | 0.177 |
| cg11630610 | 0.070 (0.062) | 0.258 | 0.089 (0.061) | 0.148 | 0.061 (0.062) | 0.327 | 0.110 | 0.223 |  | - | - |
| cg05681643 | 0.028 (0.061) | 0.643 | 0.086 (0.061) | 0.162 | 0.103 (0.064) | 0.108 | 0.103 | 0.342 |  | - | - |
| cg11754670 | 0.065 (0.062) | 0.298 | 0.018 (0.063) | 0.777 | 0.004 (0.063) | 0.954 | 0.177 | 0.848 |  | - | - |
| cg06358566 | 0.006 (0.061) | 0.919 | 0.011 (0.062) | 0.854 | -0.084 (0.062) | 0.176 | 0.128 | 0.630 |  | - | - |
| cg02591826 | -0.022 (0.061) | 0.721 | -0.096 (0.062) | 0.119 | -0.056 (0.063) | 0.376 | 0.118 | 0.257 |  | - | - |
| cg10400937 | 0.003 (0.061) | 0.966 | 0.005 (0.062) | 0.940 | -0.073 (0.062) | 0.244 | 0.187 | 0.460 |  | - | - |
| cg08484100 | -0.014 (0.061) | 0.824 | 0.032 (0.062) | 0.603 | 0.024 (0.063) | 0.698 | 0.299 | 0.622 |  | - | - |
| cg20562821 | 0.091 (0.062) | 0.146 | 0.047 (0.064) | 0.466 | 0.081 (0.065) | 0.211 | 0.167 | 0.776 |  | - | - |
| cg08106661 | 0.019 (0.063) | 0.758 | -0.086 (0.066) | 0.196 | -0.080 (0.070) | 0.256 | 0.189 | 0.378 |  | - | - |
| cg07219103 | 0.107 (0.061) | 0.081 | 0.146 (0.063) | 0.020 | -0.004 (0.065) | 0.947 | 0.214 | 0.528 |  | - | - |
| cg24792179 | 0.045 (0.062) | 0.466 | 0.030 (0.062) | 0.627 | 0.045 (0.064) | 0.481 | 0.197 | 0.960 |  | - | - |
| cg10643850 | -0.001 (0.062) | 0.989 | -0.045 (0.062) | 0.470 | 0.047 (0.063) | 0.454 | 0.239 | 0.921 |  | - | - |
| cg02386575 | 0.040 (0.061) | 0.516 | -0.008 (0.061) | 0.895 | 0.031 (0.062) | 0.621 | 0.452 | 0.629 |  | - | - |
| cg22794712 | 0.041 (0.062) | 0.510 | 0.037 (0.063) | 0.557 | -0.053 (0.064) | 0.409 | 0.338 | 0.373 |  | - | - |
| cg07560408 | -0.003 (0.062) | 0.955 | 0.005 (0.062) | 0.936 | 0.031 (0.063) | 0.617 | 0.455 | 0.186 |  | - | - |
| cg01545454 | -0.050 (0.061) | 0.411 | -0.060 (0.062) | 0.331 | -0.084 (0.062) | 0.179 | 0.734 | 0.509 |  | - | - |
| cg23398826 | -0.068 (0.061) | 0.266 | 0.002 (0.062) | 0.969 | -0.076 (0.062) | 0.223 | 0.671 | 0.739 |  | - | - |
| cg15833447 | -0.052 (0.061) | 0.394 | -0.038 (0.063) | 0.542 | -0.080 (0.063) | 0.205 | 0.577 | 0.040 |  | - | - |
| cg16639138 | 0.034 (0.061) | 0.579 | 0.044 (0.061) | 0.477 | -0.036 (0.061) | 0.558 | 0.958 | 0.373 |  | - | - |

CpG = cytosine-phosphoguanine sit;. SE = standard error; SV = surrogate variable.

Effect size is for the comparison with quartile 1. Multivariable model was adjusted for: age, sex, education level, marital status, smoking, drinking, physical activity, diet score, body mass index, fasting time, study area, and batch or SVs. Mediation analysis was performed for significant CpGs (P for trend < 0.05) only.

**Table 4–Source Data 5. Association between quartile methylation level of identified CpGs and cholesterol in high-density lipoprotein (mmol/L).**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Quartile 2 | | Quartile 3 | | Quartile 4 | | P for trend  (adjusted for batch) | P for trend (adjusted for SVs) |  | Mediation effect | |
| CpGs | Effect size (se) | P | Effect size | P | Effect size | P |  | Proportion mediated, % | P |
| cg15833447 | -0.024 (0.025) | 0.343 | 0.015 (0.026) | 0.556 | 0.037 (0.026) | 0.154 | 0.013 | 0.102 |  | -10.77 | 0.180 |
| cg21210537 | 0.044 (0.026) | 0.084 | 0.036 (0.026) | 0.178 | 0.040 (0.027) | 0.146 | 0.019 | 0.014 |  | 7.30 | 0.235 |
| cg07560408 | -0.032 (0.025) | 0.212 | 0.018 (0.025) | 0.488 | 0.031 (0.026) | 0.236 | 0.073 | 0.173 |  | - | - |
| cg16639138 | 0.007 (0.025) | 0.790 | 0.021 (0.025) | 0.393 | 0.021 (0.025) | 0.400 | 0.165 | 0.175 |  | - | - |
| cg05740632 | 0.020 (0.025) | 0.431 | 0.014 (0.026) | 0.582 | 0.039 (0.026) | 0.128 | 0.125 | 0.379 |  | - | - |
| cg10400937 | 0.011 (0.025) | 0.649 | 0.037 (0.025) | 0.142 | 0.022 (0.026) | 0.389 | 0.243 | 0.266 |  | - | - |
| cg26334131 | 0.009 (0.025) | 0.713 | 0.049 (0.025) | 0.054 | 0.028 (0.026) | 0.275 | 0.130 | 0.249 |  | - | - |
| cg11630610 | -0.040 (0.025) | 0.114 | -0.041 (0.025) | 0.106 | -0.059 (0.025) | 0.020 | 0.350 | 0.137 |  | - | - |
| cg02591826 | 0.006 (0.025) | 0.822 | -0.026 (0.025) | 0.297 | 0.009 (0.026) | 0.719 | 0.251 | 0.197 |  | - | - |
| cg24792179 | -0.007 (0.025) | 0.792 | 0.003 (0.026) | 0.921 | 0.013 (0.026) | 0.628 | 0.278 | 0.636 |  | - | - |
| cg01545454 | -0.038 (0.025) | 0.131 | -0.046 (0.025) | 0.069 | -0.027 (0.025) | 0.291 | 0.394 | 0.596 |  | - | - |
| cg19583211 | -0.033 (0.025) | 0.196 | -0.033 (0.026) | 0.190 | -0.007 (0.026) | 0.781 | 0.370 | 0.361 |  | - | - |
| cg13311494 | 0.006 (0.025) | 0.820 | 0.025 (0.025) | 0.310 | 0.016 (0.026) | 0.541 | 0.428 | 0.433 |  | - | - |
| cg08484100 | 0.019 (0.025) | 0.453 | -0.034 (0.025) | 0.184 | 0.007 (0.026) | 0.774 | 0.780 | 0.326 |  | - | - |
| cg08106661 | 0.022 (0.026) | 0.384 | -0.008 (0.027) | 0.764 | -0.020 (0.029) | 0.486 | 0.413 | 0.820 |  | - | - |
| cg10643850 | -0.041 (0.025) | 0.105 | -0.029 (0.025) | 0.261 | 0.010 (0.026) | 0.708 | 0.606 | 0.427 |  | - | - |
| cg23398826 | -0.023 (0.025) | 0.351 | -0.031 (0.025) | 0.225 | -0.020 (0.026) | 0.444 | 0.733 | 0.598 |  | - | - |
| cg07219103 | -0.004 (0.025) | 0.886 | 0.015 (0.026) | 0.549 | -0.025 (0.027) | 0.350 | 0.700 | 0.856 |  | - | - |
| cg22794712 | 0.028 (0.025) | 0.278 | 0.018 (0.026) | 0.490 | 0.025 (0.026) | 0.344 | 0.893 | 0.935 |  | - | - |
| cg02386575 | -0.011 (0.025) | 0.649 | -0.008 (0.025) | 0.747 | -0.002 (0.025) | 0.928 | 0.681 | 0.824 |  | - | - |
| cg11754670 | 0.006 (0.025) | 0.815 | 0.011 (0.026) | 0.665 | -0.004 (0.026) | 0.884 | 0.773 | 0.752 |  | - | - |
| cg20302171 | -0.006 (0.025) | 0.806 | 0.007 (0.025) | 0.768 | 0.010 (0.026) | 0.712 | 0.457 | 0.903 |  | - | - |
| cg06358566 | 0.010 (0.025) | 0.697 | 0.024 (0.025) | 0.340 | 0.016 (0.026) | 0.538 | 0.951 | 0.899 |  | - | - |
| cg20562821 | -0.017 (0.026) | 0.518 | 0.003 (0.026) | 0.908 | -0.042 (0.027) | 0.116 | 0.949 | 0.068 |  | - | - |
| cg05681643 | -0.014 (0.025) | 0.572 | 0.010 (0.025) | 0.699 | -0.001 (0.026) | 0.964 | 0.801 | 0.927 |  | - | - |

CpG = cytosine-phosphoguanine site; SE = standard error; SV = surrogate variable.

Effect size is for the comparison with quartile 1. Multivariable model was adjusted for: age, sex, education level, marital status, smoking, drinking, physical activity, diet score, body mass index, fasting time, study area, and batch or SVs. Mediation analysis was performed for significant CpGs (P for trend < 0.05) only.

**Table 4–Source Data 6. Association between quartile methylation level of identified CpGs and random glucose (mmol/L).**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Quartile 2 | | Quartile 3 | | Quartile 4 | | P for trend  (adjusted for batch) | P for trend (adjusted for SVs) |  | Mediation effect | |
| CpGs | Effect size (se) | P | Effect size | P | Effect size | P |  | Proportion mediated, % | P |
| cg10400937 | -0.466 (0.225) | 0.038 | -0.015 (0.228) | 0.949 | 0.551 (0.231) | 0.017 | 0.003 | 0.013 |  | 6.72 | 0.107 |
| cg01545454 | -0.173 (0.229) | 0.449 | -0.163 (0.234) | 0.487 | 0.203 (0.234) | 0.385 | 0.006 | 0.111 |  | 9.58 | 0.097 |
| cg11754670 | -0.020 (0.230) | 0.931 | 0.316 (0.233) | 0.177 | 0.466 (0.236) | 0.049 | 0.005 | 0.652 |  | 36.39 | 0.086 |
| cg26334131 | -0.087 (0.233) | 0.708 | -0.398 (0.231) | 0.085 | -0.517 (0.234) | 0.028 | 0.018 | 0.234 |  | 32.70 | 0.109 |
| cg07219103 | 0.197 (0.229) | 0.391 | 0.462 (0.235) | 0.049 | 0.578 (0.244) | 0.018 | 0.032 | 0.856 |  | 6.17 | 0.135 |
| cg20302171 | -0.173 (0.229) | 0.450 | -0.128 (0.229) | 0.576 | -0.556 (0.234) | 0.018 | 0.027 | 0.692 |  | 15.77 | 0.123 |
| cg02591826 | 0.040 (0.229) | 0.861 | 0.286 (0.231) | 0.215 | 0.226 (0.236) | 0.339 | 0.080 | 0.509 |  | - | - |
| cg22794712 | 0.103 (0.231) | 0.655 | -0.049 (0.235) | 0.834 | 0.442 (0.240) | 0.066 | 0.118 | 0.982 |  | - | - |
| cg08106661 | 0.021 (0.233) | 0.929 | 0.232 (0.248) | 0.349 | 0.490 (0.263) | 0.063 | 0.137 | 0.990 |  | - | - |
| cg07560408 | 0.001 (0.232) | 0.998 | -0.168 (0.231) | 0.467 | -0.336 (0.235) | 0.153 | 0.293 | 0.647 |  | - | - |
| cg05681643 | -0.019 (0.229) | 0.932 | 0.019 (0.230) | 0.934 | -0.212 (0.239) | 0.375 | 0.345 | 0.130 |  | - | - |
| cg19583211 | 0.029 (0.230) | 0.901 | -0.075 (0.232) | 0.748 | 0.212 (0.233) | 0.364 | 0.408 | 0.352 |  | - | - |
| cg15833447 | -0.331 (0.230) | 0.150 | -0.153 (0.234) | 0.514 | -0.281 (0.236) | 0.235 | 0.423 | 0.837 |  | - | - |
| cg24792179 | -0.309 (0.233) | 0.184 | -0.250 (0.234) | 0.284 | -0.176 (0.239) | 0.462 | 0.485 | 0.155 |  | - | - |
| cg05740632 | -0.073 (0.231) | 0.752 | 0.083 (0.234) | 0.724 | -0.239 (0.235) | 0.309 | 0.501 | 0.815 |  | - | - |
| cg08484100 | 0.383 (0.229) | 0.095 | 0.223 (0.233) | 0.338 | -0.105 (0.235) | 0.655 | 0.407 | 0.676 |  | - | - |
| cg21210537 | 0.131 (0.234) | 0.577 | 0.370 (0.242) | 0.126 | 0.111 (0.249) | 0.657 | 0.617 | 0.192 |  | - | - |
| cg13311494 | -0.329 (0.230) | 0.154 | -0.089 (0.229) | 0.699 | -0.044 (0.233) | 0.852 | 0.704 | 0.195 |  | - | - |
| cg20562821 | 0.412 (0.233) | 0.077 | 0.361 (0.240) | 0.133 | -0.076 (0.241) | 0.752 | 0.721 | 0.602 |  | - | - |
| cg06358566 | -0.016 (0.228) | 0.944 | 0.023 (0.230) | 0.920 | 0.020 (0.233) | 0.931 | 0.756 | 0.169 |  | - | - |
| cg16639138 | -0.125 (0.227) | 0.581 | -0.253 (0.228) | 0.268 | 0.069 (0.229) | 0.764 | 0.988 | 0.242 |  | - | - |
| cg11630610 | -0.024 (0.234) | 0.918 | -0.044 (0.230) | 0.850 | -0.014 (0.233) | 0.953 | 0.857 | 0.863 |  | - | - |
| cg10643850 | 0.004 (0.234) | 0.987 | -0.136 (0.233) | 0.559 | -0.175 (0.236) | 0.458 | 0.946 | 0.070 |  | - | - |
| cg02386575 | 0.102 (0.229) | 0.657 | 0.213 (0.228) | 0.352 | -0.008 (0.231) | 0.971 | 0.978 | 0.480 |  | - | - |
| cg23398826 | 0.154 (0.229) | 0.501 | 0.134 (0.231) | 0.563 | -0.119 (0.233) | 0.609 | 0.955 | 0.781 |  | - | - |

CpG = cytosine-phosphoguanine site; SE = standard error; SV = surrogate variable.

Effect size is for the comparison with quartile 1. Multivariable model was adjusted for: age, sex, education level, marital status, smoking, drinking, physical activity, diet score, body mass index, fasting time, study area, treatment of diabetes, and batch or SVs. Mediation analysis was performed for significant CpGs (P for trend < 0.05) only.

**Table 4–Source Data 7. Association between quartile methylation level of identified CpGs and triglyceride (mmol/L).**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Quartile 2 | | Quartile 3 | | Quartile 4 | | P for trend  (adjusted for batch) | P for trend (adjusted for SVs) |  | Mediation effect | |
| CpGs | Effect size (se) | P | Effect size | P | Effect size | P |  | Proportion mediated, % | P |
| cg15833447 | -0.225 (0.137) | 0.102 | -0.153 (0.140) | 0.274 | -0.380 (0.142) | 0.007 | 0.073 | 0.019 |  | - | - |
| cg16639138 | -0.027 (0.136) | 0.842 | -0.004 (0.137) | 0.974 | -0.088 (0.138) | 0.524 | 0.459 | 0.205 |  | - | - |
| cg08484100 | -0.059 (0.137) | 0.664 | 0.156 (0.139) | 0.264 | -0.061 (0.141) | 0.665 | 0.751 | 0.565 |  | - | - |
| cg23398826 | -0.107 (0.137) | 0.437 | -0.084 (0.138) | 0.544 | -0.120 (0.140) | 0.390 | 0.441 | 0.347 |  | - | - |
| cg20302171 | 0.192 (0.137) | 0.162 | 0.196 (0.137) | 0.155 | 0.041 (0.141) | 0.773 | 0.990 | 0.469 |  | - | - |
| cg01545454 | 0.015 (0.137) | 0.914 | 0.229 (0.139) | 0.101 | 0.164 (0.139) | 0.239 | 0.455 | 0.387 |  | - | - |
| cg07219103 | 0.143 (0.138) | 0.301 | -0.053 (0.141) | 0.704 | 0.173 (0.146) | 0.238 | 0.508 | 0.379 |  | - | - |
| cg24792179 | -0.082 (0.139) | 0.554 | -0.021 (0.140) | 0.881 | -0.077 (0.143) | 0.592 | 0.620 | 0.848 |  | - | - |
| cg22794712 | 0.013 (0.138) | 0.922 | -0.041 (0.141) | 0.772 | -0.157 (0.144) | 0.276 | 0.532 | 0.130 |  | - | - |
| cg11754670 | 0.051 (0.139) | 0.716 | 0.148 (0.141) | 0.295 | 0.093 (0.142) | 0.515 | 0.345 | 0.618 |  | - | - |
| cg07560408 | 0.111 (0.139) | 0.424 | 0.028 (0.138) | 0.838 | -0.122 (0.141) | 0.385 | 0.710 | 0.937 |  | - | - |
| cg05681643 | -0.050 (0.137) | 0.713 | -0.121 (0.138) | 0.379 | -0.077 (0.143) | 0.591 | 0.518 | 0.473 |  | - | - |
| cg02386575 | 0.072 (0.136) | 0.596 | -0.110 (0.137) | 0.422 | -0.123 (0.138) | 0.372 | 0.467 | 0.350 |  | - | - |
| cg26334131 | -0.071 (0.139) | 0.608 | -0.215 (0.139) | 0.121 | -0.091 (0.141) | 0.517 | 0.594 | 0.884 |  | - | - |
| cg10643850 | 0.058 (0.139) | 0.678 | 0.118 (0.139) | 0.397 | -0.040 (0.142) | 0.780 | 0.666 | 0.420 |  | - | - |
| cg08106661 | -0.164 (0.140) | 0.243 | -0.200 (0.149) | 0.178 | -0.037 (0.158) | 0.816 | 0.814 | 0.423 |  | - | - |
| cg13311494 | -0.097 (0.138) | 0.482 | -0.073 (0.137) | 0.595 | -0.065 (0.140) | 0.642 | 0.759 | 0.809 |  | - | - |
| cg19583211 | 0.356 (0.138) | 0.010 | 0.066 (0.139) | 0.635 | 0.082 (0.139) | 0.554 | 0.777 | 0.860 |  | - | - |
| cg11630610 | 0.077 (0.139) | 0.580 | 0.127 (0.138) | 0.358 | -0.047 (0.139) | 0.737 | 0.617 | 0.303 |  | - | - |
| cg06358566 | 0.103 (0.137) | 0.453 | 0.024 (0.138) | 0.860 | -0.082 (0.140) | 0.559 | 0.694 | 0.719 |  | - | - |
| cg02591826 | -0.188 (0.136) | 0.167 | 0.220 (0.138) | 0.110 | -0.074 (0.140) | 0.598 | 0.811 | 0.932 |  | - | - |
| cg05740632 | -0.061 (0.138) | 0.658 | 0.049 (0.140) | 0.728 | -0.082 (0.141) | 0.558 | 0.881 | 0.841 |  | - | - |
| cg10400937 | -0.013 (0.136) | 0.926 | -0.211 (0.138) | 0.127 | 0.097 (0.139) | 0.488 | 0.712 | 0.627 |  | - | - |
| cg20562821 | 0.177 (0.140) | 0.206 | 0.135 (0.143) | 0.347 | 0.124 (0.145) | 0.391 | 0.982 | 0.779 |  | - | - |
| cg21210537 | -0.134 (0.140) | 0.338 | 0.028 (0.145) | 0.848 | -0.015 (0.150) | 0.922 | 0.795 | 0.882 |  | - | - |

CpG = cytosine-phosphoguanine site; SE = standard error; SV = surrogate variable.

Effect size is for the comparison with quartile 1. Multivariable model was adjusted for: age, sex, education level, marital status, smoking, drinking, physical activity, diet score, body mass index, fasting time, study area, and batch or SVs. Mediation analysis was performed for significant CpGs (P for trend < 0.05) only.