**Recent consumption of a caffeine-containing beverage and serum biomarkers of cardiometabolic function in the UK Biobank**

Supplemental Material

# **SUPPLEMENTARY METHODS**

## Participants

UK Biobank investigators sent postal invitations to approximately 9.2 million individuals registered with the UK’s National Health Service who were aged 40–69 years and lived within approximately 40 km of one of 22 assessment centers located throughout England, Wales, and Scotland(1). Between 2006 and 2010, over 502,633 participants aged 37-73 years (5.4% participation rate) provided full informed consent to participate in UK Biobank and completed a 90-minute assessment (see Table S1 for order of operations). Participants are free to withdraw from UK Biobank at any time and request that their data no longer be used. At the time of the current analysis, data from 502,612 participants was available to researchers for analysis (Figure S1).

## Measures and procedures

Usual assessment center opening hours were Monday to Friday 8:00 am to 8:00 pm (last appointment starting at 7:00 pm) and Saturday 8:00 am to 6:00 pm (last appointment starting at 5:00 pm). The questionnaire was administered in two sequential parts during the assessment center visit: a touch-screen self-completed questionnaire followed by a computer-assisted personal interview (CAPI). A pre-visit aide memoire was provided to participants prior to attending the assessment center so they could note certain information that may be difficult or time-consuming for them to recall during the visit. Pre-coded lists of diseases, drugs, and occupations were built into the CAPI system, along with structured search facilities, to help this information to be recorded (and automatically coded). Data for the current analysis was downloaded in 2017.

**References**

1. UK Biobank Coordinating Centre (2007) UK Biobank: Protocol for a large-scale prospective epidemiological resource. <http://www.ukbiobank.ac.uk/wp-content/uploads/2011/11/UK-Biobank-Protocol.pdf>

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3. Zhong V, Kuang A, Danning R *et al.* (2018) A genome-wide association study of habitual bitter and sweet beverage consumption. *Submitted*.

4. Sulem P, Gudbjartsson DF, Geller F *et al.* (2011) Sequence variants at CYP1A1-CYP1A2 and AHR associate with coffee consumption. *Hum Mol Genet* **20**, 2071-2077.

5. Cornelis MC, Monda KL, Yu K *et al.* (2011) Genome-wide meta-analysis identifies regions on 7p21 (AHR) and 15q24 (CYP1A2) as determinants of habitual caffeine consumption. *PLoS Genet* **7**, e1002033.

6. Cornelis MC, Kacprowski T, Menni C *et al.* (2016) Genome-wide association study of caffeine metabolites provides new insights to caffeine metabolism and dietary caffeine-consumption behavior. *Hum Mol Genet* **25**, 5472-5482.

7. Amin N, Byrne E, Johnson J *et al.* (2012) Genome-wide association analysis of coffee drinking suggests association with CYP1A1/CYP1A2 and NRCAM. *Mol Psychiatry* **17**, 1116-1129.

8. Hindorf L, MacArthur J, Morales J *et al.* (accessed January 1, 2015) Catalogue of Published Genome-Wide Association Studies.

9. Li N, van der Sijde MR, LifeLines Cohort Study G *et al.* (2014) Pleiotropic effects of lipid genes on plasma glucose, HbA1c, and HOMA-IR levels. *Diabetes* **63**, 3149-3158.

# Table S1. Assessment center order of operations(1)\*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Visit station | Assessments undertaken | Variables for current analysis | Data available | Current analysis |
| All | Subset with genetic data† |
| Reception(10 min) | Welcome and registrationConsent |  |  |  |  |
| Questionnaire(40 min) | Touch screen questionnaire | AgeSexRaceSmoking statusIncomeEducationEmploymentSelf-rate healthTownsendPhysical activityCoffeeCoffee typeTea AlcoholWaterFishRed meatFruitVegetables Oral contraceptive usePost-menopausal hormone useSelf-reported diabetes/insulin use Self-reported blood pressure medicationSelf-reported heart conditionSelf-reported cholesterol medication | 502616502616502616502616425419407183496857499125501989491884500347384485500421502616497833500561501356500474498126502616502616502616502616502616502616 | 447794447794447794447794384581369598407703445927447241438199447794347830447794447794444974447040447653447032445177447794447794447794447794447794447794 | 307696307696307696307696266188254511283190306754307329300972307696243400307696307696305956307393307635307331306230307696307696307696307696307696307696 |
| Interview(10 min) | Interviewer questionnaireBlood pressure measurement | Medication use | 502616 | 447794 | 307696 |
| Physical measurements(15 min) | Anthropometrics, hand-grip strength, heel bone ultrasound, spirometry | BMIWHRCaffeine drinking in last hour (yes/no) | 499511500351460110 | 446743447407447794 | 307062307440307696 |
| Sample collection(15 min) | Blood sampleUrine sample | Fasting timeQC Genetic data Serum biomarkersApoA1ApoBLp (a)tCholHDLLDLTGCRPglucose HbA1c | 501383407206427532467232375654469615429894468732469240468594429590466530 | 447794370193390199426627343099428794392373428005428456427936392096425715 | 307696307696268191293283234376294709269679294163294473294115269510294388 |
| Exit | Consent and result summary printedTravel expense claim provided |  |  |  |  |

\*Abbreviations: tChol, total cholesterol; TG, triglycerides; ApoA1, apolipoprotein A1; ApoB, apolipoprotein B1; BMI, body mass index, CRP, C-reactive protein; HbA1c, glycated haemoglobin A1c; HDL, high density lipoprotein; LDL, low-density lipoprotein; Lp(a), lipoprotein (a); QC, quality control; WHR, waist-to-hip ratio

†The sub-set of participants for genetic analysis included unrelated individuals with high quality genetic data, who self-report as “British” and who have very similar ancestral backgrounds based on results of principal component analysis

# Table S2. SNPs for coffee- and caffeine- related traits based on genome-wide association studies\*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Locus | Closest gene(s) | SNPEA/OAfunction | EAF | Trait | Effect | Reference | Association with other traits† |
| AFR | AMR | ASN | EU |
| 2p23.3 | *GCKR* | rs1260326 C/T missense | 0.88 | 0.59 | 0.44 | 0.59 | coffee intake | + | (2; 3) | waist circumference, lipid traits, serum glucose, chronic kidney disease, C-reactive protein, gamma-glutamyl transferase, serum albumin, serum urate, leptin |
| 4q22.1 | *ABCG2* | rs1481012 A/G intronic | 0.98 | 0.85 | 0.71 | 0.89 | coffee intake | + | (2) | LDL, response to statin, serum urate, gout |
| 7p21.1 | *AHR* | rs6968554 G/A intergenic | 0.72 | 0.44 | 0.36 | 0.63 | coffee intake | + | (2-4)  | albuminuria |
| caffeine intake | + | (5) |
| plasma caffeine metabolites | - | (6) |
| 7q11.23 | *MLXIPL* | rs7800944 C/T intronic | 0.39 | 0.18 | 0.11 | 0.27 | coffee intake | + | (2; 3) | lipid traits, alcohol drinkingfasting glucose‡ |
| 7q11.23 | *POR* | rs17685  A/G 3’UTR | 0.13 | 0.22 | 0.35 | 0.30 | coffee intake | + | (2; 3) |  |
| plasma caffeine metabolites | - | (6) |  |
| 15q24.1 | *CYP1A1-CYP1A2* | rs2472297 T/Cintergenic | 0.02 | 0.09 | 0.0 | 0.24 | coffee intake | + | (2-4; 7) | albuminuria, urine albumin,  |
| caffeine intake | + | (5) |
| plasma caffeine metabolites | - | (6) |  |
| *CYP1A2* | rs762551 A/C intronic | 0.54 | 0.74 | 0.63 | 0.69 | coffee intake | + | (2) |  |
| caffeine intake | + | (5) |  |
| 22q11.23 | *SPECC1L-ADORA2A* | rs2330783  G/T intronic | 0.92 | 0.98 | 0 | 0.99 | coffee intake | + | (3) |  |
| *ADORA2A* | rs5751876  T/C intronic | 0.66 | 0.43 | 0.49 | 0.39 |  |  |  |  |

EA: effect allele, EAF: effect allele frequency (based on HapMap data), OA: other allele, AFR: African ancestry, AMR: Ad-mixed American ancestry, ASN: Asian ancestry; EU European ancestry

\*Listed are SNPs examined in the current study (see main paper for inclusion criteria). rs5751876 (*ADORA2A*) is a candidate SNP selected from the literature.

†Other GWAS catalogue traits associated with SNP(8)

‡Large follow-up study(9)

# Table S3. Associations between participant characteristics and SNP genotypes (P values)\*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Characteristic | Statistical Test | rs1260326\_C | rs1481012\_A | rs17685\_A | rs2330783\_G | rs2472297\_T | rs5751876\_T | rs6968554\_G | rs762551\_A | rs7800944\_C |
| F | M | F | M | F | M | F | M | F | M | F | M | F | M | F | M | F | M |
| Age, years | ANOVA | 0.11 | 0.59 | 0.57 | 0.07 | 0.37 | 0.008 | 0.18 | 0.37 | 0.66 | 0.77 | 0.55 | 0.09 | 0.61 | 0.42 | 0.35 | 0.30 | 0.69 | 0.76 |
| coffee, cups/d | ANOVA | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | 0.002 | <.0001 | <.0001 | 0.32 | 0.10 | <.0001 | <.0001 | <.0001 | <.0001 | 0.0005 | <.0001 |
| regular, cups/d | ANOVA | <.0001 | <.0001 | 0.0006 | <.0001 | <.0001 | <.0001 | 0.0003 | 0.004 | <.0001 | <.0001 | 0.16 | 0.22 | <.0001 | <.0001 | <.0001 | <.0001 | 0.0007 | <.0001 |
| instant, cups/d | ANOVA | <.0001 | <.0001 | 0.008 | <.0001 | <.0001 | <.0001 | 0.0003 | 0.12 | <.0001 | <.0001 | 0.03 | 0.62 | <.0001 | <.0001 | <.0001 | <.0001 | 0.006 | <.0001 |
| ground, cups/d | ANOVA | 0.008 | 0.002 | 0.006 | 0.01 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | 0.11 | 0.12 | <.0001 | <.0001 | <.0001 | <.0001 | 0.17 | 0.008 |
| decaf, cups/d | ANOVA | 0.10 | 0.02 | 0.04 | 0.008 | <.0001 | <.0001 | 0.004 | 0.18 | <.0001 | <.0001 | 0.14 | 0.79 | <.0001 | <.0001 | 0.007 | 0.003 | 0.64 | 0.18 |
| tea, cups/d | ANOVA | 0.15 | 0.75 | 0.0001 | <.0001 | <.0001 | <.0001 | 0.06 | 0.02 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | 0.007 | 0.07 |
| coffee/tea caffeine, mg/d | ANOVA | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | 0.007 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 |
| coffee/tea caffeine, mg/kg/d | ANOVA | <.0001 | 0.002 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | 0.012 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | 0.0002 | <.0001 |
| plain water, servings/d | ANOVA | 0.0003 | 0.19 | 0.004 | <.0001 | 0.0001 | 0.13 | 0.03 | 0.012 | <.0001 | <.0001 | 0.86 | 0.62 | <.0001 | <.0001 | <.0001 | 0.000 | 0.02 | 0.002 |
| BMI | ANOVA | 0.71 | <.0001 | 0.001 | 0.06 | 0.06 | 0.001 | 0.39 | 0.08 | <.0001 | 0.0001 | 0.60 | 0.16 | 0.06 | 0.03 | 0.04 | 0.49 | 0.04 | 0.07 |
| WHR | ANOVA | 0.02 | 0.008 | 0.16 | 0.18 | 0.52 | 0.50 | 0.88 | 0.11 | 0.003 | 0.002 | 0.71 | 0.22 | 0.05 | 0.18 | 0.0008 | 0.26 | 0.06 | 0.78 |
| Townsend deprivation score | ANOVA | 0.84 | 0.48 | 0.03 | 0.006 | 0.02 | 0.006 | 0.81 | 0.15 | 0.02 | 0.59 | 0.32 | 0.71 | 0.67 | 0.67 | 0.23 | 0.69 | 0.47 | 0.47 |
| moderate/vigorour physical activity, min/wk | ANOVA | 0.06 | 0.79 | 0.57 | 0.47 | 0.71 | 0.99 | 0.80 | 0.83 | 0.13 | 0.54 | 0.42 | 0.48 | 0.72 | 0.41 | 0.17 | 0.30 | 0.43 | 0.99 |
| alcohol, drinks/wk | ANOVA | <.0001 | <.0001 | 0.06 | 0.14 | 0.45 | 0.57 | 0.17 | 0.002 | <.0001 | 0.07 | 0.05 | 0.002 | 0.05 | 0.03 | 0.06 | 0.06 | 0.001 | 0.0004 |
| fish, servings/wk | ANOVA | 0.001 | 0.03 | 0.09 | 0.72 | 0.51 | 0.009 | 0.68 | 0.73 | 0.65 | 0.06 | 0.30 | 0.27 | 0.84 | 0.03 | 0.61 | 0.002 | 0.02 | 0.13 |
| red meat, servings/wk | ANOVA | 0.01 | 0.97 | 0.40 | 0.21 | 0.26 | 0.76 | 0.31 | 0.58 | 0.72 | 0.007 | 0.31 | 0.39 | 0.69 | 0.19 | 0.40 | 0.08 | 0.04 | 0.0005 |
| fruit, servings/wk | ANOVA | 0.09 | 0.80 | 0.51 | 0.60 | 0.68 | 0.55 | 0.05 | 0.25 | 0.001 | 0.0002 | 0.11 | 0.04 | 0.05 | 0.06 | 0.38 | 0.14 | 0.04 | 0.09 |
| vegetables, servings/wk | ANOVA | 0.03 | 0.01 | 0.41 | 0.49 | 0.95 | 0.26 | 0.34 | 0.73 | 0.47 | 0.61 | 0.13 | 0.13 | 0.91 | 0.36 | 0.66 | 0.19 | 0.94 | 0.03 |
| fasting time, h | ANOVA | 0.13 | 0.60 | 0.49 | 0.06 | 0.38 | 0.81 | 0.18 | 0.07 | 0.23 | 0.15 | 0.66 | 0.74 | 0.07 | 0.77 | 0.36 | 1.00 | 0.90 | 0.54 |
| **recent caffeine intake, yes/no** | Chi-Square | 0.07 | 0.63 | 0.18 | 0.46 | 0.26 | 0.39 | 0.88 | 0.73 | 0.18 | 0.02 | 0.61 | 0.03 | 0.004 | 0.02 | 0.62 | 0.16 | 0.05 | 0.02 |
| coffee intake, categorical | Chi-Square | 0.0002 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | 0.0002 | 0.07 | <.0001 | <.0001 | <.0001 | 0.0007 | <.0001 | <.0001 | <.0001 | <.0001 | 0.005 | <.0001 |
| tea intake, categorical | Chi-Square | 0.18 | 0.07 | <.0001 | <.0001 | <.0001 | <.0001 | 0.79 | 0.64 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | 0.004 | 0.04 |
| coffee type | Chi-Square | 0.47 | 0.86 | 0.14 | 0.98 | 0.004 | 0.21 | 0.22 | 0.11 | <.0001 | <.0001 | 0.006 | 0.13 | <.0001 | 0.009 | 0.009 | 0.08 | 0.72 | 0.30 |
| smoking status | Chi-Square | 0.70 | 0.77 | 0.09 | 0.27 | 0.003 | 0.62 | 0.58 | 0.80 | 0.89 | 0.62 | 0.66 | 0.71 | 0.20 | 0.04 | 0.10 | 0.60 | 0.06 | 0.53 |
| income | Chi-Square | 0.69 | 0.70 | 0.32 | 0.72 | 0.002 | 0.02 | 0.23 | 0.86 | 0.14 | 0.16 | 0.11 | 0.57 | 0.08 | 0.20 | 0.90 | 0.21 | 0.09 | 0.79 |
| education | Chi-Square | 0.44 | 0.05 | 0.24 | 0.93 | 0.07 | 0.02 | 0.18 | 0.37 | 0.04 | 0.44 | 0.010 | 0.04 | 0.67 | 0.008 | 0.002 | 0.79 | 0.12 | 0.83 |
| employment  | Chi-Square | 0.20 | 0.74 | 0.24 | 0.40 | 0.57 | 0.64 | 0.14 | 0.87 | 0.42 | 0.07 | 0.70 | 0.81 | 0.86 | 0.58 | 0.23 | 0.85 | 0.78 | 0.33 |
| home owner, yes/no | Chi-Square | 0.17 | 0.04 | 0.93 | 0.29 | 0.24 | 0.13 | 0.67 | 0.18 | 0.05 | 0.28 | 0.45 | 0.82 | 0.05 | 0.65 | 0.33 | 0.45 | 0.44 | 0.07 |
| fasting time, categorical | Chi-Square | 0.11 | 0.88 | 0.36 | 0.06 | 0.81 | 0.03 | 1.00 | 0.11 | 0.09 | 0.90 | 0.03 | 0.25 | 0.60 | 0.76 | 0.68 | 0.81 | 0.98 | 0.46 |
| caffeine intake, categorical | Chi-Square | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | 0.0001 | 0.0004 | <.0001 | <.0001 | 0.002 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 |
| aspirin use, yes/no | Chi-Square | 0.05 | 0.67 | 0.08 | 0.68 | 0.47 | 0.07 | 0.89 | 0.33 | 0.62 | 0.37 | 0.99 | 0.24 | 0.72 | 0.50 | 0.12 | 0.10 | 0.16 | 0.59 |
| blood pressure medication use, yes/n | Chi-Square | 0.03 | 0.93 | 0.33 | 0.35 | 0.52 | 0.18 | 0.17 | 0.22 | 0.38 | 0.61 | 0.18 | 0.74 | 0.004 | 0.001 | <.0001 | <.0001 | 0.50 | 0.11 |
| cholesterol medication use, yes/no | Chi-Square | <.0001 | <.0001 | 0.02 | 0.30 | 0.28 | 0.03 | 0.64 | 0.08 | 0.52 | 0.54 | 0.20 | 0.03 | 0.002 | 0.27 | 0.23 | 0.0009 | 0.38 | 0.10 |
| self-reported diabetes or insulin use, yes/no | Chi-Square | 0.008 | <.0001 | 0.03 | 0.14 | 0.25 | 0.16 | 0.79 | 0.22 | 0.25 | 0.23 | 0.26 | 0.09 | 0.50 | 0.06 | 0.94 | 0.008 | 0.002 | 0.43 |
| self-reported heart disease, yes/no | Chi-Square | 0.11 | 0.31 | 0.72 | 0.41 | 0.11 | 0.56 | 0.37 | 0.29 | 0.88 | 0.11 | 0.48 | 0.36 | 0.65 | 0.35 | 0.79 | 0.71 | 0.96 | 0.25 |
| post-menopausal hormone use, yes/no | Chi-Square | 0.39 |  | 0.61 |  | 0.06 |  | 0.51 |  | 0.52 |  | 0.44 |  | 0.79 |  | 0.03 |  | 0.02 |  |
| oral contraceptive use, yes/no | Chi-Square | 0.35 |  | 0.63 |  | 0.57 |  | 0.07 |  | 0.92 |  | 0.23 |  | 0.12 |  | 0.49 |  | 0.94 |  |
| self-reported overall health rating | Chi-Square | 0.01 | 0.17 | 0.58 | 0.57 | 0.28 | 0.88 | 0.72 | 0.02 | 0.46 | 0.30 | 0.82 | 0.66 | 0.12 | 0.58 | 0.27 | 0.67 | 0.07 | 0.74 |

F: female, M: male

\*Shown are results (p values) from univariate statistical tests. Color shading corresponds to results meeting statistical significance (orange, P<0.005) or nominal significance (tan, P<0.05).

# Table S4. Crude [MEAN (SD)] and adjusted\* [LSMEAN (SD)] mean biomarker concentrations by recent caffeine drinking

|  |  |  |
| --- | --- | --- |
| Biomarker, units | Women | Men |
| Recent caffeine: No | Recent caffeine: Yes | Recent caffeine: No | Recent caffeine: Yes |
| N | MEAN (SD) | LSMEAN (SD) | N | MEAN (SD) | LSMEAN (SD) | N | MEAN (SD) | LSMEAN (SD) | N | MEAN (SD) | LSMEAN (SD) |
| ApoA1, g/L | 206709 | 1.64 (0.27) | 1.63 (0.46) | 4106 | 1.62 (0.26) | 1.63 (0.26) | 175078 | 1.43 (0.23) | 1.43 (0.35) | 3991 | 1.41 (0.22) | 1.42 (0.22) |
| ApoB, g/L | 228783 | 1.04 (0.24) | 1.04 (0.41) | 4549 | 1.02 (0.23) | 1.04 (0.23) | 188953 | 1.03 (0.24) | 1.03 (0.37) | 4316 | 1.04 (0.24) | 1.04 (0.23) |
| ApoB/ApoA1 | 205616 | 0.65 (0.19) | 0.65 (0.33) | 4084 | 0.65 (0.19) | 0.65 (0.18) | 173996 | 0.74 (0.21) | 0.74 (0.32) | 3956 | 0.75 (0.21) | 0.74 (0.2) |
| Lp(a), log nmol/L | 184240 | 3.22 (1.12) | 3.21 (2.1) | 3696 | 3.2 (1.12) | 3.2 (1.18) | 151683 | 3.16 (1.13) | 3.16 (1.9) | 3480 | 3.15 (1.14) | 3.16 (1.2) |
| cholesterol,mmol/L | 229429 | 5.88 (1.11) | 5.88 (1.91) | 4564 | 5.82 (1.11) | 5.88 (1.07) | 190220 | 5.5 (1.12) | 5.5 (1.67) | 4353 | 5.56 (1.11) | 5.53 (1.06) |
| HDL, mmol/L | 208308 | 1.6 (0.37) | 1.59 (0.62) | 4129 | 1.58 (0.37) | 1.59 (0.35) | 175183 | 1.28 (0.3) | 1.28 (0.46) | 4000 | 1.26 (0.3) | 1.27 (0.29) |
| LDL, mmol/L | 229080 | 3.63 (0.86) | 3.63 (1.49) | 4559 | 3.6 (0.86) | 3.64 (0.83) | 189815 | 3.49 (0.86) | 3.5 (1.27) | 4347 | 3.54 (0.85) | 3.52 (0.81) |
| TG, log mmol/L | 227842 | 0.3 (0.47) | 0.29 (0.77) | 4529 | 0.29 (0.48) | 0.29 (0.43) | 188723 | 0.53 (0.51) | 0.52 (0.81) | 4311 | 0.56 (0.52) | 0.53 (0.52) |
| non-HDL, mmol/L | 208405 | 4.28 (1.07) | 4.28 (1.84) | 4129 | 4.24 (1.06) | 4.28 (1.03) | 175529 | 4.22 (1.07) | 4.22 (1.61) | 4002 | 4.3 (1.07) | 4.26 (1.02) |
| CRP, log mg/L | 226713 | 0.3 (1.04) | 0.29 (1.78) | 4517 | 0.27 (1.05) | 0.32 (0.99) | 187683 | 0.23 (0.96) | 0.23 (1.49) | 4299 | 0.24 (0.96) | 0.24 (0.94) |
| glucose, mmol/L | 206590 | 4.99 (0.69) | 4.98 (1.24) | 4079 | 5.04 (0.84) | 5.07 (0.69) | 173301 | 5.06 (0.85) | 5.06 (1.31) | 3945 | 5.1 (0.98) | 5.14 (0.83) |
| HbA1c, mmol/mol | 225768 | 35.35 (4.35) | 35.34 (6.79) | 4531 | 34.91 (4.18) | 35.18 (3.81) | 186810 | 35.84 (5.42) | 35.9 (7.2) | 4280 | 35.64 (5.28) | 35.86 (4.55) |

\*Adjusted for age, race, date of blood draw, fasting time, assessment center, Townsend deprivation index, education, income, employment status, home ownership, smoking, physical activity, waist-to-hip ratio, body mass index, oral contraceptive use (women only), post-menopausal hormone use (women only), self-rated health, aspirin use, cholesterol-lowering medication use, antihypertension medication use, history or diabetes, history of CVD and habitual intakes of coffee, tea, water, alcohol, fish, red meat, fruits and vegetables. Geometric means are presented for Lp(a), TG and CRP.

# Table S5. SNP-Biomarker Associations\*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Sex | Biomarker | SNP | β | 95% CI | P value |
| LL | UL |
| F | ApoA1 | rs1260326\_C | -0.0091 | -0.0109 | -0.0074 | <.0001 |
| M | ApoA1 | rs1260326\_C | -0.0078 | -0.0094 | -0.0061 | <.0001 |
| F | ApoB | rs1260326\_C | -0.0136 | -0.0151 | -0.0121 | <.0001 |
| M | ApoB | rs1260326\_C | -0.0150 | -0.0166 | -0.0133 | <.0001 |
| F | ApoB/ApoA1 | rs1260326\_C | -0.0049 | -0.0062 | -0.0037 | <.0001 |
| M | ApoB/ApoA1 | rs1260326\_C | -0.0061 | -0.0075 | -0.0046 | <.0001 |
| F | Lp(a) | rs1260326\_C | 0.0091 | 0.0002 | 0.0180 | 0.046 |
| M | Lp(a) | rs1260326\_C | 0.0020 | -0.0079 | 0.0118 | 0.699 |
| F | cholesterol | rs1260326\_C | -0.0595 | -0.0665 | -0.0525 | <.0001 |
| M | cholesterol | rs1260326\_C | -0.0724 | -0.0798 | -0.0650 | <.0001 |
| F | HDL | rs1260326\_C | 0.0006 | -0.0018 | 0.0030 | 0.639 |
| M | HDL | rs1260326\_C | -0.0017 | -0.0038 | 0.0005 | 0.126 |
| F | LDL | rs1260326\_C | -0.0389 | -0.0442 | -0.0335 | <.0001 |
| M | LDL | rs1260326\_C | -0.0415 | -0.0471 | -0.0358 | <.0001 |
| F | TG | rs1260326\_C | -0.0475 | -0.0503 | -0.0446 | <.0001 |
| M | TG | rs1260326\_C | -0.0564 | -0.0601 | -0.0528 | <.0001 |
| F | non-HDL | rs1260326\_C | -0.0614 | -0.0683 | -0.0544 | <.0001 |
| M | non-HDL | rs1260326\_C | -0.0696 | -0.0769 | -0.0622 | <.0001 |
| F | CRP | rs1260326\_C | -0.0887 | -0.0949 | -0.0826 | <.0001 |
| M | CRP | rs1260326\_C | -0.0662 | -0.0729 | -0.0596 | <.0001 |
| F | glucose | rs1260326\_C | 0.0210 | 0.0161 | 0.0258 | <.0001 |
| M | glucose | rs1260326\_C | 0.0163 | 0.0102 | 0.0225 | <.0001 |
| F | HbA1c | rs1260326\_C | 0.0836 | 0.0584 | 0.1087 | <.0001 |
| M | HbA1c | rs1260326\_C | 0.1058 | 0.0739 | 0.1378 | <.0001 |
| F | ApoA1 | rs1481012\_A | 0.0038 | 0.0010 | 0.0066 | 0.008 |
| M | ApoA1 | rs1481012\_A | 0.0021 | -0.0004 | 0.0046 | 0.096 |
| F | ApoB | rs1481012\_A | -0.0032 | -0.0056 | -0.0009 | 0.007 |
| M | ApoB | rs1481012\_A | -0.0002 | -0.0027 | 0.0024 | 0.894 |
| F | ApoB/ApoA1 | rs1481012\_A | -0.0038 | -0.0057 | -0.0018 | 0.0001 |
| M | ApoB/ApoA1 | rs1481012\_A | -0.0014 | -0.0037 | 0.0009 | 0.233 |
| F | Lp(a) | rs1481012\_A | -0.0048 | -0.0186 | 0.0090 | 0.496 |
| M | Lp(a) | rs1481012\_A | 0.0027 | -0.0125 | 0.0179 | 0.731 |
| F | cholesterol | rs1481012\_A | -0.0043 | -0.0151 | 0.0066 | 0.440 |
| M | cholesterol | rs1481012\_A | 0.0008 | -0.0106 | 0.0121 | 0.895 |
| F | HDL | rs1481012\_A | 0.0044 | 0.0007 | 0.0081 | 0.020 |
| M | HDL | rs1481012\_A | 0.0041 | 0.0008 | 0.0073 | 0.014 |
| F | LDL | rs1481012\_A | -0.0078 | -0.0161 | 0.0006 | 0.067 |
| M | LDL | rs1481012\_A | 0.0016 | -0.0070 | 0.0103 | 0.711 |
| F | TG | rs1481012\_A | -0.0004 | -0.0048 | 0.0041 | 0.875 |
| M | TG | rs1481012\_A | -0.0077 | -0.0133 | -0.0021 | 0.007 |
| F | non-HDL | rs1481012\_A | -0.0098 | -0.0206 | 0.0010 | 0.076 |
| M | non-HDL | rs1481012\_A | -0.0017 | -0.0130 | 0.0097 | 0.776 |
| F | CRP | rs1481012\_A | 0.0115 | 0.0019 | 0.0210 | 0.019 |
| M | CRP | rs1481012\_A | 0.0126 | 0.0023 | 0.0229 | 0.016 |
| F | glucose | rs1481012\_A | -0.0034 | -0.0110 | 0.0041 | 0.372 |
| M | glucose | rs1481012\_A | 0.0039 | -0.0055 | 0.0133 | 0.420 |
| F | HbA1c | rs1481012\_A | -0.1353 | -0.1742 | -0.0964 | <.0001 |
| M | HbA1c | rs1481012\_A | -0.0889 | -0.1380 | -0.0398 | 0.0004 |
| F | ApoA1 | rs17685\_A | -0.0006 | -0.0025 | 0.0014 | 0.574 |
| M | ApoA1 | rs17685\_A | 0.0005 | -0.0013 | 0.0022 | 0.604 |
| F | ApoB | rs17685\_A | 0.0043 | 0.0026 | 0.0059 | <.0001 |
| M | ApoB | rs17685\_A | 0.0019 | 0.0001 | 0.0036 | 0.042 |
| F | ApoB/ApoA1 | rs17685\_A | 0.0027 | 0.0014 | 0.0041 | <.0001 |
| M | ApoB/ApoA1 | rs17685\_A | 0.0012 | -0.0004 | 0.0029 | 0.134 |
| F | Lp(a) | rs17685\_A | -0.0016 | -0.0113 | 0.0081 | 0.746 |
| M | Lp(a) | rs17685\_A | -0.0035 | -0.0142 | 0.0073 | 0.528 |
| F | cholesterol | rs17685\_A | 0.0182 | 0.0106 | 0.0258 | <.0001 |
| M | cholesterol | rs17685\_A | 0.0139 | 0.0059 | 0.0219 | 0.001 |
| F | HDL | rs17685\_A | -0.0026 | -0.0052 | 0.0000 | 0.050 |
| M | HDL | rs17685\_A | -0.0001 | -0.0024 | 0.0022 | 0.946 |
| F | LDL | rs17685\_A | 0.0153 | 0.0094 | 0.0212 | <.0001 |
| M | LDL | rs17685\_A | 0.0086 | 0.0025 | 0.0147 | 0.006 |
| F | TG | rs17685\_A | 0.0067 | 0.0036 | 0.0099 | <.0001 |
| M | TG | rs17685\_A | 0.0048 | 0.0008 | 0.0088 | 0.018 |
| F | non-HDL | rs17685\_A | 0.0194 | 0.0118 | 0.0269 | <.0001 |
| M | non-HDL | rs17685\_A | 0.0149 | 0.0068 | 0.0229 | 0.000 |
| F | CRP | rs17685\_A | -0.0097 | -0.0165 | -0.0030 | 0.005 |
| M | CRP | rs17685\_A | -0.0097 | -0.0170 | -0.0024 | 0.009 |
| F | glucose | rs17685\_A | -0.0038 | -0.0091 | 0.0015 | 0.163 |
| M | glucose | rs17685\_A | -0.0114 | -0.0181 | -0.0048 | 0.001 |
| F | HbA1c | rs17685\_A | 0.0094 | -0.0181 | 0.0368 | 0.503 |
| M | HbA1c | rs17685\_A | 0.0062 | -0.0286 | 0.0410 | 0.728 |
| F | ApoA1 | rs2330783\_G | 0.0014 | -0.0060 | 0.0089 | 0.704 |
| M | ApoA1 | rs2330783\_G | -0.0017 | -0.0085 | 0.0051 | 0.620 |
| F | ApoB | rs2330783\_G | 0.0023 | -0.0040 | 0.0085 | 0.483 |
| M | ApoB | rs2330783\_G | 0.0025 | -0.0043 | 0.0094 | 0.468 |
| F | ApoB/ApoA1 | rs2330783\_G | 0.0004 | -0.0048 | 0.0056 | 0.892 |
| M | ApoB/ApoA1 | rs2330783\_G | 0.0004 | -0.0058 | 0.0067 | 0.890 |
| F | Lp(a) | rs2330783\_G | -0.0087 | -0.0459 | 0.0285 | 0.647 |
| M | Lp(a) | rs2330783\_G | -0.0287 | -0.0699 | 0.0126 | 0.174 |
| F | cholesterol | rs2330783\_G | 0.0180 | -0.0111 | 0.0471 | 0.225 |
| M | cholesterol | rs2330783\_G | 0.0225 | -0.0084 | 0.0534 | 0.153 |
| F | HDL | rs2330783\_G | 0.0005 | -0.0095 | 0.0104 | 0.927 |
| M | HDL | rs2330783\_G | -0.0027 | -0.0115 | 0.0062 | 0.550 |
| F | LDL | rs2330783\_G | 0.0141 | -0.0083 | 0.0365 | 0.218 |
| M | LDL | rs2330783\_G | 0.0153 | -0.0082 | 0.0389 | 0.203 |
| F | TG | rs2330783\_G | 0.0136 | 0.0017 | 0.0255 | 0.026 |
| M | TG | rs2330783\_G | 0.0232 | 0.0079 | 0.0385 | 0.003 |
| F | non-HDL | rs2330783\_G | 0.0130 | -0.0160 | 0.0419 | 0.381 |
| M | non-HDL | rs2330783\_G | 0.0169 | -0.0141 | 0.0478 | 0.286 |
| F | CRP | rs2330783\_G | -0.0104 | -0.0362 | 0.0153 | 0.427 |
| M | CRP | rs2330783\_G | -0.0083 | -0.0363 | 0.0197 | 0.560 |
| F | glucose | rs2330783\_G | 0.0129 | -0.0075 | 0.0332 | 0.215 |
| M | glucose | rs2330783\_G | -0.0016 | -0.0273 | 0.0240 | 0.900 |
| F | HbA1c | rs2330783\_G | 0.0339 | -0.0708 | 0.1385 | 0.526 |
| M | HbA1c | rs2330783\_G | -0.0218 | -0.1549 | 0.1113 | 0.749 |
| F | ApoA1 | rs2472297\_T | 0.0011 | -0.0009 | 0.0031 | 0.285 |
| M | ApoA1 | rs2472297\_T | 0.0038 | 0.0020 | 0.0056 | <.0001 |
| F | ApoB | rs2472297\_T | 0.0012 | -0.0005 | 0.0028 | 0.174 |
| M | ApoB | rs2472297\_T | 0.0020 | 0.0002 | 0.0038 | 0.031 |
| F | ApoB/ApoA1 | rs2472297\_T | 0.0007 | -0.0007 | 0.0021 | 0.340 |
| M | ApoB/ApoA1 | rs2472297\_T | -0.0011 | -0.0027 | 0.0006 | 0.211 |
| F | Lp(a) | rs2472297\_T | -0.0031 | -0.0130 | 0.0067 | 0.535 |
| M | Lp(a) | rs2472297\_T | -0.0043 | -0.0152 | 0.0066 | 0.436 |
| F | cholesterol | rs2472297\_T | 0.0070 | -0.0007 | 0.0148 | 0.075 |
| M | cholesterol | rs2472297\_T | 0.0117 | 0.0035 | 0.0198 | 0.005 |
| F | HDL | rs2472297\_T | 0.0021 | -0.0005 | 0.0048 | 0.118 |
| M | HDL | rs2472297\_T | 0.0043 | 0.0020 | 0.0066 | 0.0003 |
| F | LDL | rs2472297\_T | 0.0046 | -0.0013 | 0.0106 | 0.127 |
| M | LDL | rs2472297\_T | 0.0084 | 0.0022 | 0.0146 | 0.008 |
| F | TG | rs2472297\_T | -0.0029 | -0.0061 | 0.0003 | 0.073 |
| M | TG | rs2472297\_T | -0.0028 | -0.0068 | 0.0012 | 0.175 |
| F | non-HDL | rs2472297\_T | 0.0069 | -0.0008 | 0.0147 | 0.078 |
| M | non-HDL | rs2472297\_T | 0.0072 | -0.0010 | 0.0153 | 0.086 |
| F | CRP | rs2472297\_T | -0.0138 | -0.0206 | -0.0069 | <.0001 |
| M | CRP | rs2472297\_T | -0.0107 | -0.0181 | -0.0033 | 0.005 |
| F | glucose | rs2472297\_T | 0.0018 | -0.0037 | 0.0072 | 0.526 |
| M | glucose | rs2472297\_T | 0.0012 | -0.0056 | 0.0080 | 0.726 |
| F | HbA1c | rs2472297\_T | -0.0095 | -0.0373 | 0.0184 | 0.505 |
| M | HbA1c | rs2472297\_T | 0.0219 | -0.0135 | 0.0572 | 0.225 |
| F | ApoA1 | rs5751876\_T | 0.0008 | -0.0010 | 0.0026 | 0.412 |
| M | ApoA1 | rs5751876\_T | -0.0003 | -0.0020 | 0.0013 | 0.691 |
| F | ApoB | rs5751876\_T | 0.0022 | 0.0006 | 0.0037 | 0.005 |
| M | ApoB | rs5751876\_T | -0.0001 | -0.0017 | 0.0016 | 0.917 |
| F | ApoB/ApoA1 | rs5751876\_T | 0.0017 | 0.0004 | 0.0029 | 0.009 |
| M | ApoB/ApoA1 | rs5751876\_T | -0.0001 | -0.0016 | 0.0014 | 0.918 |
| F | Lp(a) | rs5751876\_T | 0.0044 | -0.0046 | 0.0133 | 0.339 |
| M | Lp(a) | rs5751876\_T | -0.0003 | -0.0102 | 0.0096 | 0.953 |
| F | cholesterol | rs5751876\_T | 0.0121 | 0.0051 | 0.0191 | 0.001 |
| M | cholesterol | rs5751876\_T | 0.0022 | -0.0052 | 0.0095 | 0.568 |
| F | HDL | rs5751876\_T | 0.0014 | -0.0010 | 0.0038 | 0.251 |
| M | HDL | rs5751876\_T | -0.0005 | -0.0026 | 0.0016 | 0.646 |
| F | LDL | rs5751876\_T | 0.0085 | 0.0032 | 0.0139 | 0.002 |
| M | LDL | rs5751876\_T | 0.0013 | -0.0044 | 0.0069 | 0.663 |
| F | TG | rs5751876\_T | 0.0009 | -0.0020 | 0.0037 | 0.558 |
| M | TG | rs5751876\_T | 0.0018 | -0.0019 | 0.0054 | 0.343 |
| F | non-HDL | rs5751876\_T | 0.0113 | 0.0043 | 0.0183 | 0.002 |
| M | non-HDL | rs5751876\_T | 0.0028 | -0.0046 | 0.0102 | 0.461 |
| F | CRP | rs5751876\_T | 0.0025 | -0.0037 | 0.0087 | 0.423 |
| M | CRP | rs5751876\_T | -0.0004 | -0.0071 | 0.0063 | 0.901 |
| F | glucose | rs5751876\_T | 0.0026 | -0.0023 | 0.0075 | 0.290 |
| M | glucose | rs5751876\_T | -0.0040 | -0.0101 | 0.0022 | 0.205 |
| F | HbA1c | rs5751876\_T | 0.0103 | -0.0149 | 0.0355 | 0.422 |
| M | HbA1c | rs5751876\_T | 0.0128 | -0.0192 | 0.0447 | 0.434 |
| F | ApoA1 | rs6968554\_G | -0.0020 | -0.0038 | -0.0002 | 0.033 |
| M | ApoA1 | rs6968554\_G | -0.0003 | -0.0019 | 0.0014 | 0.732 |
| F | ApoB | rs6968554\_G | 0.0017 | 0.0001 | 0.0032 | 0.034 |
| M | ApoB | rs6968554\_G | 0.0014 | -0.0003 | 0.0030 | 0.111 |
| F | ApoB/ApoA1 | rs6968554\_G | 0.0016 | 0.0003 | 0.0029 | 0.013 |
| M | ApoB/ApoA1 | rs6968554\_G | 0.0012 | -0.0003 | 0.0027 | 0.126 |
| F | Lp(a) | rs6968554\_G | -0.0099 | -0.0190 | -0.0008 | 0.033 |
| M | Lp(a) | rs6968554\_G | 0.0062 | -0.0039 | 0.0162 | 0.227 |
| F | cholesterol | rs6968554\_G | 0.0049 | -0.0022 | 0.0120 | 0.179 |
| M | cholesterol | rs6968554\_G | 0.0060 | -0.0015 | 0.0135 | 0.118 |
| F | HDL | rs6968554\_G | -0.0041 | -0.0065 | -0.0017 | 0.001 |
| M | HDL | rs6968554\_G | -0.0014 | -0.0035 | 0.0008 | 0.208 |
| F | LDL | rs6968554\_G | 0.0055 | 0.0001 | 0.0110 | 0.048 |
| M | LDL | rs6968554\_G | 0.0032 | -0.0025 | 0.0090 | 0.270 |
| F | TG | rs6968554\_G | 0.0079 | 0.0050 | 0.0108 | <.0001 |
| M | TG | rs6968554\_G | 0.0077 | 0.0039 | 0.0114 | <.0001 |
| F | non-HDL | rs6968554\_G | 0.0101 | 0.0030 | 0.0172 | 0.005 |
| M | non-HDL | rs6968554\_G | 0.0079 | 0.0003 | 0.0154 | 0.041 |
| F | CRP | rs6968554\_G | -0.0102 | -0.0165 | -0.0040 | 0.001 |
| M | CRP | rs6968554\_G | -0.0111 | -0.0179 | -0.0043 | 0.001 |
| F | glucose | rs6968554\_G | 0.0057 | 0.0007 | 0.0107 | 0.024 |
| M | glucose | rs6968554\_G | 0.0040 | -0.0022 | 0.0103 | 0.206 |
| F | HbA1c | rs6968554\_G | 0.0442 | 0.0186 | 0.0698 | 0.001 |
| M | HbA1c | rs6968554\_G | 0.0438 | 0.0113 | 0.0763 | 0.008 |
| F | ApoA1 | rs762551\_A | 0.0007 | -0.0013 | 0.0026 | 0.511 |
| M | ApoA1 | rs762551\_A | 0.0037 | 0.0019 | 0.0055 | <.0001 |
| F | ApoB | rs762551\_A | 0.0011 | -0.0005 | 0.0028 | 0.183 |
| M | ApoB | rs762551\_A | 0.0024 | 0.0005 | 0.0042 | 0.011 |
| F | ApoB/ApoA1 | rs762551\_A | 0.0002 | -0.0012 | 0.0016 | 0.774 |
| M | ApoB/ApoA1 | rs762551\_A | -0.0002 | -0.0018 | 0.0015 | 0.852 |
| F | Lp(a) | rs762551\_A | -0.0002 | -0.0100 | 0.0096 | 0.968 |
| M | Lp(a) | rs762551\_A | 0.0064 | -0.0045 | 0.0172 | 0.249 |
| F | cholesterol | rs762551\_A | 0.0043 | -0.0033 | 0.0120 | 0.268 |
| M | cholesterol | rs762551\_A | 0.0109 | 0.0027 | 0.0190 | 0.009 |
| F | HDL | rs762551\_A | 0.0002 | -0.0025 | 0.0028 | 0.901 |
| M | HDL | rs762551\_A | 0.0032 | 0.0009 | 0.0055 | 0.007 |
| F | LDL | rs762551\_A | 0.0046 | -0.0013 | 0.0105 | 0.127 |
| M | LDL | rs762551\_A | 0.0083 | 0.0021 | 0.0145 | 0.009 |
| F | TG | rs762551\_A | -0.0049 | -0.0080 | -0.0017 | 0.003 |
| M | TG | rs762551\_A | -0.0040 | -0.0080 | 0.0000 | 0.051 |
| F | non-HDL | rs762551\_A | 0.0046 | -0.0031 | 0.0122 | 0.239 |
| M | non-HDL | rs762551\_A | 0.0094 | 0.0013 | 0.0176 | 0.023 |
| F | CRP | rs762551\_A | -0.0017 | -0.0085 | 0.0050 | 0.615 |
| M | CRP | rs762551\_A | -0.0100 | -0.0174 | -0.0027 | 0.008 |
| F | glucose | rs762551\_A | -0.0037 | -0.0091 | 0.0017 | 0.178 |
| M | glucose | rs762551\_A | -0.0007 | -0.0075 | 0.0060 | 0.830 |
| F | HbA1c | rs762551\_A | 0.0078 | -0.0199 | 0.0354 | 0.582 |
| M | HbA1c | rs762551\_A | 0.0353 | 0.0001 | 0.0704 | 0.049 |
| F | ApoA1 | rs7800944\_C | -0.0009 | -0.0029 | 0.0010 | 0.341 |
| M | ApoA1 | rs7800944\_C | -0.0003 | -0.0020 | 0.0015 | 0.764 |
| F | ApoB | rs7800944\_C | -0.0055 | -0.0072 | -0.0039 | <.0001 |
| M | ApoB | rs7800944\_C | -0.0047 | -0.0065 | -0.0030 | <.0001 |
| F | ApoB/ApoA1 | rs7800944\_C | -0.0035 | -0.0048 | -0.0021 | <.0001 |
| M | ApoB/ApoA1 | rs7800944\_C | -0.0032 | -0.0048 | -0.0016 | 0.0001 |
| F | Lp(a) | rs7800944\_C | -0.0019 | -0.0115 | 0.0077 | 0.705 |
| M | Lp(a) | rs7800944\_C | -0.0058 | -0.0165 | 0.0049 | 0.289 |
| F | cholesterol | rs7800944\_C | -0.0176 | -0.0252 | -0.0101 | <.0001 |
| M | cholesterol | rs7800944\_C | -0.0126 | -0.0206 | -0.0047 | 0.002 |
| F | HDL | rs7800944\_C | 0.0102 | 0.0076 | 0.0128 | <.0001 |
| M | HDL | rs7800944\_C | 0.0080 | 0.0057 | 0.0103 | <.0001 |
| F | LDL | rs7800944\_C | -0.0115 | -0.0173 | -0.0057 | 0.0001 |
| M | LDL | rs7800944\_C | -0.0020 | -0.0080 | 0.0041 | 0.531 |
| F | TG | rs7800944\_C | -0.0410 | -0.0441 | -0.0379 | <.0001 |
| M | TG | rs7800944\_C | -0.0460 | -0.0499 | -0.0420 | <.0001 |
| F | non-HDL | rs7800944\_C | -0.0280 | -0.0355 | -0.0205 | <.0001 |
| M | non-HDL | rs7800944\_C | -0.0203 | -0.0283 | -0.0123 | <.0001 |
| F | CRP | rs7800944\_C | -0.0263 | -0.0329 | -0.0196 | <.0001 |
| M | CRP | rs7800944\_C | -0.0112 | -0.0184 | -0.0039 | 0.003 |
| F | glucose | rs7800944\_C | 0.0080 | 0.0028 | 0.0133 | 0.003 |
| M | glucose | rs7800944\_C | 0.0072 | 0.0005 | 0.0138 | 0.034 |
| F | HbA1c | rs7800944\_C | 0.0773 | 0.0502 | 0.1044 | <.0001 |
| M | HbA1c | rs7800944\_C | 0.0763 | 0.0418 | 0.1108 | <.0001 |

F: female, M: male

\*Shown are results from linear regressions assuming an additive genetic model and adjusted for age, race, date of blood draw, fasting time, assessment center, Townsend deprivation index, education, income, employment status, home ownership, smoking, physical activity, waist-to-hip ratio, body mass index, oral contraceptive use (women only), post-menopausal hormone use (women only), self-rated health, aspirin use, cholesterol-lowering medication use, antihypertension medication use, history or diabetes, history of CVD and habitual intakes of coffee, tea, water, alcohol, fish, red meat, fruits and vegetables. Color shading corresponds to results meeting statistical significance (orange, P<0.005) or nominal significance (tan, P<0.05).