SUPPLEMENAL MATERIAL

Supplemental Methods: Detailed information for each cohort

Atherosclerosis Risk in Communities Study (ARIC)

The ARIC Study is a prospective longitudinal investigation of the development of atherosclerosis and its clinical sequelae in which 15,792 individuals aged 45 to 64 years were enrolled at baseline in 1987-1989 from four communities in the United States: Forsyth County, North Carolina; Jackson, Mississippi (African-Americans only); the suburbs of Minneapolis, Minnesota; and Washington County, Maryland.[1] Four examinations were carried out at three-year intervals (exam 1, 1987-1989; exam 2, 1990-1992; exam 3, 1993-1995; exam 4, 1996-1998.) A fifth clinical examination was completed in 2011-2013. Subjects were contacted annually to update their medical histories between examinations. Written informed consent was provided by all study participants, and the study design and methods were approved by institutional review boards at the collaborating medical institutions: University of Mississippi Medical Center Institutional Review Board (Jackson Field Center); Wake Forest University Health Sciences Institutional Review Board (Forsyth County Field Center); University of Minnesota Institutional Review Board (Minnesota Field Center); and the Johns Hopkins School of Public Health Institutional Review Board (Washington County Field Center). DNA methylation data was only for African-Americans of the ARIC cohort, from the Jackson, MS and Forsyth County, NC study sites of the cohort. Incident cardiovascular events occurring between the time of the methylation measurement at either exam 2 or exam 3 and December 31, 2011 were identified during annual phone contact with study participants and by surveillance of local hospital discharge records and death records. Incident CHD was validated by physician review. Bisulfite converted DNA extracted from peripheral blood leukocytes was hybridized to the Illumina HumanMethylation450[2] BeadChip (Illumina Inc., San Diego, CA), following the Illumina HD Methylation protocol (Illumina Inc., San Diego, CA). Individuals were excluded from the analyses if the pass rate for the DNA sample for the participant was < 99% (probes with a detection p-value <0.01/all probes on the array). CpG sites were not analyzed in this study if more than 5% of the samples showed a detection p-value > 0.01, or if the average detection p-value was > 0.01 on the Y chromosome for males. Methylation values were normalized using the Beta MIxture Quantile dilation (BMIQ) method for type I/type II bias correction.[3] Cox proportional hazards models were adjusted for age, sex, years of education, smoking status (current, former, or never), field center, clinical examination (exam 2 or exam 3), body mass index (BMI), technical variables including plate number, column number, and row number, four principal components from the Illumina Infinium HumanExome BeadChip genotype array to account for potential confounding by genetic ancestry, ten surrogate variables (to control for unmeasured batch effects), and cell type proportion estimates. The proportions of neutrophils, lymphocytes, monocytes, eosinophils, and basophils were imputed using the Houseman method[4] based on the measured differential cell counts available for a subset of ARIC participants at exam 2 (n = 175).

Cardiovascular Health Study (CHS)

The CHS is a population-based cohort study of risk factors for coronary heart disease and stroke in adults ≥65 years conducted across four field centers.[5] The original predominantly European ancestry cohort of 5,201 persons was recruited in 1989-1990 from random samples of the Medicare eligibility lists; subsequently, an additional predominantly African-American cohort of 687 persons was enrolled for a total sample of 5,888. DNA methylation was measured on 200 European ancestry and 200 African-American ancestry participants. The samples were randomly selected among participants without presence of coronary heart disease, congestive heart failure, peripheral vascular disease, valvular heart disease, stroke or transient ischemic attack at study baseline or lack of available DNA at study year 5. CHS was approved by institutional review committees at each field center and individuals in the present analysis had available DNA and gave informed consent including consent to use of genetic information for the study of cardiovascular disease. Between enrollment in the CHS study and 1998–1999, participants were seen in the clinic annually, and contacted by phone at 6-month intervals to collect information about hospitalizations and potential cardiovascular events. Subsequently, telephone calls occurred every 6 months. Hospital records of all potential events were obtained, and all events were adjudicated by a CHS Events Committee. MI was indicated by symptoms of coronary ischemia, elevated serum levels of troponin and cardiac enzymes, and specified electrocardiographic changes.[6] Deaths were identified by a review of obituaries, medical records, death certificates, and the Centers of Medicare and Medicaid Service health care utilization data base for hospitalization, and from household contacts; 100% complete follow-up for mortality status was achieved. Deaths from cardiovascular causes included deaths by coronary heart disease, heart failure, peripheral vascular disease, or

cerebrovascular disease.[7] Methylation measurements were performed using the Infinium HumanMethylation450 BeadChip. Quality control was performed in in the minfi[8] R package. Samples with low median intensities of below 10.5 (log_2) across the methylated and unmethylated channels, samples with a proportion of probes falling detection of greater than 0.5%, samples with QC probes falling greater than 3 standard deviation from the mean, sex-check mismatches, or failed concordance with prior genotyping were removed. In total, 11 samples were removed for sample QC resulting in a sample of 191 European-ancestry and 198 African-American samples. Methylation values were normalized using the SWAN quantile normalization method.[9] White blood cell proportions were estimated from the methylation data using the Houseman method.[4] Analyses were conducted with penalized cox regression, adjusting for age, sex, years of education, smoking status (never/former/current), BMI, as well as cell count composition as estimated using the Housmann method. Analyses were stratified by European or African-American ancestry. Analyses of African-Americans were additionally adjusted for two genetic principal components.

long-tErm follow-up of antithrombotic management Patterns In acute CORonary syndrome patients (EPICOR)

EPICOR is a case-control study nested within the Italian section of the EPIC cohort (about 50,000 volunteers) EPIC-Italy subjects included in EPICOR were recruited between 1992-1998 in 4 Italian centers, Turin and Varese (Northern Italy), Naples (Central-Southern Italy), and Ragusa (Southern Italy). All subjects were healthy at enrollment and have been followed up for major events (mainly cancer, cardiovascular disease, and other chronic diseases of the adulthood).[10] This current analysis included 584 individuals healthy at the time of recruitment: 292 who developed non-fatal Myocardial Infarction (MI) at follow-up (average Time to Disease (TTD) 6.92 ± 3.77 years), and 292 controls matched to cases by age (± 2.5 years), gender, Center of recruitment (Sampling method: Incidence density method). EPICOR MI cases were identified from hospital discharge databases of clinical reports identifying events based on International Classification of Diseases (ICD)-9 codes. Cases were cross-checked with mortality files to identify fatal and nonfatal cases. Subjects with CHD at EPIC cohort entry were excluded from this study. DNA methylation was measured in bisulfite-converted DNA from white blood cells using the Infinium HumanMethylation450 BeadChip (Illumina). Methylation signals (beta-values) were excluded if they had detection p-value≥ 0.05; CpG loci were excluded if they had detection p-value ≥ 0.05 in more than 1% of the assayed samples.Samples with a global call rate $\leq$99% were excluded as well. Normalization was performed on raw methylation data, including color bias adjustment, Quantile Normalization, and BMIQ for type I/type II bias correction.[3] Penalized logistic regression model adjusting for matching variables: age (± 2.5 years), gender, and center of recruitment. Additional covariates included in the model are education (numeric in years), BMI (numeric), smoking status (categorical: current, former, never), and cell type proporsions estimated using the Houseman method.

The Framingham Heart Study (FHS)

The Framingham Heart Study (FHS) offspring cohort, as previously described,[11] is a community-based cohort recruited in 1971 and included the offspring (and their spouses) of the FHS original cohort.[12] The eligible sample for this investigation was drawn from participants in the FHS offspring cohort who gave consent for genomic studies and had DNA methylation assays completed on whole blood samples collected at the eighth examination cycle (2005-2008). At each examination, participants provided fasting blood samples and had a standardized medical examination, including obtaining smoking history, current medication use, and height and weight. Details are available at http://www.framinghamheartstudy.org/. Participants provided written informed consent at the time of each examination visit. The study protocol was approved by the Institutional Review Board at Boston University Medical Center (Boston, MA). CHD and MI events were prospectively ascertained via periodic health updates with the participants and surveillance of the local medical centers. All events were adjudicated by a panel of three physicians, who reviewed participants' medical records, laboratory findings and clinic examination notes. Offspring cohort participants who had prevalent CHD at the eighth examination cycle (2005-2008) were excluded from the analyses (n=261). In FHS, buffy coat preparations were obtained from peripheral whole blood samples. DNA was extracted using the Gentra Puregene DNA extraction kit (Qiagen, Venlo, Netherlands) and then underwent bisulfite conversion using the EZ DNA Methylation kit (Zymo Research, Irvine, CA). Samples underwent whole genome amplification, fragmentation, array hybridization, and single-base pair extension. DNA methylation arrays were run in two laboratory batches at the Johns Hopkins Center for Inherited Disease Research (lab batch #1) and University of Minnesota Biomedical Genomics Center (lab batch #2). The first batch included 576 samples from an earlier

cardiovascular disease case-control study[13] and the second batch included 2270 samples from the remainder of the offspring cohort participants. DNA methylation results underwent normalization within laboratory batches using the DASEN methodology implemented in the wateRmelon package[14] in R (version 3.0.2). We excluded samples with a missing rate >1% at p<0.01 (n=10 for batch #1 and n=35 for batch #2), poor single nucleotide polymorphism (SNP) matching to the 65 SNP control probe locations (n=38 for batch #1 and n=41 for batch #2), and outliers by multi-dimensional scaling techniques (n=25 for batch #1 and n=48 for batch #2). We excluded probes with a missing rate >20% at p<0.01 (n=466 from batch #1 and n=366 from batch #2), as well as probes previously identified to map to multiple locations[15] or to have an underlying SNP (minor allele frequency >5% in European ancestry (EUR) 1000 genomes project data) at the CpG site or within 10 bp of the single base extension (n=42,251). Genotype data were obtained from buffy coat samples, assayed using the MIPS 50K and Affymetrix 500K platforms. After quality control for Hardy-Weinberg Equilibrium, excessive Mendelian errors, and low call rate, imputation using the 1000 Genomes reference panel was conducted, yielding approximately 39 million SNPs. Mixed effect Cox proportional hazards regression models were conducted to test the association of genome-wide DNA methylation with time to CHD or MI event using the *coxme* package in R. The untransformed DNA methylation beta value was specified as the independent variable of interest adjusted for age, sex, body mass index (kg/m^2) , smoking (current/former/never), educational attainment, imputed cell counts (obtained via the Houseman method,[4] and surrogate variables to account for unmeasured batch effects as fixed effects.[16] The model was also adjusted as a random effect for a covariance matrix that comprises the familial relatedness, which are obtained by self-report and genetic similarity calculated by identity-by-descent probabilities. The methylation quantitative trait loci (meQTL) model utilized a two-step approach. First, the DNA methylation beta value was residualized with adjustment for age, sex, imputed cell count proportions, measured technical covariates (row, chip, column), and the family structure covariance matrix. Second, the residual of the DNA methylation was specified as the dependent variable, SNP genotype dosage as the independent variable of interest and additionally adjusted for 50 methylation SVAs (surrogate variable analysis) to account for unmeasured technical and batch effects.

The Invecchiare in Chianti study (InCHIANTI)

The InCHIANTI study is a population-based epidemiological study aimed at evaluating the factors that influence mobility in the older population living in the Chianti region in Tuscany, Italy.[17] Briefly, 1616 residents were selected from the population registry of Greve in Chianti (a rural area: 11709 residents with 19.3% of the population greater than 65 years of age), and Bagno a Ripoli (Antella village near Florence; 4,704 inhabitants, with 20.3% greater than 65 years of age). The participation rate was 90% (n=1453), and the age of the participants ranged between 21 and 102 years. The study protocol was approved by the Italian National Institute of Research and Care of Aging Institutional Review and Medstar Research Institute (Baltimore, MD).Assessment of DNA methylation has been previously described[18]. Briefly, DNA was extracted from buffy coat samples and bisulfite converted using Zymo EZ-96 DNA Methylation kit (Zymo Research Corp., Irvine, CA) and methylation status of 485,577 CpG sites was assessed with Illumina Infinium HumanMethylation450 BeadChip (Illumina Inc, San Diego, CA). Quality control filtering and normalization accomplished using the wateRmelon package.8 Markers were exluced if the bead count was less than 3 in $\geq$ 5% of samples. Samples and markers where also excluded if $\geq$ 5% of detection p-values were greater than 0.01. A background adjustment and quantile normalization were applied to the filtered data set; followed by the BMIQ method[3] for type I/type II bias correction. Methylation markers on the X and Y chromosome, as well as markers with potentially cross-reactive probes and probes that may be polymorphic in European populations (AF $\geq$ .01) were excluded from analyses. Analyses were conducted with penalized Cox regression, adjusting for age, sex, smoking status (never/former/current), categorical education, BMI, and CD8T, CD4T, NK, and monocytes cell type proportions estimated with the Houseman method,[4] as well as complete blood count (CBC) neutrophils and monocytes.

The Kooperative Gesundheitsforschung in der Region Augsburg study (KORA)

The Cooperative Health Research in the Region of Augsburg, Germany Survey 4 (KORA S4) is a population based survey of 4,261 individuals recruited from Augsburg, Germany from October, 1999 – April, 2001.[19] This study was approved by the ethics committee of the Bavarian Medical Association in Munich, Germany. Non-fatal MI events

were reported to the Coronary Events Registry and linked to the cohorts using name and date of birth.[20,21] For individuals who moved out of the study area, mailed questionnaires and general practitioner notes were used to validate MI. In the event that the questionnaires were not returned the date of move was used as the loss to follow-up date. Fatal MI events found in population registries but not the Coronary Events Registry were classified using the general practitioner's notes, hospital discharge letter, or ICD-9 code of the underlying cause of death.
For the current analysis, all participants with a myocardial infarction (MI) prior to their baseline exam were excluded. Additionally, only participants with blood samples available for DNA methylation assaying were used for this study. Genome-wide DNA methylation measurement at 485,577 genomic sites was performed using the Infinium HumanMethylation450K BeadChip®[2,22]) in 1814 KORA F4, and 1535 KORA S4 samples. The laboratory process has been described previously.[23] Briefly, denaturated single-stranded genomic DNA was subjected to bisulfite treatment using the EZ-96 DNA Methylation Kit (Zymo Research, Orange, CA, USA). Bisulfite-converted samples were subjected to whole genome amplification, followed by enzymatic fragmentation and application to the BeadChips. The arrays were fluorescently stained and scanned with the Illumina HiScan SQ scanner. Background correction was performed using the R package *minfi*, version 1.6.0.[8] Detection p-values were defined as the probability of a signal being detected above the background signal level, as estimated from negative control probes. Data were normalized using quantile normalization (QN) on the raw signal intensities [24] using the R package *limma*, version 3.16.5 [25]. Furthermore, beta-mixture quantile normalization (BMIQ)[3] was applied using the R package *watermelon*, version 1.0.3.[14] Before analyses all samples with detection p-values > 0.05 for 1% of all probes were removed followed by the removal of all probes with detection p-values > 0.05 for 1% or more of the remaining samples. Proportions of selected cell types (i.e., granulocytes, monocytes, B cells, CD4+ T cells, CD8+ T cells and natural killer cells) were estimated using the method of Houseman et al.[4] Twnenty principal components created from the control probes were used as technical covariates. Models were run under penalized Cox regression model (incident MI). Models were additionally adjusted for age, sex, smoking status, and BMI.

Normative Aging Study (NAS)
The ongoing longitudinal US Department of Veterans Affairs (VA) Normative Aging Study (NAS) was established in 1963 and included men, 21-80 years old and free of known chronic medical conditions at entry.[26] Subsequently participants were invited to medical examinations every three to five years. At each visit, men provided information on medical history, lifestyle, and demographic factors, and underwent physical examinations and laboratory tests. DNA samples were collected from 675 active participants between 1999-2007. All subjects were evaluated at the baseline examination for preexisting cardiovascular disease (including nonfatal ischemic heart disease or stroke) based on medical records and physician exams from the current or past study visits.26 Hospital records and any other clinical documentation for every report of cardiovascular event were reviewed by a board-certified cardiologist. Experienced research staff coded cardiovascular outcomes using ICD-9 codes. DNA was extracted from buffy coat using the QIAamp DNA Blood Kit (QIAGEN, Valencia, CA), bisulfite converted using the EZ-96 DNA Methylation Kit (Zymo Research, Orange, CA), and analyzed using the Infinium HumanMethylation450K BeadChip®. Quality control analysis was performed to remove samples and probes, where >1% of probes or samples, respectively, had a detection p-value > 0.05. The remaining samples were preprocessed using the Illumina-type background correction[27] and normalized with the dye-bias and BMIQ adjustments.[3] For the current analysis, participants were excluded if they had previously developed coronary heart disease at the 'baseline' examination 1(i.e. 1st examination from which DNA methylation data was derived). Analyses were performed with Cox Proportional Hazards models, adjusting for age, years of education, smoking status, BMI. Proportions of selected cell types (i.e., granulocytes, monocytes, B cells, CD4+ T cells, CD8+ T cells and natural killer cells) were estimated using the procedure proposed by Houseman et al.,[4] and included as adjustment variables in the model. To avoid any batch effect of DNA methylation levels, technical covariates for plate, position of the chip, row and column were included as fixed effect in the analyses.

The Women's Health Initiative Epigenetic Mechanisms of PM-Mediated CVD (WHI-EMPC)
WHI-EMPC is an ancillary study of epigenetic mechanisms underlying associations between ambient particulate matter (PM) air pollution and cardiovascular disease (CVD) in the Women's Health Initiative clinical trials (CT) cohort. The WHI-EMPC study population is a stratified, random sample of 2,200 WHI CT participants who were examined between 1993 and 2001; had available buffy coat, core analytes, electrocardiograms, and ambient concentrations of PM; but were not taking anti-arrhythmic medications at the time. As such, WHI-EMPC is representative of the larger, multiethnic WHI CT population from which it was sampled: n = 68,132 participants aged 50-79 years who were randomized to hormone therapy, calcium / vitamin D supplementation, and / or dietary modification in 40 U.S. clinical centers at the baseline exam (1993-1998) and re-examined in the fasting state one,

three, six, and nine years later.[28,29] Self-reported CHD cases were confirmed by physician-review, classification, and local / central adjudication of medical records. Genome-wide DNAm at CpG sites was measured using the Illumina 450K Infinium Methylation BeadChip, quality controlled using the following filters: detection p-values > 0.01 in > 10% of samples, detection p-values > 0.01 or missing in > 1% of probes, and probes with a coefficient of variation < 5%. Analyses were conducted with Firth's penalized likelihood Cox (for incident CHD) or mixed-effects Cox (for incident MI) models, adjusted for age, categorical education (vocational or high school; any college / college graduate; post-graduate, professional, or advanced degree), smoking status (never; former; current), BMI, cell type proportions (derived using method of Houseman et al.[4]), cohort-specific sampling variables, and batch variables including plate, chip, row, and column, which were treated as random effects for incident MI analyses.

Integrative genomics and risk of CHD and related phenotypes in the Women's Health Initiative (WHI-BAA23)

The WHI-BAA23 Ancillary study included a subsample of participants of the Women's Health Initiative (WHI) study, a national study that began in 1993 which enrolled postmenopausal women between the ages of 50-79 years into either one of two three randomized clinical trials (RCTs). None of these women had CHD at baseline but about half of these women had developed CHD by 2010. Women were selected from one of two WHI large sub cohorts that had previously undergone genome wide genotyping as well as profiling for 7 cardiovascular disease related biomarkers including total cholesterol, HDL, LDL, triglycerides, CRP, creatinine, insulin, and glucose through 2 core WHI ancillary studies. The first cohort is the WHI SNP Health Association Resource (SHARe) cohort of minorities that includes >8000 African American (AA) women and >3500 Hispanic women. The second cohort consists of a combination of European Americans (EA) from the two Hormonal Therapy (HT) trials selected for GWAS and biomarkers in core studies W58 and W63 From these two cohorts, two sample sets were formed. The first (sample set 1) is a sample set of 637 CHD cases and 631 non-CHD cases as of Sept 30, 2010. The second sample set (sample set 2) is a non-overlapping sample of 432 cases of coronary heart disease and 472 non-cases as of September 17, 2012. Adjudication methods for cardiovascular disease outcomes in the WHI have been previously described extensively.[30] Adjudication of these events occurred for all participants through the clinical trial and intervention phase (1993-2005) as well as the first extension (2005-2010). Adjudication of CHD events during the second extension study (2010-2015) was restricted to a subset of participants in the Medical Record Cohort (MRC). DNA methylation data was derived from DNA extracted from buffy coat of whole blood. Methylation analysis was performed at HudsonAlpha Institute of Biotechnology using the Illumina Infinium HumanMethylation450 BeadChip, following the standard protocol of Illumina methylation assays. Any value with a detection p-value above 0.01 was set to missing, and samples with more than 1.5% missing data were removed. Additionally, CpGs with greater than 10% missing data were removed. Batch normalization was carried out using non-parametric empirical Bayes normalization using the Combat[31] function in R. Probes using Infinium I chemistry were normalized separately from those using Infinium II chemistry, and a chemistry correction was applied after normalization.[32] Models run under penalized logistic regression, adjusting for age, BMI, 3-category smoking (never/former/current), and categorical education. We additionally included as covariates in the models cell-count estimation using Houseman's method (i.e., granulocytes, monocytes, B cells, CD4+ T cells, CD8+ T cells and natural killer cells) and 20 principal components created from the control probes.

Supplemental Table 1. Genomic details for the 30 CpG sites associated (FDR<0.05) with risk of coronary heart disease (CHD).

CpG name	Chromosome	Genomic location	Gene region*
cg22617878	3	10417183	Body
cg13827209	9	101912842	3'UTR;3'UTR
cg14185717	9	16864746	Body
cg10307345	11	18771567	Body
cg13822123	2	54197256	Body
cg23245316	2	3260005	Body
cg24977276	7	74105270	Body
cg24447788	19	795310	--
cg08422803	21	46341067	TSS200;5'UTR
cg01751802	19	11309639	TSS1500
cg02449373	19	49256123	5'UTR
cg02683350	5	178658501	Body;Body
cg05820312	8	141468672	1stExon;TSS1500;5'UTR
cg06639874	2	238417703	Body
cg06582394	3	121902622	5'UTR;1stExon
cg02155262	4	178363707	TSS200
cg12766383	1	19403306	Body
cg05892484	7	2143507	Body
cg03031868	13	47371523	TSS200
cg25497530	7	158059944	Body
cg06596307	15	99405016	Body
cg10702366	1	60070383	Body
cg26470101	2	173099597	--
cg26042024	8	135610009	Body;3'UTR;TSS1500
cg00466121	1	86174151	TSS200
cg04987302	14	57476116	--
cg08853494	4	76439657	TSS200;1stExon;5'UTR
cg26467725	15	92647041	Body
cg06442192	19	48059856	TSS1500
cg00393373	4	10456597	5'UTR

*gene region information is according to annotation data from Illumina. Dashed lines within table cells indicate that no gene was mapped to that specific CpG

Supplemental Table 2. Genomic details for the 29 CpG sites associated with risk of myocardial infarction (MI).

CpG name	Chromosome	Genomic location	Gene region*
cg22871797	15	22992526	Body
cg24977276	7	74105270	Body
cg18598861	14	24635529	3'UTR
cg09777776	19	24269890	TSS200
cg20545941	22	43821227	Body
cg19935845	6	32074856	5'UTR
cg24423782	7	129410417	TSS200
cg00393373	4	10456597	5'UTR
cg00466121	1	86174151	TSS200
cg19227382	10	73521606	Body
cg03467256	2	10556515	5'UTR
cg25196881	15	39780412	--
cg02321112	7	156810523	--
cg00355799	1	244109212	--
cg17556588	11	32854320	Body
cg04987302	14	57476116	--
cg07289306	3	44039357	--
cg05892484	7	2143507	Body
cg10702366	1	60070383	Body
cg22618720	20	55959549	--
cg14010194	6	42152817	Body
cg13827209	9	101912842	3'UTR
cg24318598	11	70034186	3'UTR;Body
cg07015775	1	86174125	TSS200
cg21018156	6	134061814	--
cg07475527	1	24864545	--
cg20000562	14	36978633	Body
cg07436807	10	90712767	TSS200;5'UTR
cg14029912	3	5027616	--

*gene region information is according to annotation information from Illumina.
Dashed lines within table cells indicate that no gene was mapped to that specific CpG

Supplemental Table 3. Comparison of effect estimates for the CHD-associated CpGs results from a meta-analysis of European-ancestry participants vs meta-analysis of African-American ancestry participants

CpG	β (Eur.)	β (Af. Am.)	SE (Eur.)	SE (Af. Am.)	t-statistic	p-value*
cg07436807	0.139	-1.859	0.445	0.396	4.249	0.002
cg05892484	-0.197	-1.507	0.341	0.269	3.751	0.004
cg09777776	0.455	-0.104	0.117	0.199	3.411	0.007
cg24977276	0.142	-0.818	0.303	0.139	3.365	0.007
cg06596307	-0.036	-1.077	0.376	0.205	2.887	0.016
cg22617878	-0.789	0.454	0.135	0.691	-2.741	0.021
cg22871797	-0.302	-1.271	0.338	0.305	2.703	0.022
cg24318598	0.171	-0.376	0.230	0.132	2.468	0.033
cg23245316	-0.245	-1.138	0.378	0.205	2.467	0.033
cg18598861	-1.180	-0.189	0.272	0.516	-2.436	0.035
cg02155262	0.095	1.150	0.465	0.222	-2.401	0.037
cg14185717	-0.426	-0.795	0.142	0.172	2.215	0.051
cg22618720	-0.243	-0.803	0.221	0.249	2.214	0.051
cg13827209	0.698	0.401	0.145	0.132	1.928	0.083
cg21018156	-0.395	-0.143	0.152	0.059	-1.791	0.103
cg06582394	0.427	0.238	0.099	0.098	1.744	0.112
cg06639874	-0.277	-0.602	0.188	0.127	1.743	0.112
cg13822123	0.248	0.926	0.418	0.172	-1.743	0.112
cg14029912	-0.819	-0.419	0.264	0.153	-1.568	0.148
cg02449373	0.856	0.506	0.184	0.268	1.479	0.170
cg10702366	-0.244	-0.126	0.053	0.102	-1.469	0.173
cg03467256	-0.703	-0.369	0.185	0.259	-1.436	0.181
cg07015775	0.487	0.988	0.461	0.202	-1.161	0.272
cg04987302	-0.601	-0.866	0.172	0.276	1.135	0.283
cg05820312	0.583	1.095	0.504	0.231	-1.080	0.306
cg25497530	-0.379	-0.529	0.127	0.143	1.039	0.323
cg02321112	0.459	0.679	0.197	0.196	-1.025	0.330
cg26467725	-0.616	-0.946	0.332	0.221	1.008	0.337
cg00355799	-0.157	-0.361	0.227	0.092	0.969	0.356
cg07475527	-0.096	-0.253	0.160	0.123	0.961	0.359
cg07289306	0.973	0.616	0.343	0.334	0.960	0.360
cg00393373	-0.661	-0.391	0.147	0.413	-0.925	0.377
cg26470101	0.499	0.688	0.204	0.171	-0.892	0.393
cg06442192	-1.133	-0.817	0.268	0.442	-0.858	0.411
cg01751802	0.254	0.332	0.087	0.083	-0.833	0.424
cg19935845	-0.510	-0.370	0.146	0.166	-0.832	0.425
cg20000562	0.247	0.350	0.117	0.121	-0.800	0.442
cg14010194	-0.783	-0.572	0.221	0.287	-0.788	0.449
cg03031868	0.567	0.755	0.253	0.180	-0.742	0.475
cg24447788	-0.519	-0.689	0.112	0.336	0.726	0.484
cg24423782	-0.500	-0.661	0.205	0.253	0.659	0.525
cg08853494	0.139	0.452	0.533	0.097	-0.652	0.529
cg17556588	-0.296	-0.180	0.207	0.063	-0.614	0.553
cg25196881	-0.268	-0.414	0.335	0.120	0.472	0.647
cg20545941	-1.456	-1.253	0.429	0.438	-0.429	0.677

cg26042024	-0.606	-0.717	0.144	0.358	0.425	0.680
cg00466121	0.826	0.958	0.425	0.226	-0.327	0.751
cg19227382	-0.634	-0.724	0.290	0.212	0.307	0.765
cg10307345	-0.305	-0.279	0.070	0.097	-0.287	0.780
cg08422803	0.392	0.404	0.121	0.108	-0.090	0.930
cg02683350	-1.016	-0.998	0.238	0.450	-0.051	0.960
cg12766383	-1.259	-1.234	0.612	0.288	-0.044	0.966

Abbreviations: Af. Am.: African American ancestry; Eur: European ancestry.

* p-value for t-statistic difference when comparing results from a meta-analysis of European ancestry individuals only with that of African-American ancestry individuals only

Supplemental Table 4. DNA methylation at 30 CpG sites associated with the risk of incident coronary heart disease (discovered via Fixed effects meta-analysis) - comparison to results obtained with Random-effects meta-analysis.

	Fixed-effects meta-analysis results		Random-effects meta-analysis results	
CpG name	beta coefficient* (95% CI)	nominal p-value	beta coefficient* (95% CI)	nominal p-value
cg00393373	0.73(0.64,0.84)	4.91E-06	0.73(0.64,0.84)	4.90681E-06
cg00466121	1.59(1.31,1.93)	3.16E-06	1.59(1.31,1.93)	3.16075E-06
cg01751802	1.16(1.09,1.23)	9.35E-07	1.16(1.09,1.23)	9.3515E-07
cg02155262	1.61(1.32,1.96)	1.97E-06	1.24(0.85,1.8)	0.264812801
cg02449373	1.45(1.25,1.68)	9.98E-07	1.45(1.25,1.68)	9.97915E-07
cg02683350	0.6(0.49,0.74)	1.55E-06	0.6(0.49,0.74)	1.54868E-06
cg03031868	1.41(1.22,1.63)	2.29E-06	1.34(1.09,1.64)	0.00491481
cg04987302	0.71(0.62,0.82)	3.71E-06	0.71(0.62,0.82)	4.00642E-06
cg05820312	1.65(1.35,2.03)	1.60E-06	1.6(1.25,2.05)	0.000184416
cg05892484	0.61(0.49,0.74)	2.01E-06	0.71(0.5,1.02)	0.060823449
cg06442192	0.59(0.47,0.74)	4.89E-06	0.59(0.47,0.74)	4.88514E-06
cg06582394	1.18(1.1,1.26)	1.90E-06	1.18(1.1,1.26)	1.89777E-06
cg06596307	0.66(0.55,0.78)	2.99E-06	0.83(0.59,1.17)	0.28261177
cg06639874	0.78(0.7,0.86)	1.83E-06	0.85(0.71,1.01)	0.060399808
cg08422803	1.22(1.13,1.32)	7.52E-07	1.22(1.13,1.32)	7.51693E-07
cg08853494	1.25(1.14,1.37)	4.03E-06	1.14(0.9,1.43)	0.280226903
cg10307345	0.86(0.82,0.91)	1.86E-07	0.86(0.82,0.91)	1.85973E-07
cg10702366	0.90(0.86,0.94)	3.09E-06	0.90(0.86,0.94)	3.08604E-06
cg12766383	0.54(0.42,0.69)	1.98E-06	0.54(0.42,0.69)	1.9811E-06
cg13822123	1.51(1.29,1.77)	2.03E-07	1.36(1.04,1.78)	0.024174101
cg13827209	1.31(1.19,1.44)	3.76E-08	1.33(1.16,1.51)	2.29709E-05
cg14185717	0.75(0.67,0.83)	1.38E-07	0.78(0.66,0.93)	0.004977918
cg22617878	0.69(0.61,0.79)	1.99E-08	0.94(0.49,1.80)	0.863486095
cg23245316	0.63(0.53,0.75)	2.17E-07	0.69(0.48,0.99)	0.043840849
cg24447788	0.76(0.69,0.85)	4.33E-07	0.8(0.66,0.96)	0.019465698
cg24977276	0.72(0.64,0.82)	2.54E-07	0.87(0.68,1.11)	0.25543627
cg25497530	0.80(0.73,0.88)	2.62E-06	0.81(0.72,0.9)	0.000164888
cg26042024	0.73(0.64,0.84)	3.13E-06	0.79(0.63,0.99)	0.037875082
cg26467725	0.66(0.55,0.78)	4.22E-06	0.72(0.56,0.92)	0.009886641
cg26470101	1.36(1.19,1.54)	3.09E-06	1.36(1.19,1.54)	3.08655E-06

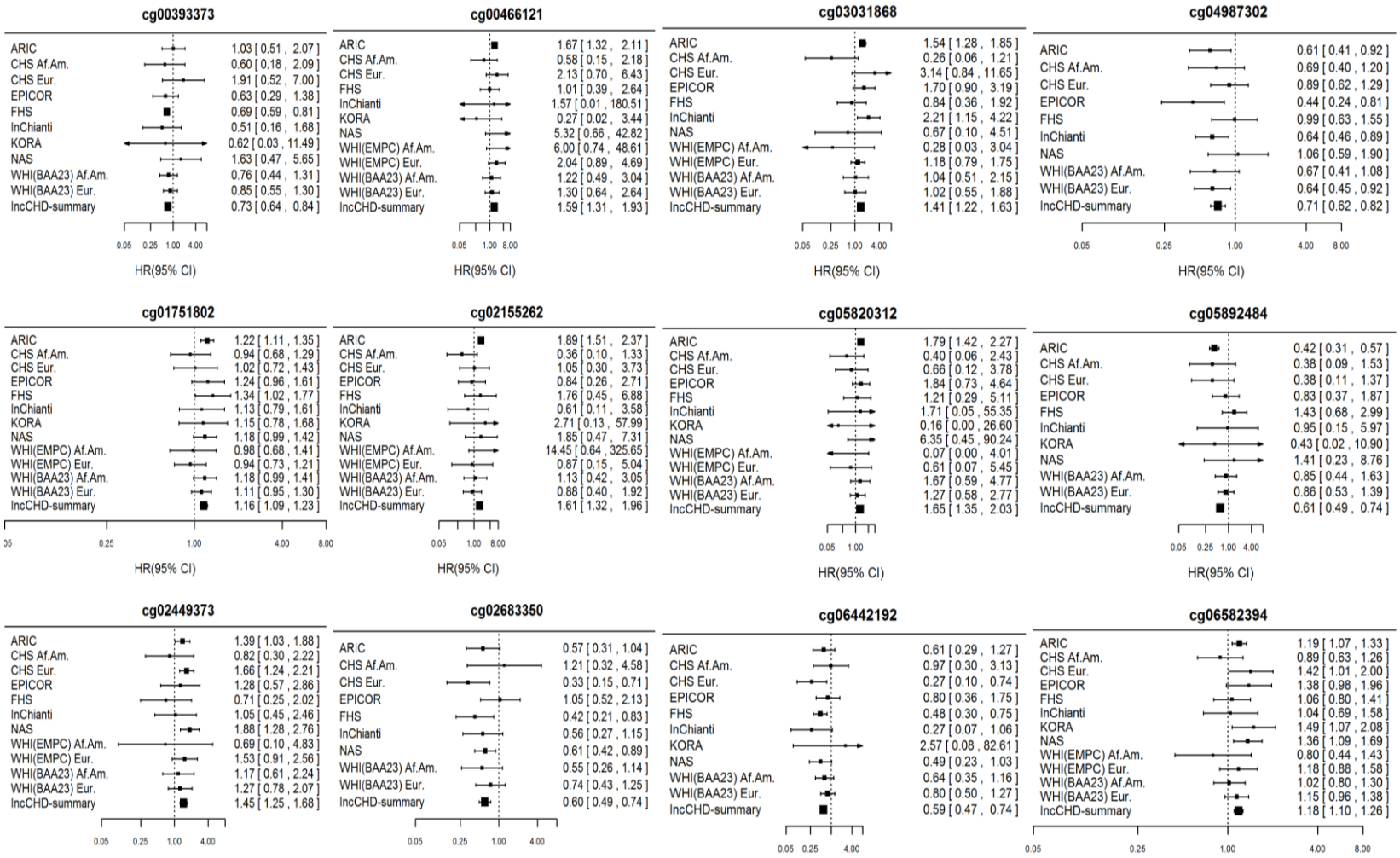
* effect estimates represent log hazard ratio per 5% increase in DNA methylation

Supplemental Table 5. Associations of cis genetic variants (meQTLs) with corresponding phenotypes from previous GWAS studies.

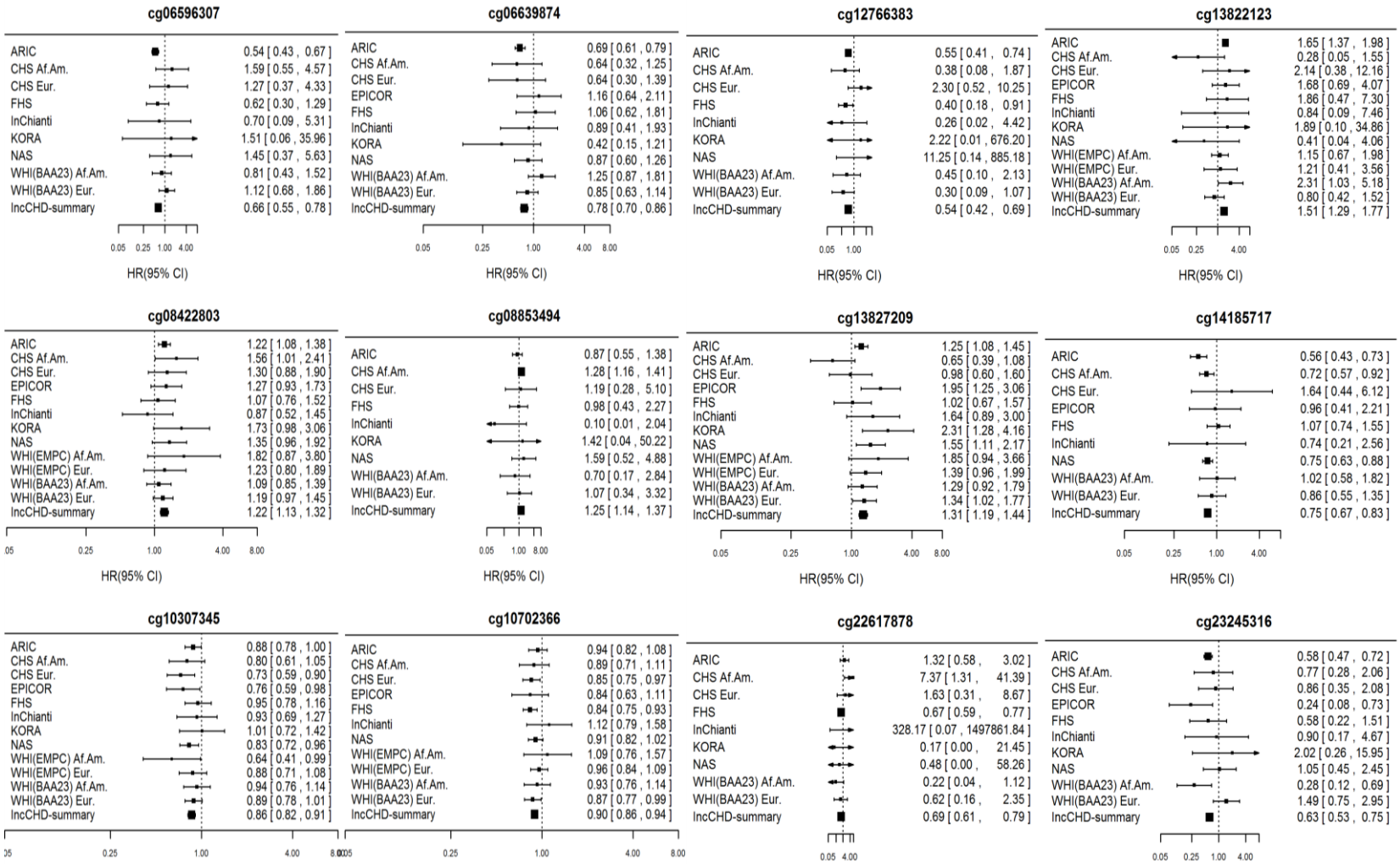
Genomic Locus	Lead SNP	chr	bp	rsID	PMID	First Author	Journal	Trait	P-value
8	rs1013186	9	101908365	rs334353	23455636	Fritsche LG[33]	Nat Genet	Age-related macular degeneration	3.00E-11
3	rs10187185	2	238443226	rs2292884	21743057	Schumacher FR[34]	Hum Mol Genet	Prostate cancer	4.00E-08
3	rs10187185	2	238387228	rs7584330	21743467	Kote-Jarai Z[35]	Nat Genet	Prostate cancer	3.00E-09
1	rs12740006	1	60084516	rs12727131	21507922	Ramsuran V[36]	Clin Infect Dis	Neutrophil count	3.00E-06
5	rs2255214	3	121769522	rs2681424	22190364	Patsopoulos NA[37]	Ann Neurol	Multiple sclerosis	2.00E-07
5	rs2681416	3	121817613	rs2681416	25279986	Skibola CF[38]	Am J Hum Genet	Follicular lymphoma	2.00E-07
5	rs2681416	3	121817613	rs2681416	25261932	Cerhan JR[39]	Nat Genet	Diffuse large B cell lymphoma	8.00E-08
9	rs3887900	11	18738718	rs10766496	26305897	Iyengar SK[40]	PLoS Genet	Diabetic kidney disease	5.00E-06
5	rs4308217	3	121793187	rs4308217	21833088	Sawcer S[41]	Nature	Multiple sclerosis	6.00E-08
5	rs7614486	3	121946099	rs7627468	26272126	Oddsson A[42]	Nat Commun	Kidney stones	2.00E-08

Abbreviations: chr: chromosome; meQTL: methylation quantitative trait loci; GWAS: genome-wide association study; PMID: pubmed ID

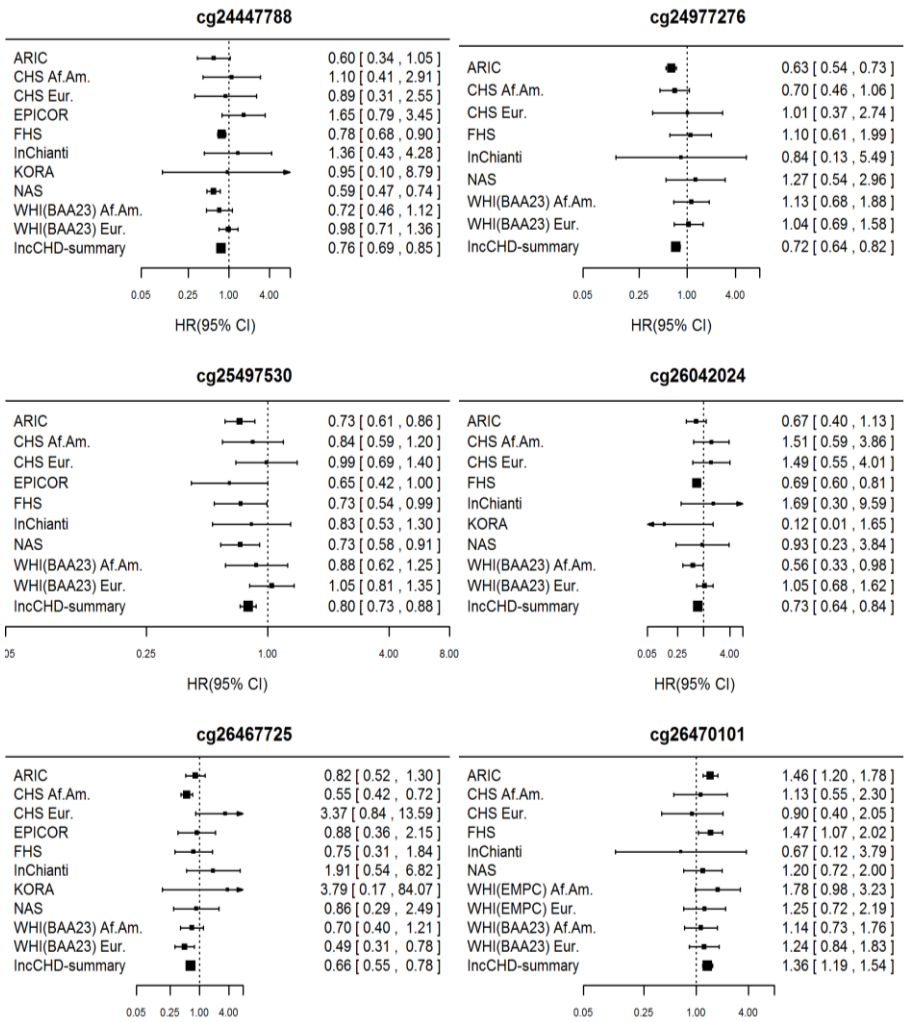
Results obtained via FUMA functional annotation tool (http://fuma.ctglab.nl/).



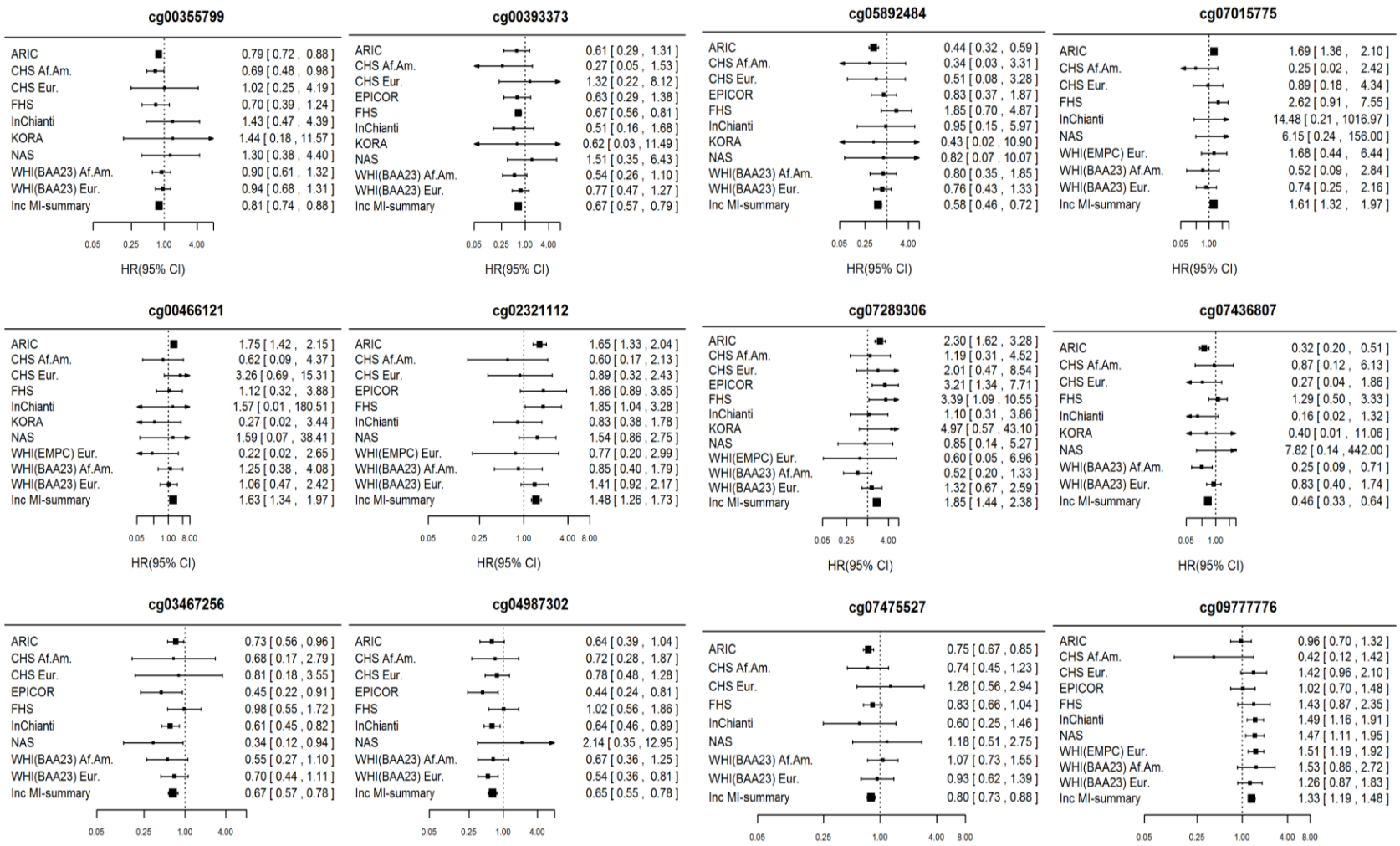
Supplemental Figure 1 (part I). Forest plots for the 30 CpG sites with FDR p-value <0.05 in the incident coronary heart disease (CHD) meta-analysis. Abbreviations: HR: hazard ratio; CI: confidence interval. Hazard ratios represent CHD risk per 5% increase in DNA methylation. X-axis is presented on log scale in order to facilitate the presentation of HRs across the different cohorts and CpGs.



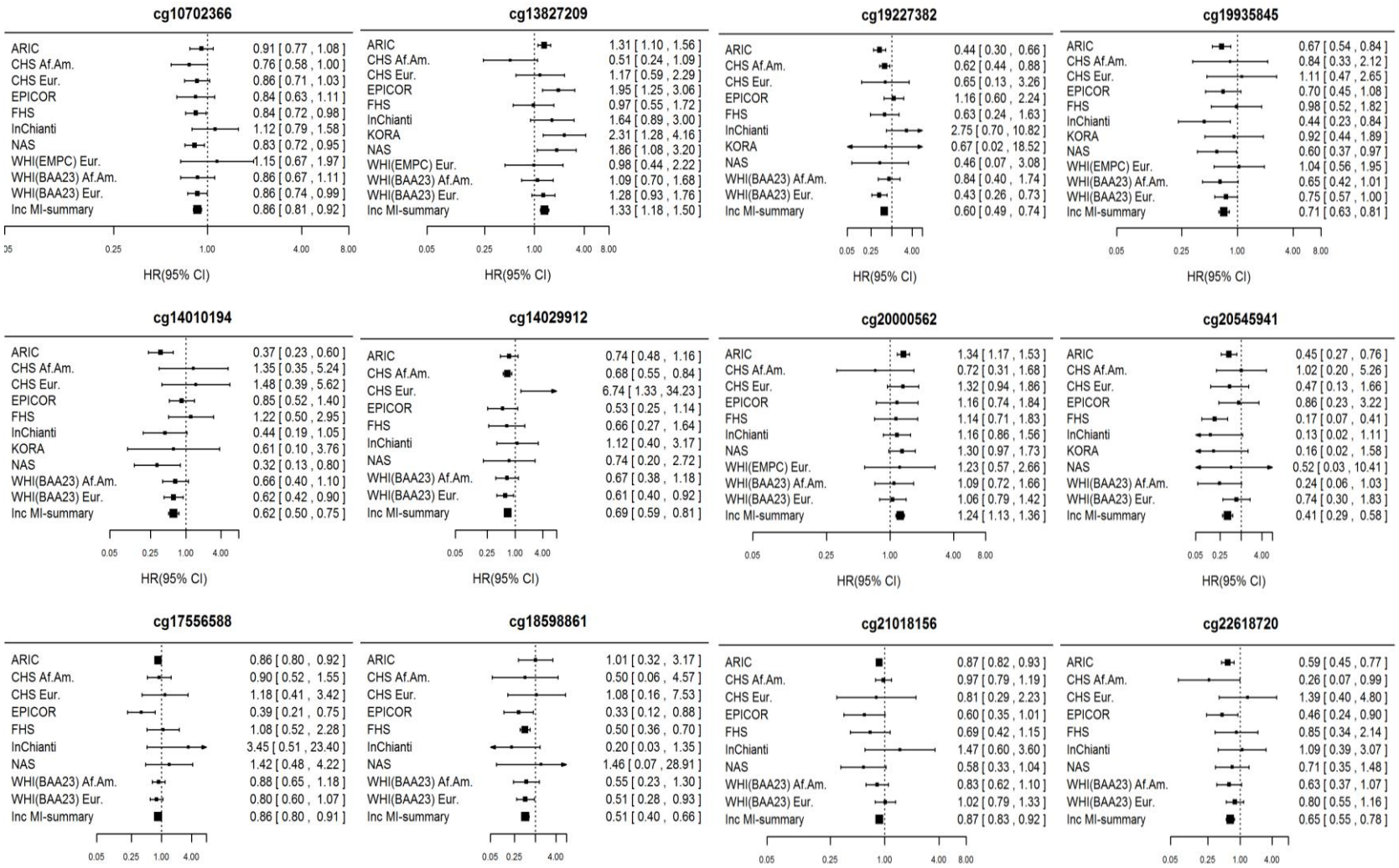
Supplemental Figure 1 (part II). Forest plots for the 30 CpG sites with FDR p-value <0.05 in the incident coronary heart disease (CHD) meta-analysis. Abbreviations: HR: hazard ratio; CI: confidence interval. Hazard ratios represent CHD risk per 5% increase in DNA methylation. X-axis is presented on log scale in order to facilitate the presentation of HRs across the different cohorts and CpGs.



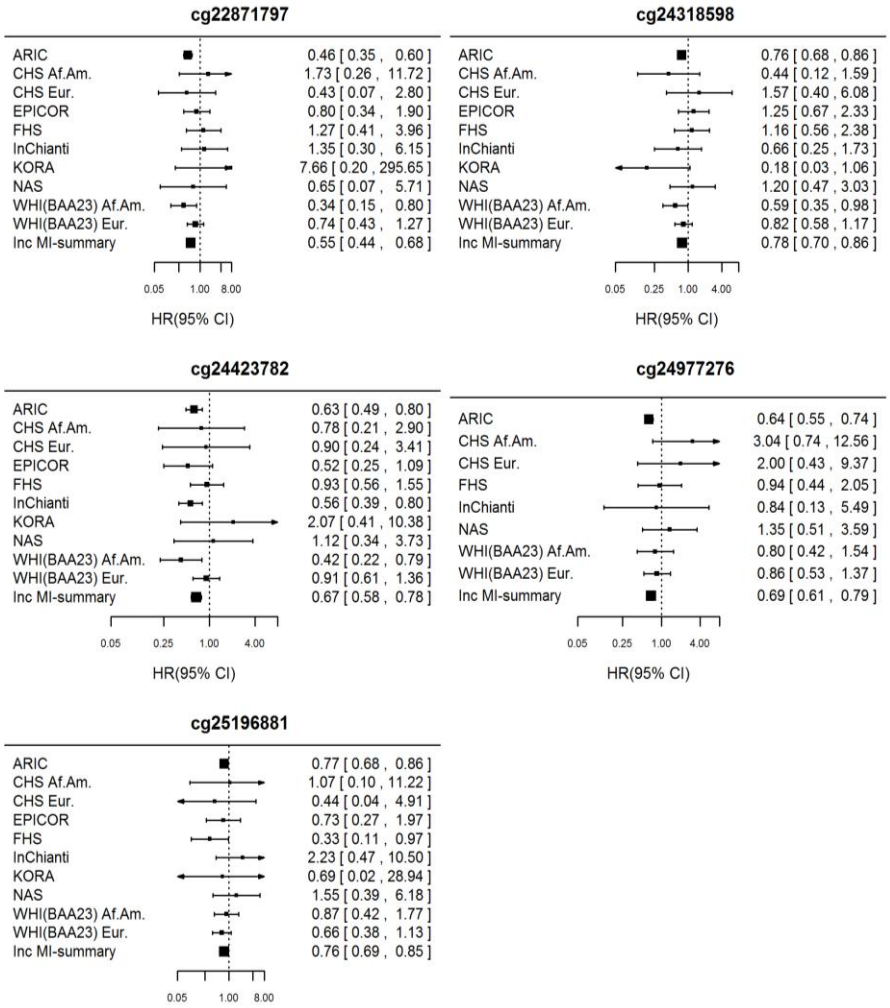
Supplemental Figure 1 (part III). Forest plots for the 30 CpG sites with FDR p-value <0.05 in the incident coronary heart disease (CHD) meta-analysis. Abbreviations: HR: hazard ratio; CI: confidence interval. Hazard ratios represent CHD risk per 5% increase in DNA methylation. X-axis is presented on log scale in order to facilitate the presentation of HRs across the different cohorts and CpGs.



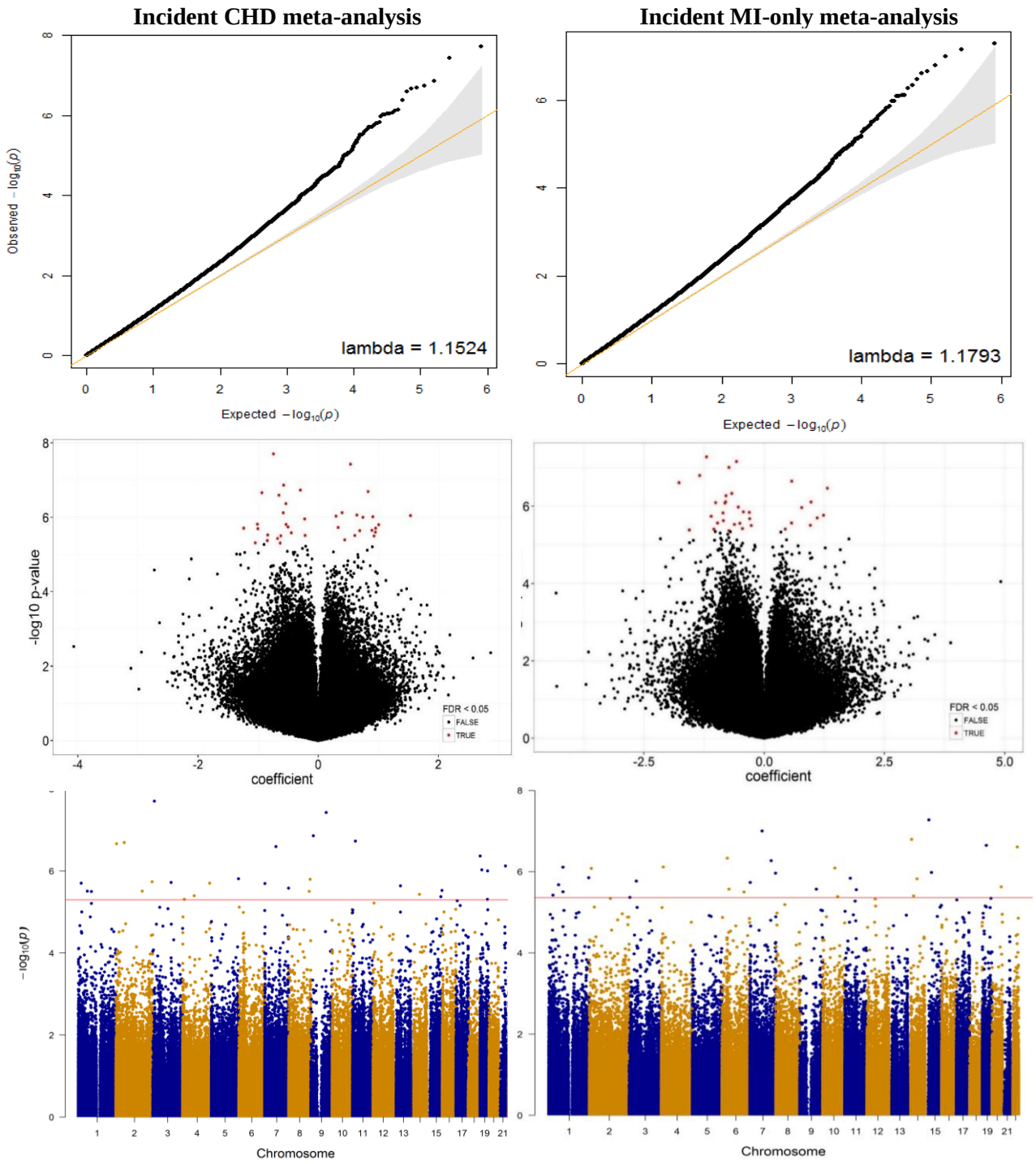
Supplemental Figure 2 (part I). Forest plots for the 29 CpG sites with FDR p-value <0.05 in the incident myocardial infarction (MI) meta-analysis. Abbreviations: HR: hazard ratio; CI: confidence interval. Hazard ratios represent CHD risk per 5% increase in DNA methylation. X-axis is presented on log scale in order to facilitate the presentation of HRs across the different cohorts and CpGs.



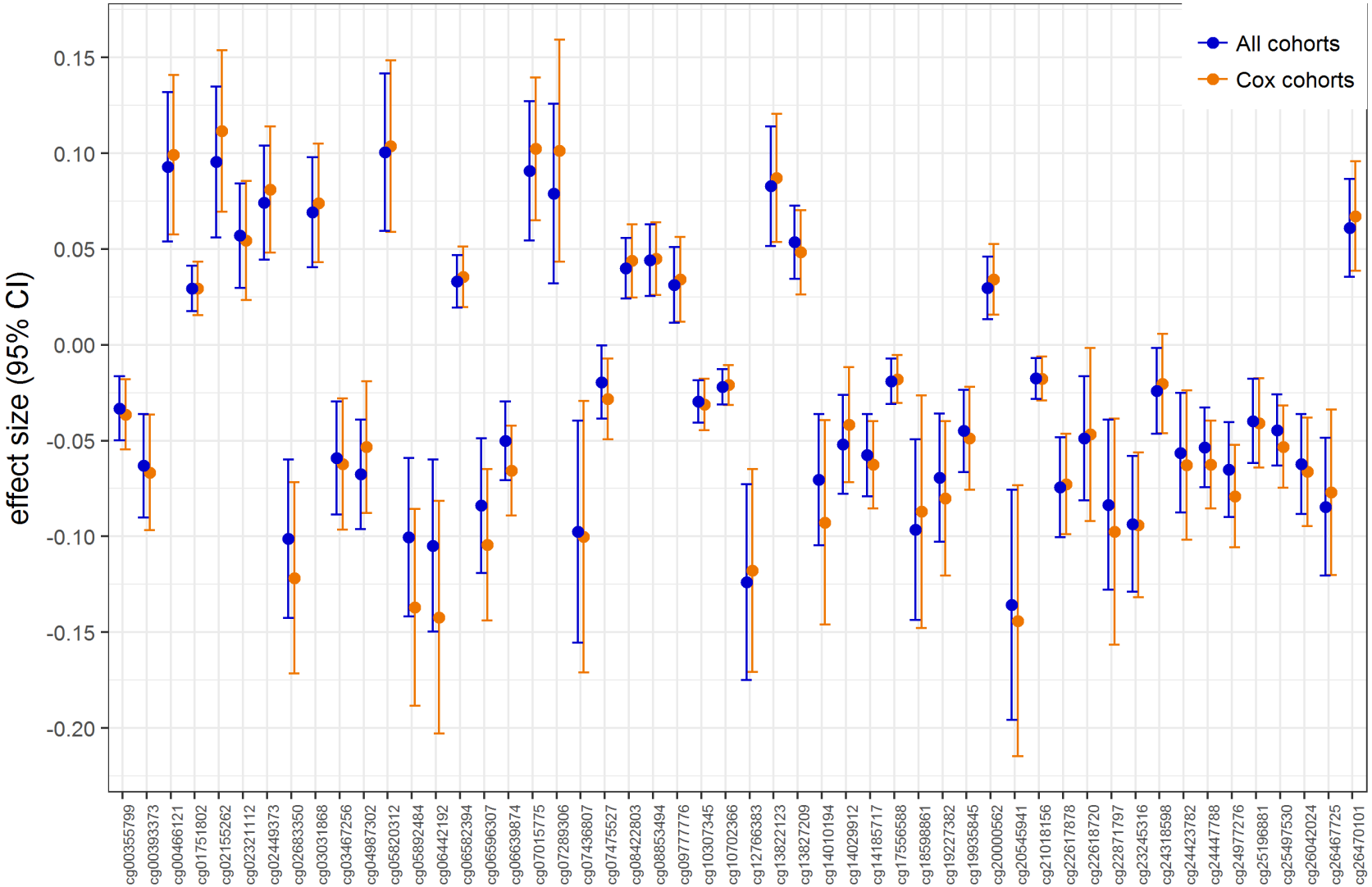
Supplemental Figure 2 (part II). Forest plots for the 29 CpG sites with FDR p-value <0.05 in the incident myocardial infarction (MI) meta-analysis. Abbreviations: HR: hazard ratio; CI: confidence interval. Hazard ratios represent CHD risk per 5% increase in DNA methylation. X-axis is presented on log scale in order to facilitate the presentation of HRs across the different cohorts and CpGs.



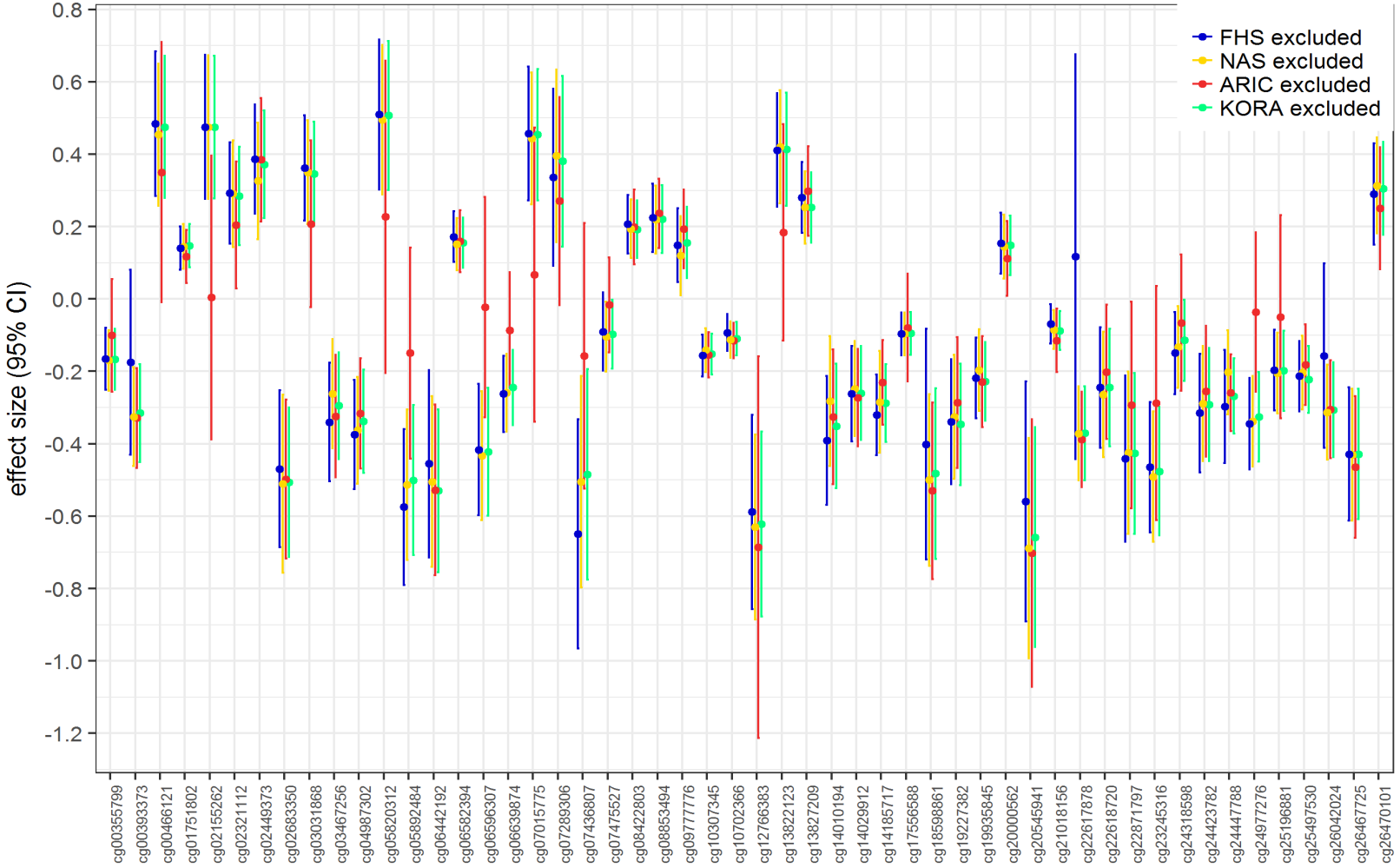
Supplemental Figure 2 (part III). Forest plots for the 29 CpG sites with FDR p-value <0.05 in the incident myocardial infarction (MI) meta-analysis. Abbreviations: HR: hazard ratio; CI: confidence interval. Hazard ratios represent CHD risk per 5% increase in DNA methylation. X-axis is presented on log scale in order to facilitate the presentation of HRs across the different cohorts and CpGs.



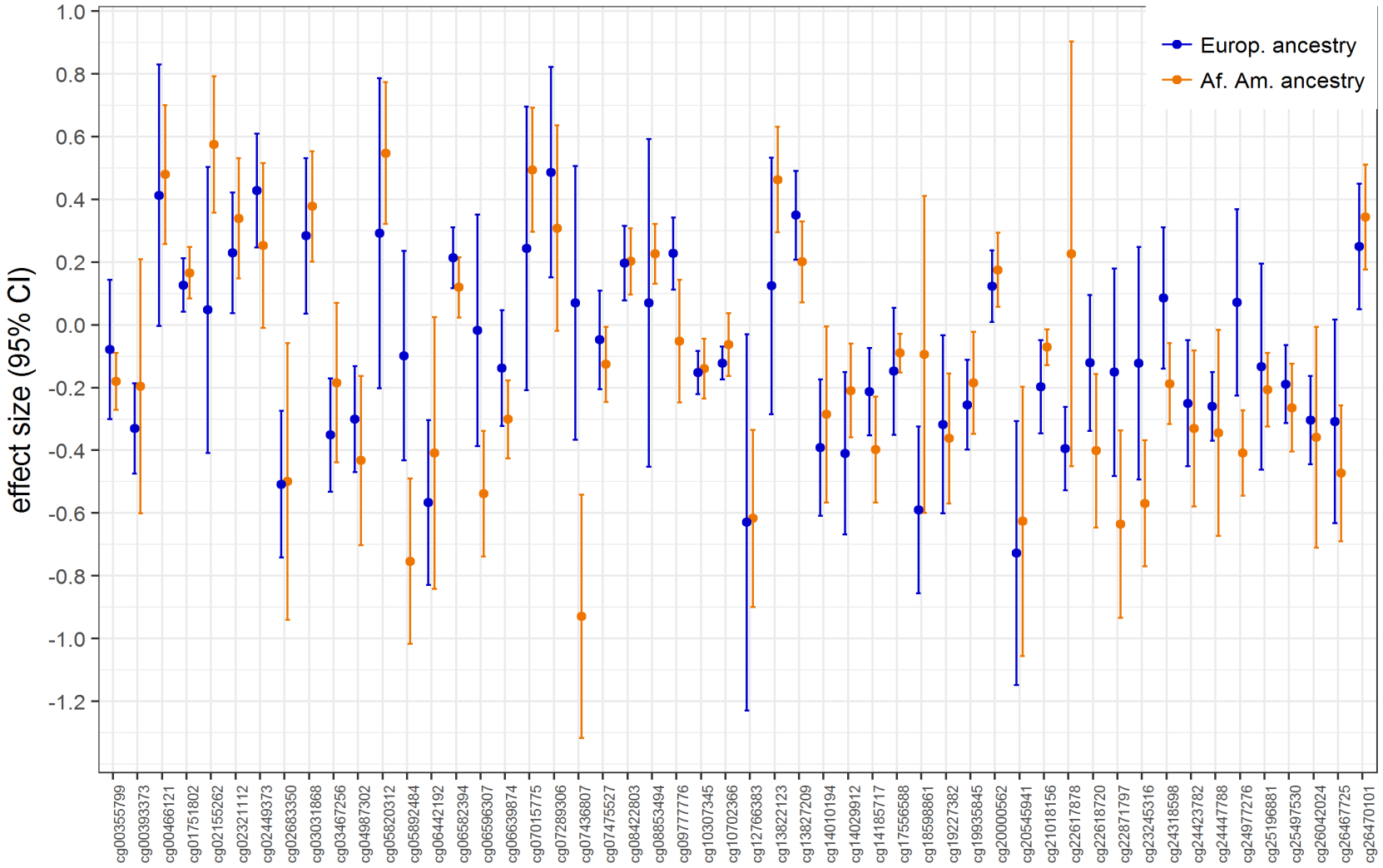
Supplemental Figure 3. Quantile-quantile plots (top), volcano plots (middle), and manhattan plots (bottom) for meta-analysis epigenome-wide association coefficients and p-values for incident coronary heart disease (CHD; No. CpGs included=442,192) and incident myocardial infarction (MI; No. CpGs included=442,175)



Supplemental Figure 4. Plots of effect sizes (i.e., log hazard ratios) and 95% confidence intervals (CIs) for the 52 coronary heart disease-associated CpGs, comparing results of meta-analysis including all cohorts (blue) vs. meta-analysis with only cohorts that used cox regression (orange).



Supplemental Figure 5. Plots of effect sizes (i.e., log hazard ratios) and 95% confidence intervals (CIs) for the 52 coronary heart disease-associated CpGs – Comparing results from four meta-analyses, each time excluding one cohort.



Supplemental Figure 6. Plots of effect sizes (i.e., log hazard ratios) and 95% confidence intervals (CIs) for the 52 coronary heart disease-associated CpGs - Comparing results from a meta-analysis of participants from European-ancestry vs meta-analysis of participants from African-American ancestry.

1. The atherosclerosis risk in communities (aric) study: Design and objectives. The aric investigators. *American journal of epidemiology*. 1989;129:687-702.
2. Sandoval J, Heyn H, Moran S, Serra-Musach J, Pujana MA, Bibikova M, Esteller M. Validation of a DNA methylation microarray for 450,000 cpg sites in the human genome. *Epigenetics : official journal of the DNA Methylation Society*. 2011;6:692-702.
3. Teschendorff AE, Marabita F, Lechner M, Bartlett T, Tegner J, Gomez-Cabrero D, Beck S. A beta-mixture quantile normalization method for correcting probe design bias in illumina infinium 450 k DNA methylation data. *Bioinformatics*. 2013;29:189-196.
4. Houseman EA, Accomando WP, Koestler DC, Christensen BC, Marsit CJ, Nelson HH, Wiencke JK, Kelsey KT. DNA methylation arrays as surrogate measures of cell mixture distribution. *BMC bioinformatics*. 2012;13:86.
5. Tell GS, Fried LP, Hermanson B, Manolio TA, Newman AB, Borhani NO. Recruitment of adults 65 years and older as participants in the cardiovascular health study. *Annals of epidemiology*. 1993;3:358-366.
6. Ives DG, Fitzpatrick AL, Bild DE, Psaty BM, Kuller LH, Crowley PM, Cruise RG, Theroux S. Surveillance and ascertainment of cardiovascular events. The cardiovascular health study. *Annals of epidemiology*. 1995;5:278-285.
7. Psaty BM, Kuller LH, Bild D, Burke GL, Kittner SJ, Mittelmark M, Price TR, Rautaharju PM, Robbins J. Methods of assessing prevalent cardiovascular disease in the cardiovascular health study. *Annals of epidemiology*. 1995;5:270-277.
8. Aryee MJ, Jaffe AE, Corrada-Bravo H, Ladd-Acosta C, Feinberg AP, Hansen KD, Irizarry RA. Minfi: A flexible and comprehensive bioconductor package for the analysis of infinium DNA methylation microarrays. *Bioinformatics*. 2014;30:1363-1369.
9. Maksimovic J, Gordon L, Oshlack A. Swan: Subset-quantile within array normalization for illumina infinium humanmethylation450 beadchips. *Genome biology*. 2012;13:R44.
10. Riboli E, Kaaks R. The epic project: Rationale and study design. European prospective investigation into cancer and nutrition. *International journal of epidemiology*. 1997;26 Suppl 1:S6-14.
11. Kannel WB, Feinleib M, McNamara PM, Garrison RJ, Castelli WP. An investigation of coronary heart disease in families. The framingham offspring study. *American journal of epidemiology*. 1979;110:281-290.
12. Dawber TR, Meadors GF, Moore FE, Jr. Epidemiological approaches to heart disease: The framingham study. *American journal of public health and the nation's health*. 1951;41:279-281.
13. Joehanes R, Ying S, Huan T, Johnson AD, Raghavachari N, Wang R, Liu P, Woodhouse KA, Sen SK, Tanriverdi K, Courchesne P, Freedman JE, O'Donnell CJ, Levy D, Munson PJ. Gene expression signatures of coronary heart disease. *Arteriosclerosis, thrombosis, and vascular biology*. 2013;33:1418-1426.
14. Pidsley R, CC YW, Volta M, Lunnon K, Mill J, Schalkwyk LC. A data-driven approach to preprocessing illumina 450k methylation array data. *BMC genomics*. 2013;14:293.
15. Chen YA, Lemire M, Choufani S, Butcher DT, Grafodatskaya D, Zanke BW, Gallinger S, Hudson TJ, Weksberg R. Discovery of cross-reactive probes and polymorphic cpgs in the illumina infinium humanmethylation450 microarray. *Epigenetics : official journal of the DNA Methylation Society*. 2013;8:203-209.
16. Leek JT, Johnson WE, Parker HS, Jaffe AE, Storey JD. The sva package for removing batch effects and other unwanted variation in high-throughput experiments. *Bioinformatics*. 2012;28:882-883
17. Ferrucci L, Bandinelli S, Benvenuti E, Di Iorio A, Macchi C, Harris TB, Guralnik JM. Subsystems contributing to the decline in ability to walk: Bridging the gap between epidemiology and

geriatric practice in the inchianti study. *Journal of the American Geriatrics Society*. 2000;48:1618-1625.
18. Moore AZ, Hernandez DG, Tanaka T, Pilling LC, Nalls MA, Bandinelli S, Singleton AB, Ferrucci L. Change in epigenome-wide DNA methylation over 9 years and subsequent mortality: Results from the inchianti study. *The journals of gerontology. Series A, Biological sciences and medical sciences*. 2016;71:1029-1035.
19. Holle R, Happich M, Lowel H, Wichmann HE, Group MKS. Kora--a research platform for population based health research. *Gesundheitswesen*. 2005;67 Suppl 1:S19-25
20. Kirchberger I, Heier M, Kuch B, von Scheidt W, Meisinger C. Presenting symptoms of myocardial infarction predict short- and long-term mortality: The monica/kora myocardial infarction registry. *American heart journal*. 2012;164:856-861.
21. Ziegler D, Rathmann W, Dickhaus T, Meisinger C, Mielck A, Group KS. Neuropathic pain in diabetes, prediabetes and normal glucose tolerance: The monica/kora augsburg surveys s2 and s3. *Pain medicine*. 2009;10:393-400.
22. Bibikova M, Barnes B, Tsan C, Ho V, Klotzle B, Le JM, Delano D, Zhang L, Schroth GP, Gunderson KL, Fan JB, Shen R. High density DNA methylation array with single cpg site resolution. *Genomics*. 2011;98:288-295.
23. Zeilinger S, Kuhnel B, Klopp N, Baurecht H, Kleinschmidt A, Gieger C, Weidinger S, Lattka E, Adamski J, Peters A, Strauch K, Waldenberger M, Illig T. Tobacco smoking leads to extensive genome-wide changes in DNA methylation. *PloS one*. 2013;8:e63812.
24. Lehne B, Drong AW, Loh M, Zhang W, Scott WR, Tan ST, Afzal U, Scott J, Jarvelin MR, Elliott P, McCarthy MI, Kooner JS, Chambers JC. A coherent approach for analysis of the illumina humanmethylation450 beadchip improves data quality and performance in epigenome-wide association studies. *Genome biology*. 2015;16:37.
25. Smyth G. Limma: linear models for microarray data. Bioinformatics and computational biology solutions using R and Bioconductor 2005:397-420.
26. Bell B, Rose CL, Damon A. The veterans administration longitudinal study of healthy aging. *The Gerontologist*. 1966;6:179-184.
27. Triche TJ, Jr., Weisenberger DJ, Van Den Berg D, Laird PW, Siegmund KD. Low-level processing of illumina infinium DNA methylation beadarrays. *Nucleic acids research*. 2013;41:e90.
28. Design of the women's health initiative clinical trial and observational study. The women's health initiative study group. *Controlled clinical trials*. 1998;19:61-109.
29. Anderson GL, Manson J, Wallace R, Lund B, Hall D, Davis S, Shumaker S, Wang CY, Stein E, Prentice RL. Implementation of the women's health initiative study design. *Annals of epidemiology*. 2003;13:S5-17.
30. Curb JD, McTiernan A, Heckbert SR, Kooperberg C, Stanford J, Nevitt M, Johnson KC, Proulx-Burns L, Pastore L, Criqui M, Daugherty S, Morbidity WHI, Mortality C. Outcomes ascertainment and adjudication methods in the women's health initiative. *Annals of epidemiology*. 2003;13:S122-128.
31. Johnson WE, Li C, Rabinovic A. Adjusting batch effects in microarray expression data using empirical bayes methods. *Biostatistics*. 2007;8:118-127.
32. Absher DM, Li X, Waite LL, Gibson A, Roberts K, Edberg J, Chatham WW, Kimberly RP. Genome-wide DNA methylation analysis of systemic lupus erythematosus reveals persistent hypomethylation of interferon genes and compositional changes to cd4+ t-cell populations. *PLoS genetics*. 2013;9:e1003678.
33. Fritsche LG, Chen W, Schu M, Yaspan BL, Yu Y, Thorleifsson G, Zack DJ, Arakawa S, Cipriani V, Ripke S, Igo RP, Jr., Buitendijk GH, Sim X, Weeks DE, Guymer RH, Merriam JE, Francis PJ, Hannum G, Agarwal A, Armbrecht AM, Audo I, Aung T, Barile GR, Benchaboune M, Bird AC, Bishop PN,

Branham KE, Brooks M, Brucker AJ, Cade WH, Cain MS, Campochiaro PA, Chan CC, Cheng CY, Chew EY, Chin KA, Chowers I, Clayton DG, Cojocaru R, Conley YP, Cornes BK, Daly MJ, Dhillon B, Edwards AO, Evangelou E, Fagerness J, Ferreyra HA, Friedman JS, Geirsdottir A, George RJ, Gieger C, Gupta N, Hagstrom SA, Harding SP, Haritoglou C, Heckenlively JR, Holz FG, Hughes G, Ioannidis JP, Ishibashi T, Joseph P, Jun G, Kamatani Y, Katsanis N, C NK, Khan JC, Kim IK, Kiyohara Y, Klein BE, Klein R, Kovach JL, Kozak I, Lee CJ, Lee KE, Lichtner P, Lotery AJ, Meitinger T, Mitchell P, Mohand-Said S, Moore AT, Morgan DJ, Morrison MA, Myers CE, Naj AC, Nakamura Y, Okada Y, Orlin A, Ortube MC, Othman MI, Pappas C, Park KH, Pauer GJ, Peachey NS, Poch O, Priya RR, Reynolds R, Richardson AJ, Ripp R, Rudolph G, Ryu E, Sahel JA, Schaumberg DA, Scholl HP, Schwartz SG, Scott WK, Shahid H, Sigurdsson H, Silvestri G, Sivakumaran TA, Smith RT, Sobrin L, Souied EH, Stambolian DE, Stefansson H, Sturgill-Short GM, Takahashi A, Tosakulwong N, Truitt BJ, Tsironi EE, Uitterlinden AG, van Duijn CM, Vijaya L, Vingerling JR, Vithana EN, Webster AR, Wichmann HE, Winkler TW, Wong TY, Wright AF, Zelenika D, Zhang M, Zhao L, Zhang K, Klein ML, Hageman GS, Lathrop GM, Stefansson K, Allikmets R, Baird PN, Gorin MB, Wang JJ, Klaver CC, Seddon JM, Pericak-Vance MA, Iyengar SK, Yates JR, Swaroop A, Weber BH, Kubo M, Deangelis MM, Leveillard T, Thorsteinsdottir U, Haines JL, Farrer LA, Heid IM, Abecasis GR, Consortium AMDG. Seven new loci associated with age-related macular degeneration. *Nature genetics*. 2013;45:433-439, 439e431-432.

34. Schumacher FR, Berndt SI, Siddiq A, Jacobs KB, Wang Z, Lindstrom S, Stevens VL, Chen C, Mondul AM, Travis RC, Stram DO, Eeles RA, Easton DF, Giles G, Hopper JL, Neal DE, Hamdy FC, Donovan JL, Muir K, Al Olama AA, Kote-Jarai Z, Guy M, Severi G, Gronberg H, Isaacs WB, Karlsson R, Wiklund F, Xu J, Allen NE, Andriole GL, Barricarte A, Boeing H, Bueno-de-Mesquita HB, Crawford ED, Diver WR, Gonzalez CA, Gaziano JM, Giovannucci EL, Johansson M, Le Marchand L, Ma J, Sieri S, Stattin P, Stampfer MJ, Tjonneland A, Vineis P, Virtamo J, Vogel U, Weinstein SJ, Yeager M, Thun MJ, Kolonel LN, Henderson BE, Albanes D, Hayes RB, Feigelson HS, Riboli E, Hunter DJ, Chanock SJ, Haiman CA, Kraft P. Genome-wide association study identifies new prostate cancer susceptibility loci. *Human molecular genetics*. 2011;20:3867-3875.

35. Kote-Jarai Z, Olama AA, Giles GG, Severi G, Schleutker J, Weischer M, Campa D, Riboli E, Key T, Gronberg H, Hunter DJ, Kraft P, Thun MJ, Ingles S, Chanock S, Albanes D, Hayes RB, Neal DE, Hamdy FC, Donovan JL, Pharoah P, Schumacher F, Henderson BE, Stanford JL, Ostrander EA, Sorensen KD, Dork T, Andriole G, Dickinson JL, Cybulski C, Lubinski J, Spurdle A, Clements JA, Chambers S, Aitken J, Gardiner RA, Thibodeau SN, Schaid D, John EM, Maier C, Vogel W, Cooney KA, Park JY, Cannon-Albright L, Brenner H, Habuchi T, Zhang HW, Lu YJ, Kaneva R, Muir K, Benlloch S, Leongamornlert DA, Saunders EJ, Tymrakiewicz M, Mahmud N, Guy M, O'Brien LT, Wilkinson RA, Hall AL, Sawyer EJ, Dadaev T, Morrison J, Dearnaley DP, Horwich A, Huddart RA, Khoo VS, Parker CC, Van As N, Woodhouse CJ, Thompson A, Christmas T, Ogden C, Cooper CS, Lophatonanon A, Southey MC, Hopper JL, English DR, Wahlfors T, Tammela TL, Klarskov P, Nordestgaard BG, Roder MA, Tybjaerg-Hansen A, Bojesen SE, Travis R, Canzian F, Kaaks R, Wiklund F, Aly M, Lindstrom S, Diver WR, Gapstur S, Stern MC, Corral R, Virtamo J, Cox A, Haiman CA, Le Marchand L, Fitzgerald L, Kolb S, Kwon EM, Karyadi DM, Orntoft TF, Borre M, Meyer A, Serth J, Yeager M, Berndt SI, Marthick JR, Patterson B, Wokolorczyk D, Batra J, Lose F, McDonnell SK, Joshi AD, Shahabi A, Rinckleb AE, Ray A, Sellers TA, Lin HY, Stephenson RA, Farnham J, Muller H, Rothenbacher D, Tsuchiya N, Narita S, Cao GW, Slavov C, Mitev V, Easton DF, Eeles RA, Oncology UKGPCSCBAoUSSo, Uk ProtecT Study Collaborators TAPCB, Consortium P. Seven prostate cancer susceptibility loci identified by a multi-stage genome-wide association study. *Nature genetics*. 2011;43:785-791.

36. Ramsuran V, Kulkarni H, He W, Mlisana K, Wright EJ, Werner L, Castiblanco J, Dhanda R, Le T, Dolan MJ, Guan W, Weiss RA, Clark RA, Karim SS, Ahuja SK, Ndung'u T. Duffy-null-associated low

neutrophil counts influence hiv-1 susceptibility in high-risk south african black women. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2011;52:1248-1256.

37. Patsopoulos NA, Bayer Pharma MSGWG, Steering Committees of Studies Evaluating I-b, a CCRA, Consortium AN, GeneMsa, International Multiple Sclerosis Genetics C, Esposito F, Reischl J, Lehr S, Bauer D, Heubach J, Sandbrink R, Pohl C, Edan G, Kappos L, Miller D, Montalban J, Polman CH, Freedman MS, Hartung HP, Arnason BG, Comi G, Cook S, Filippi M, Goodin DS, Jeffery D, O'Connor P, Ebers GC, Langdon D, Reder AT, Traboulsee A, Zipp F, Schimrigk S, Hillert J, Bahlo M, Booth DR, Broadley S, Brown MA, Browning BL, Browning SR, Butzkueven H, Carroll WM, Chapman C, Foote SJ, Griffiths L, Kermode AG, Kilpatrick TJ, Lechner-Scott J, Marriott M, Mason D, Moscato P, Heard RN, Pender MP, Perreau VM, Perera D, Rubio JP, Scott RJ, Slee M, Stankovich J, Stewart GJ, Taylor BV, Tubridy N, Willoughby E, Wiley J, Matthews P, Boneschi FM, Compston A, Haines J, Hauser SL, McCauley J, Ivinson A, Oksenberg JR, Pericak-Vance M, Sawcer SJ, De Jager PL, Hafler DA, de Bakker PI. Genome-wide meta-analysis identifies novel multiple sclerosis susceptibility loci. *Annals of neurology*. 2011;70:897-912.
38. Skibola CF, Berndt SI, Vijai J, Conde L, Wang Z, Yeager M, de Bakker PI, Birmann BM, Vajdic CM, Foo JN, Bracci PM, Vermeulen RC, Slager SL, de Sanjose S, Wang SS, Linet MS, Salles G, Lan Q, Severi G, Hjalgrim H, Lightfoot T, Melbye M, Gu J, Ghesquieres H, Link BK, Morton LM, Holly EA, Smith A, Tinker LF, Teras LR, Kricker A, Becker N, Purdue MP, Spinelli JJ, Zhang Y, Giles GG, Vineis P, Monnereau A, Bertrand KA, Albanes D, Zeleniuch-Jacquotte A, Gabbas A, Chung CC, Burdett L, Hutchinson A, Lawrence C, Montalvan R, Liang L, Huang J, Ma B, Liu J, Adami HO, Glimelius B, Ye Y, Nowakowski GS, Dogan A, Thompson CA, Habermann TM, Novak AJ, Liebow M, Witzig TE, Weiner GJ, Schenk M, Hartge P, De Roos AJ, Cozen W, Zhi D, Akers NK, Riby J, Smith MT, Lacher M, Villano DJ, Maria A, Roman E, Kane E, Jackson RD, North KE, Diver WR, Turner J, Armstrong BK, Benavente Y, Boffetta P, Brennan P, Foretova L, Maynadie M, Staines A, McKay J, Brooks-Wilson AR, Zheng T, Holford TR, Chamosa S, Kaaks R, Kelly RS, Ohlsson B, Travis RC, Weiderpass E, Clavel J, Giovannucci E, Kraft P, Virtamo J, Mazza P, Cocco P, Ennas MG, Chiu BC, Fraumeni JF, Jr., Nieters A, Offit K, Wu X, Cerhan JR, Smedby KE, Chanock SJ, Rothman N. Genome-wide association study identifies five susceptibility loci for follicular lymphoma outside the hla region. *American journal of human genetics*. 2014;95:462-471.
39. Cerhan JR, Berndt SI, Vijai J, Ghesquieres H, McKay J, Wang SS, Wang Z, Yeager M, Conde L, de Bakker PI, Nieters A, Cox D, Burdett L, Monnereau A, Flowers CR, De Roos AJ, Brooks-Wilson AR, Lan Q, Severi G, Melbye M, Gu J, Jackson RD, Kane E, Teras LR, Purdue MP, Vajdic CM, Spinelli JJ, Giles GG, Albanes D, Kelly RS, Zucca M, Bertrand KA, Zeleniuch-Jacquotte A, Lawrence C, Hutchinson A, Zhi D, Habermann TM, Link BK, Novak AJ, Dogan A, Asmann YW, Liebow M, Thompson CA, Ansell SM, Witzig TE, Weiner GJ, Veron AS, Zelenika D, Tilly H, Haioun C, Molina TJ, Hjalgrim H, Glimelius B, Adami HO, Bracci PM, Riby J, Smith MT, Holly EA, Cozen W, Hartge P, Morton LM, Severson RK, Tinker LF, North KE, Becker N, Benavente Y, Boffetta P, Brennan P, Foretova L, Maynadie M, Staines A, Lightfoot T, Crouch S, Smith A, Roman E, Diver WR, Offit K, Zelenetz A, Klein RJ, Villano DJ, Zheng T, Zhang Y, Holford TR, Kricker A, Turner J, Southey MC, Clavel J, Virtamo J, Weinstein S, Riboli E, Vineis P, Kaaks R, Trichopoulos D, Vermeulen RC, Boeing H, Tjonneland A, Angelucci E, Di Lollo S, Rais M, Birmann BM, Laden F, Giovannucci E, Kraft P, Huang J, Ma B, Ye Y, Chiu BC, Sampson J, Liang L, Park JH, Chung CC, Weisenburger DD, Chatterjee N, Fraumeni JF, Jr., Slager SL, Wu X, de Sanjose S, Smedby KE, Salles G, Skibola CF, Rothman N, Chanock SJ. Genome-wide association study identifies multiple susceptibility loci for diffuse large b cell lymphoma. *Nature genetics*. 2014;46:1233-1238.
40. Iyengar SK, Sedor JR, Freedman BI, Kao WH, Kretzler M, Keller BJ, Abboud HE, Adler SG, Best LG, Bowden DW, Burlock A, Chen YD, Cole SA, Comeau ME, Curtis JM, Divers J, Drechsler C,

Duggirala R, Elston RC, Guo X, Huang H, Hoffmann MM, Howard BV, Ipp E, Kimmel PL, Klag MJ, Knowler WC, Kohn OF, Leak TS, Leehey DJ, Li M, Malhotra A, Marz W, Nair V, Nelson RG, Nicholas SB, O'Brien SJ, Pahl MV, Parekh RS, Pezzolesi MG, Rasooly RS, Rotimi CN, Rotter JI, Schelling JR, Seldin MF, Shah VO, Smiles AM, Smith MW, Taylor KD, Thameem F, Thornley-Brown DP, Truitt BJ, Wanner C, Weil EJ, Winkler CA, Zager PG, Igo RP, Jr., Hanson RL, Langefeld CD, Family Investigation of N, Diabetes. Genome-wide association and trans-ethnic meta-analysis for advanced diabetic kidney disease: Family investigation of nephropathy and diabetes (find). *PLoS genetics*. 2015;11:e1005352.

41. International Multiple Sclerosis Genetics C, Wellcome Trust Case Control C, Sawcer S, Hellenthal G, Pirinen M, Spencer CC, Patsopoulos NA, Moutsianas L, Dilthey A, Su Z, Freeman C, Hunt SE, Edkins S, Gray E, Booth DR, Potter SC, Goris A, Band G, Oturai AB, Strange A, Saarela J, Bellenguez C, Fontaine B, Gillman M, Hemmer B, Gwilliam R, Zipp F, Jayakumar A, Martin R, Leslie S, Hawkins S, Giannoulatou E, D'Alfonso S, Blackburn H, Martinelli Boneschi F, Liddle J, Harbo HF, Perez ML, Spurkland A, Waller MJ, Mycko MP, Ricketts M, Comabella M, Hammond N, Kockum I, McCann OT, Ban M, Whittaker P, Kemppinen A, Weston P, Hawkins C, Widaa S, Zajicek J, Dronov S, Robertson N, Bumpstead SJ, Barcellos LF, Ravindrarajah R, Abraham R, Alfredsson L, Ardlie K, Aubin C, Baker A, Baker K, Baranzini SE, Bergamaschi L, Bergamaschi R, Bernstein A, Berthele A, Boggild M, Bradfield JP, Brassat D, Broadley SA, Buck D, Butzkueven H, Capra R, Carroll WM, Cavalla P, Celius EG, Cepok S, Chiavacci R, Clerget-Darpoux F, Clysters K, Comi G, Cossburn M, Cournu-Rebeix I, Cox MB, Cozen W, Cree BA, Cross AH, Cusi D, Daly MJ, Davis E, de Bakker PI, Debouverie M, D'Hooghe M B, Dixon K, Dobosi R, Dubois B, Ellinghaus D, Elovaara I, Esposito F, Fontenille C, Foote S, Franke A, Galimberti D, Ghezzi A, Glessner J, Gomez R, Gout O, Graham C, Grant SF, Guerini FR, Hakonarson H, Hall P, Hamsten A, Hartung HP, Heard RN, Heath S, Hobart J, Hoshi M, Infante-Duarte C, Ingram G, Ingram W, Islam T, Jagodic M, Kabesch M, Kermode AG, Kilpatrick TJ, Kim C, Klopp N, Koivisto K, Larsson M, Lathrop M, Lechner-Scott JS, Leone MA, Leppa V, Liljedahl U, Bomfim IL, Lincoln RR, Link J, Liu J, Lorentzen AR, Lupoli S, Macciardi F, Mack T, Marriott M, Martinelli V, Mason D, McCauley JL, Mentch F, Mero IL, Mihalova T, Montalban X, Mottershead J, Myhr KM, Naldi P, Ollier W, Page A, Palotie A, Pelletier J, Piccio L, Pickersgill T, Piehl F, Pobywajlo S, Quach HL, Ramsay PP, Reunanen M, Reynolds R, Rioux JD, Rodegher M, Roesner S, Rubio JP, Ruckert IM, Salvetti M, Salvi E, Santaniello A, Schaefer CA, Schreiber S, Schulze C, Scott RJ, Sellebjerg F, Selmaj KW, Sexton D, Shen L, Simms-Acuna B, Skidmore S, Sleiman PM, Smestad C, Sorensen PS, Sondergaard HB, Stankovich J, Strange RC, Sulonen AM, Sundqvist E, Syvanen AC, Taddeo F, Taylor B, Blackwell JM, Tienari P, Bramon E, Tourbah A, Brown MA, Tronczynska E, Casas JP, Tubridy N, Corvin A, Vickery J, Jankowski J, Villoslada P, Markus HS, Wang K, Mathew CG, Wason J, Palmer CN, Wichmann HE, Plomin R, Willoughby E, Rautanen A, Winkelmann J, Wittig M, Trembath RC, Yaouanq J, Viswanathan AC, Zhang H, Wood NW, Zuvich R, Deloukas P, Langford C, Duncanson A, Oksenberg JR, Pericak-Vance MA, Haines JL, Olsson T, Hillert J, Ivinson AJ, De Jager PL, Peltonen L, Stewart GJ, Hafler DA, Hauser SL, McVean G, Donnelly P, Compston A. Genetic risk and a primary role for cell-mediated immune mechanisms in multiple sclerosis. *Nature*. 2011;476:214-219.

42. Oddsson A, Sulem P, Helgason H, Edvardsson VO, Thorleifsson G, Sveinbjornsson G, Haraldsdottir E, Eyjolfsson GI, Sigurdardottir O, Olafsson I, Masson G, Holm H, Gudbjartsson DF, Thorsteinsdottir U, Indridason OS, Palsson R, Stefansson K. Common and rare variants associated with kidney stones and biochemical traits. *Nature communications*. 2015;6:7975.