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BRIEF COMMUNICATION

Genetically Predicted Midlife Blood Pressure and Coronary Artery Disease Risk: Mendelian Randomization Analysis

Dipender Gill, BMBCh, PhD*; Marios K. Georgakis, MD*; Verena Zuber, PhD; Ville Karhunen, MSc; Stephen Burgess, PhD; Rainer Malik, PhD; Martin Dichgans, MD

BACKGROUND: Elevated blood pressure is a major cause of cardiovascular morbidity and mortality. However, it is not known whether midlife blood pressure affects later life cardiovascular risk independent of later life blood pressure.

METHODS AND RESULTS: Using genetic association estimates from the UK Biobank and CARDIoGRAMplusC4D consortium, univariable mendelian randomization was performed to investigate the total effect of genetically predicted mean arterial pressure (MAP) at age ≤55 years on coronary artery disease (CAD) risk, and multivariable mendelian randomization was performed to investigate the effect of genetically predicted MAP on CAD risk after adjusting for genetically predicted MAP at age >55 years. In both univariable and multivariable mendelian randomization analyses, there was consistent evidence of higher genetically predicted MAP at age ≤55 years increasing CAD risk. This association persisted after adjusting for genetically predicted MAP at age >55 years, when considering nonoverlapping populations for the derivation of MAP and CAD risk genetic association estimates, when investigating only incident CAD events after age >55 years, and when restricting the analysis to variants with most heterogeneity in their associations with MAP ≤55 and >55 years. For a 10–mm Hg increase in genetically predicted MAP at age ≤55 years, the odds ratio of later life CAD was 1.43 (95% CI, 1.16–1.77; *P*=0.001) after adjusting for genetically predicted MAP at age >55 years.

CONCLUSIONS: These mendelian randomization findings support a cumulative lifetime effect of elevated blood pressure on increasing CAD risk. Clinical and public health efforts toward cardiovascular disease reduction should optimize blood pressure control throughout life.

Key Words: age ■ blood pressure ■ coronary artery disease ■ mendelian randomization

Elevated blood pressure is a powerful predictor of cardiovascular morbidity and mortality. In international surveys, the 874 million adults estimated to have a systolic blood pressure (SBP) >140 mm Hg in 2015 accounted for 106 deaths per 100 000 people and loss of 143 million disability-adjusted life years.[1] Lowering blood pressure can decrease cardiovascular risk, with a 10–mm Hg reduction in SBP estimated to reduce all-cause mortality by 13%.[2]

To optimize clinical and public health strategies toward minimizing the burden of cardiovascular disease, it is important to understand whether there is a specific period in life when elevated blood pressure increases risk, or rather whether it is that elevated blood pressure throughout life has a cumulative effect. Observational studies have shown that elevated blood pressure in midlife is associated with increased risk of cardiovascular disease in later life and represents an independent risk factor, even after adjusting for blood pressure in older age.[3–5] However, inferring causal effects from such associations can be difficult because of the possibility of confounding, reverse causation,

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and measurement error. The mendelian randomization (MR) paradigm overcomes some of these limitations by using genetic variants as instrumental variables for studying the effect of an exposure on an outcome. The random allocation of genetic variants at conception means that their associations are less vulnerable to environmental confounding and reverse causation, and their cumulative lifelong effect reduces the impact of measurement error.

The aim of the current study was to generate genetic instruments for mean arterial pressure (MAP) at age ≤55 years and MAP at age >55 years, and thus investigate within the MR paradigm whether genetically predicted MAP in midlife affects risk of coronary artery disease (CAD) in later life, independent of genetically predicted MAP in later life.

METHODS

Overall Study Design

Separate genome-wide association study (GWAS) analyses for MAP in individuals aged ≤55 years and in individuals aged >55 years were performed in UK Biobank. These age categories were selected because they reflect the approximate transition toward increasing arterial stiffness,[6] and also split the UK Biobank cohort approximately in half. MAP was selected as the blood pressure trait of interest because it provides an estimate of overall arterial blood pressure during a complete cardiac cycle[7] and represents a predictor of cardiovascular risk in both younger and older adults.[8] Instruments for MAP in individuals aged ≤55 years were applied in univariable and multivariable MR analysis to investigate their effect on CAD risk. Two models were applied for univariable MR: model 1 considered outcome genetic association estimates from CARDIoGRAMplusC4D,[9] and model 2 considered outcome genetic association estimates based on incident CAD events at age >55 years in UK Biobank. In model 2, the UK Biobank cohort was split on the basis of participant linkage to primary care data and genetic association estimates for MAP and CAD were obtained from the different subsets to avoid potential bias related to participant overlap[10]; model 2 further served as a sensitivity analysis to explore potential bias related to the inclusion of recurrent CAD events and CAD events at age ≤55 years in the CARDIoGRAMplusC4D data used for model 1. For multivariable MR, the effect of genetically predicted MAP at age ≤55 years was adjusted for the effect of genetically predicted MAP at age >55 years when investigating effects on CAD risk. A further third model was also applied in the multivariable MR setting, which only included the instrument variants from model 1 that demonstrated heterogeneity between their associations with MAP in those aged ≤55 and >55 years outside the interdecile range of the distribution expected under the null hypothesis of homogeneity. Model 3 was performed as a sensitivity analysis to explore the potential impact of weak instrument bias in the multivariable MR setting, particularly as the genetic predictors of MAP in individuals aged ≤55 years may be closely related to those for individuals aged >55 years.[11] The data sources used to obtain genetic association estimates in the different analysis models are summarized in the Table. Baseline characteristics for the UK Biobank participants used in the GWAS analyses for MAP and CAD are detailed in Table S1.

MAP GWAS

MAP was calculated using the mean SBP and diastolic blood pressure readings (1/3×mean SBP+2/3×mean diastolic blood pressure) obtained at baseline assessment in UK Biobank, after correcting for antihypertensive medication use by adding 15 mm Hg to SBP and

Table. Data Sources Used to Obtain Genetic Association Estimates in the Univariable and Multivariable MR Analysis Models

Variable	Univariable MR		Multivariable MR		
	Model 1	Model 2	Model 1	Model 2	Model 3
MAP instruments and genetic association estimates	Individuals aged ≤55 y in the whole UK Biobank	UK Biobank participants aged ≤55 y without linked primary care data	Individuals aged ≤55 and >55 y in the whole UK Biobank	UK Biobank participants aged ≤55 y without linked primary care data	Individuals aged ≤55 and >55 y in the whole UK Biobank. Only instruments demonstrating heterogeneity between their associations with MAP in those ≤55 and >55 y outside the interdecile range of the distribution expected under the null hypothesis of homogeneity were included.
Coronary artery disease genetic association estimates	CARDIoGRAMplusC4D	UK Biobank participants aged >55 y with linked primary care data	CARDIoGRAMplusC4D	UK Biobank participants aged >55 y with linked primary care data	CARDIoGRAMplusC4D

MAP indicates mean arterial pressure; and MR, mendelian randomization.

10 mm Hg to diastolic blood pressure for individuals who self-reported use of any antihypertensive medication.[12] Only white British participants were included in GWAS analyses, and exclusions were made for up to second-degree related individuals (relatedness coefficient <0.0884). For the MAP GWAS used to obtain genetic association estimates in model 2, we limited participants to those not included in the UK Biobank primary care data set. After dichotomization on age (≤55 and >55 years), all MAP GWAS analyses were performed using linear regression, with age, sex, principal components 1 to 20, genotyping chip, and assessment center included as covariates. The final sample sizes for the analyses used in model 1 were as follows: ≤55 years: N=162 967; and >55 years: N=245 261. The final sample sizes in model 2 were as follows: ≤55 years: N=131 435; and >55 years: N=131 584.

Instrument Selection

For univariable MR, instruments for MAP at age ≤55 years were selected as single-nucleotide polymorphisms that associated with MAP in individuals aged ≤55 years at genome-wide significance ($P<5\times10^{-8}$) and were in pair-wise linkage disequilibrium ($r^2<0.001$). For models 1 and 2 of the multivariable MR, instruments were selected as single-nucleotide polymorphisms related at genome-wide significance to MAP at age ≤55 years or to MAP at age >55 years in the GWAS analyses considering the whole UK Biobank cohort, after clumping to pairwise linkage disequilibrium ($r^2<0.001$) on the basis of the lowest P value for association with either trait. All clumping was performed using the TwoSampleMR package in R.[13] In model 3 of the multivariable MR, only variants that had heterogeneity between their associations with MAP in those ≤55 and >55 years outside the interdecile range of the distribution expected under the null hypothesis of homogeneity were included.

Outcome Genetic Association Estimates

Genetic association estimates for CAD that were used in models 1 and 3 were obtained from the CARDIoGRAMplusC4D Consortium 1000G multiethnic GWAS (77% European ancestry) of 60 801 cases and 123 504 controls.[9]

Genetic association estimates for CAD used in model 2 were obtained from UK Biobank participants with linked primary care data. These CAD diagnoses were derived from multiple sources: death records (*International Classification of Diseases, Tenth Revision* [*ICD-10*]), hospital records (*ICD-10* and Office of Population Censuses and Surveys-4), and primary care data (release readV2 and readV3). We used the following codes: *ICD-10* I20 to I25; and Office of Population Censuses and Surveys-4 K40 to K46, K49, K50, and K75. ReadV2 and readV3 codes were extracted using a mapping from *ICD-10* codes provided by the UK Biobank (resource 592). We retained only incident events recorded after inclusion in the UK Biobank. Only white British participants aged >55 years were included in GWAS analyses, and exclusions were made for up to second-degree related individuals (relatedness coefficient <0.0884). GWAS analysis was performed using logistic regression, with age, sex, principal components 1 to 20, genotyping chip, and assessment center included as covariates. The final sample size was 8788 cases and 184 201 controls.

Statistical Analysis

Univariable MR

Multiplicative random-effects inverse-variance–weighted MR was used as the main analysis for estimating the effect of genetically predicted MAP in individuals aged ≤55 years on CAD risk in the univariable setting.[14] Contamination-mixture method and weighted median MR were further incorporated as sensitivity analyses to explore the robustness of the findings to potential pleiotropic variants[14] (Data S1). The MendelianRandomization package in R was used for performing inverse-variance–weighted, contamination-mixture, and weighted median MR.[14]

Multivariable MR

To estimate the effect of genetically predicted MAP at age ≤55 years on CAD risk independent of genetically predicted MAP at age >55 years, summary data multivariable MR was performed.[11] Specifically, the CAD risk association estimates for each instrument were regressed on the association estimates for MAP in individuals aged ≤55 and >55 years, weighted for the precision of the CAD risk estimates and with the intercept fixed at 0.

Ethical Approval and Data Availability

The data used in these analyses are publicly available. The UK Biobank study was approved by the North West Multicentre Research Ethics Committee, and all its participants provided informed consent. The UK Biobank data were accessed through application 2532. All generated results are presented in the article and its supplement. A study protocol was not preregistered. This study was reported with consideration of the STROBE-MR Guidelines (Data S2).

RESULTS

All instruments and genetic association estimates used in the MR analyses are provided in Tables S2

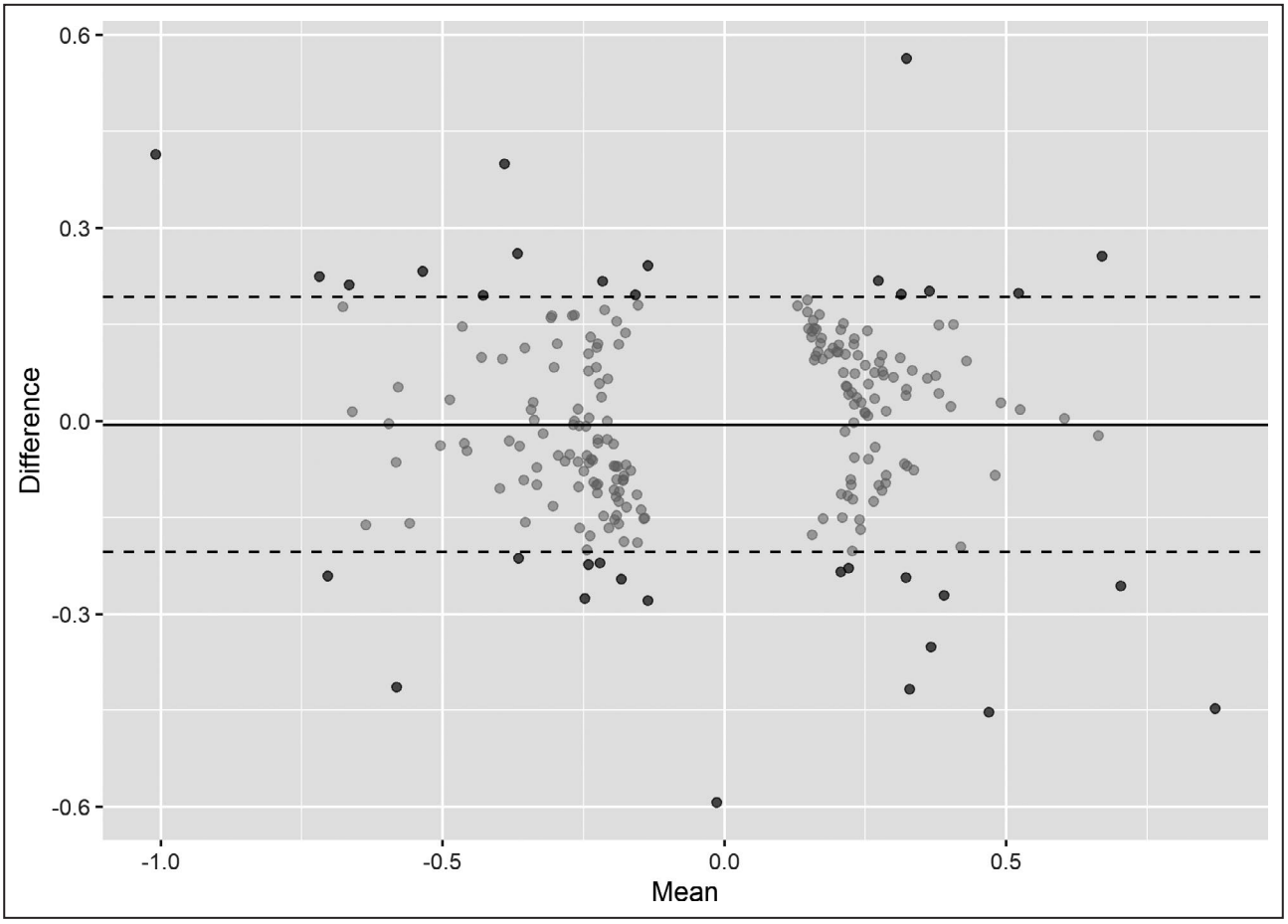

Figure 1. Bland-Altman plot depicting the heterogeneity in associations with mean arterial blood pressure (MAP) at age ≤55 and >55 years for the variants identified as having genome-wide significant association with either trait in analyses considering the whole UK Biobank cohort.

For each variant, the *x* axis depicts the mean of the association with MAP at age ≤55 and >55 years, and the *y* axis represents the difference in association with MAP at age ≤55 and >55 years. The dashed lines depict 10th and 90th percentiles of the expected distribution of heterogeneity statistics under the null hypothesis of homogeneity (ie, the interdecile range). A total of 34 variants (colored black rather than gray) fall outside this and were used in model 3 of the multivariable mendelian randomization.

through S5. A Bland-Altman plot identified 34 variants in model 1 of the multivariable MR as having heterogeneity in their associations with MAP in those aged ≤55 and >55 years outside the interdecile range of the distribution expected under the null hypothesis of homogeneity (Figure 1, Table S4), and these were applied in model 3 of the multivariable MR.

The univariable and multivariable MR analyses demonstrated consistent evidence of an effect of genetically predicted MAP at age ≤55 years on CAD risk across all models (Figure 2). For the univariable MR, similar results were obtained when performing the inverse-variance–weighted, contamination-mixture, and weighted median MR methods, which each make different assumptions about the potential inclusion of pleiotropic variants that affect CAD risk through pathways unrelated to MAP (Figure 2). Similar results were also obtained when considering CAD outcome genetic association estimates from CARDIoGRAMplusC4D or UK Biobank (Figure 2). The inverse-variance–weighted analysis in model 2 of the univariable MR, which used nonoverlapping populations for exposure and outcome genetic association estimates and only considered incident CAD events after the age of 55 years, produced an odds ratio (OR) of 1.58 per 10–mm Hg increase in genetically predicted MAP (95% CI, 1.38–1.70; $P<0.001$).

The multivariable MR analysis, which adjusted the effect of genetically predicted MAP at age ≤55 years for genetically predicted MAP at age >55 years, produced smaller MR estimates with wider 95% CIs than the univariable MR analysis that did not make such an adjustment (Figure 2). As with the univariable MR, similar results were obtained in the various multivariable MR models considered (Figure 2). Model 2 of the multivariable MR, which adjusted for genetically predicted MAP at >55 years of age, used nonoverlapping populations for exposure and outcome genetic

association estimates, and only considered incident CAD events after the age of 55 years produced an OR of 1.43 per 10–mm Hg increase in genetically predicted MAP (95% CI, 1.16–1.77; *P*=0.001).

DISCUSSION

This work applied the MR paradigm to generate evidence supporting an effect of midlife blood pressure on later life CAD risk independent of later life blood pressure. This finding reinforces the importance of adequate blood pressure control throughout life and is consistent with a cumulative temporal effect of elevated blood pressure on CAD risk. Our findings therefore have direct clinical and public health implications for optimizing management of blood pressure toward the goal of minimizing the burden of cardiovascular disease on both individuals and health systems.

The findings of this work build on previous conventional epidemiological research that has supported a cumulative lifetime effect of blood pressure on a range of cardiovascular outcomes, including atherosclerosis, stroke, and heart failure.[3–5] These previous efforts have also investigated effects of blood pressure across a range of ages, including adolescence and midlife.[3–5] Findings from these distinct populations and study designs can therefore be triangulated to generate complementary evidence supporting the case that it is cumulative and prolonged exposure to higher blood pressure that leads to the pathological processes underlying cardiovascular disease.[15]

Our study has several strengths. To our knowledge, this is the first MR study to investigate the direct effect of genetically predicted blood pressure in midlife after adjusting for genetically predicted blood pressure in older age. Compared with conventional epidemiological research, such application of the MR approach may potentially be more robust to biases related to environmental confounding, reverse causation, and measurement error. For example, by using randomly allocated genetic variants as instrumental variables for studying the effect of modifying MAP, the MR approach that we use is able to overcome confounding from factors such as smoking and lipid status. Our study also incorporates an innovative design and comprehensive range of sensitivity analyses to explore the robustness

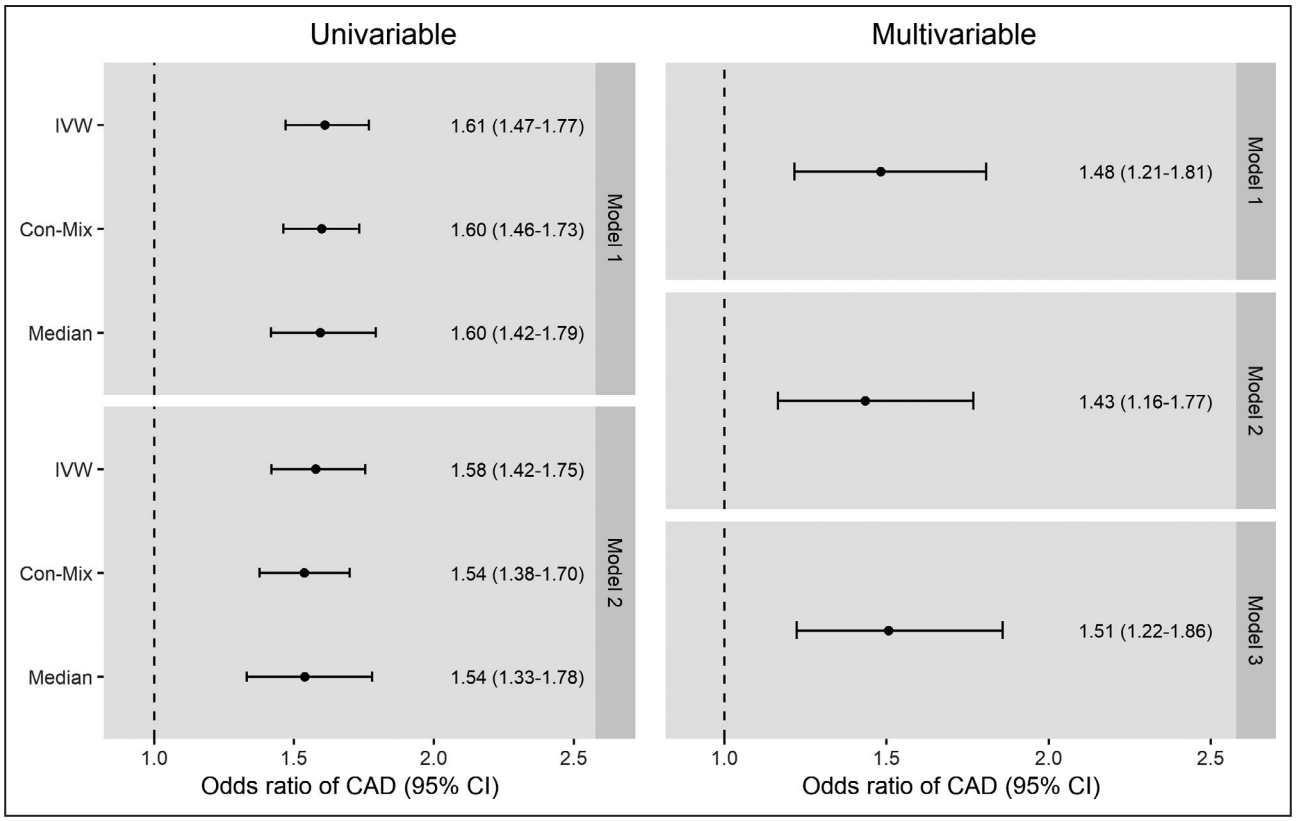

Figure 2. Effect of genetically predicted mean arterial blood pressure (MAP) at age ≤55 years on risk of coronary artery disease (CAD) in univariable and multivariable mendelian randomization analyses.
All effect estimates are given per 10–mm Hg increase in MAP. Multivariable estimates are adjusted for genetically predicted MAP at age >55 years. Con-Mix indicates contamination mixture model mendelian randomization; IVW, inverse-variance–weighted mendelian randomization; and Median, weighted median mendelian randomization.

of the findings to possible violations of the underlying assumptions of the applied MR approach. Consistent evidence supporting a direct effect of midlife blood pressure on CAD risk was obtained after adjusting for genetically predicted MAP at age >55 years, when considering nonoverlapping populations for the derivation of MAP and CAD risk genetic association estimates, when investigating only incident CAD events after age >55 years, and when restricting the analysis to variants with most heterogeneity in their associations with MAP ≤55 and >55 years.

Our work also has several limitations. First, the MR paradigm measures the lifelong effect of genetic variants, and its estimates should therefore not be directly translated to assume the effect of clinical intervention on blood pressure in a given age group. Second, it was not possible to exclude the possibility that some of our analyses might have been influenced by weak instrument bias. This is particularly relevant for the multivariable MR analysis, as the associations of the genetic variants with MAP in those aged ≤55 and >55 years were closely related (Tables S4 and S5). In the univariable analyses, such bias would have been toward the null, and is therefore unlikely to be affecting our conclusions.[10] However, in the multivariable MR settings, weak instrument bias can be either toward or away from the null.[11] In any case, some assurance against this was provided by the consistent findings in our multivariable MR sensitivity analysis that restricted to variants with most heterogeneity in their associations with MAP in those aged ≤55 years and those aged >55 years (Figure 1), as these would be least likely to experience such weak instrument bias.[11] Third, the use of antihypertensive medications varied between those aged ≤55 years and those aged >55 years in our GWAS analyses for MAP (Table S1). Although correction was made for antihypertensive drug use in these GWAS analyses, there may still have been some residual bias that could affect the analysis results.

In conclusion, this study uses the MR approach to generate evidence supporting an effect of midlife blood pressure on later life CAD risk that is independent of later life blood pressure. These findings build on existing conventional epidemiological research, and by considering distinct populations and analytical methods, they add to the body of science supporting that it is a cumulative effect of higher blood pressure that increases cardiovascular disease risk. Clinical and public health inventions should therefore be directed toward optimizing blood pressure control across all age groups.

ARTICLE INFORMATION

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Author contributions: Drs Gill, Georgakis, and Malik designed the study. Drs Gill, Malik, and Georgakis performed statistical analyses. All authors interpreted results. Drs Gill and Malik wrote the manuscript. All authors edited the manuscript for intellectual content. All authors take responsibility for the integrity of the study.

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Disclosures

Dr Gill is employed part-time by Novo Nordisk. The remaining authors have no disclosures to report.

Supplementary Materials

Data S1–S2
Tables S1–S5
References 16 and 17

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SUPPLEMENTAL MATERIAL

Data S1.

Supplemental Methods

Univariable Mendelian randomization

n sensitivity analyses

Contamination-mixture method and weighted median Mendelian randomization (MR) were incorporated as sensitivity analyses in univariable MR to explore the robustness of the findings to potential pleiotropic variants (16, 17). The contamination-mixture method assumes that the MR estimates obtained from valid instruments follow a normal distribution centered on the true causal effect estimate and that those derived from invalid instruments follow a normal distribution centered on the null (16). A likelihood function is then specified and maximized for allocating each instrument variant to one of the two mixture distributions (16). The weighted median method first orders the MR estimates obtained from individual variants by their magnitude weighted for their precision (17). The median value is then selected as the overall MR estimate and standard errors are calculated by bootstrapping (17).

Data S2.

Supplemental Checklist

Research Checklist – STROBE-MR Reporting Guidelines

Davey Smith G, Davies NM, Dimou N, Egger M, Gallo V, Golub R, et al. STROBE-MR: Guidelines for strengthening the reporting of Mendelian randomization studies. https://doi.org/10.7287/peerj.preprints.27857v1. PeerJ Preprints. 2019;7:e27857v1.

1. TITLE and ABSTRACT

Indicate Mendelian randomization as the study's design in the title and/or the abstract.

Title and Abstract

INTRODUCTION

2. Background

Explain the scientific background and rationale for the reported study. Is causality between exposure and outcome plausible? Justify why MR is a helpful method to address the study question.

Introduction

3. Objectives

State specific objectives clearly, including pre-specified causal hypotheses (if any).

Abstract and Background

METHODS

4. Study design and data sources

Present key elements of study design early in the paper. Consider including a table listing sources of data for all phases of the study. For each data source contributing to the analysis, describe the following:

a) Describe the study design and the underlying population from which it was drawn.

Describe also the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection, if available.

b) Give the eligibility criteria, and the sources and methods of selection of participants.

c) Explain how the analysed sample size was arrived at.

d) Describe measurement, quality and selection of genetic variants.

e) For each exposure, outcome and other relevant variables, describe methods of assessment and, in the case of diseases, the diagnostic criteria used.

f) Provide details of ethics committee approval and participant informed consent, if relevant.

Methods

5. Assumptions

Explicitly state assumptions for the main analysis (e.g. relevance, exclusion, independence, homogeneity) as well assumptions for any additional or sensitivity analysis.

Methods

6. Statistical methods: main analysis

Describe statistical methods and statistics used.

a) Describe how quantitative variables were handled in the analyses (i.e., scale, units, model).

b) Describe the process for identifying genetic variants and weights to be included in the analyses (i.e, independence and model). Consider a flow diagram.

c) Describe the MR estimator, e.g. two-stage least squares, Wald ratio, and related statistics.

Detail the included covariates and, in case of two-sample MR, whether the same covariate set was used for adjustment in the two samples.

d) Explain how missing data were addressed.

e) If applicable, say how multiple testing was dealt with.

Methods

7. Assessment of assumptions

Describe any methods used to assess the assumptions or justify their validity.

Methods and Discussion

8. Sensitivity analyses

Describe any sensitivity analyses or additional analyses performed.

Methods

9. Software and pre-registration

a) Name statistical software and package(s), including version and settings used.

Methods

b) State whether the study protocol and details were pre-registered (as well as when and where).

Methods

RESULTS

10. Descriptive data

a) Report the numbers of individuals at each stage of included studies and reasons for exclusion. Consider use of a flow-diagram.

b) Report summary statistics for phenotypic exposure(s), outcome(s) and other relevant variables (e.g. means, standard deviations, proportions).

c) If the data sources include meta-analyses of previous studies, provide the number of studies, their reported ancestry, if available, and assessments of heterogeneity across these studies. Consider using a supplementary table for each data source.

d) For two-sample Mendelian randomization:

i. Provide information on the similarity of the genetic variant-exposure associations between the exposure and outcome samples.

ii. Provide information on extent of sample overlap between the exposure and outcome data sources.

Methods, Results and Supplement

11. Main results

a) Report the associations between genetic variant and exposure, and between genetic variant and outcome, preferably on an interpretable scale (e.g. comparing 25th and 75th percentile of allele count or genetic risk score, if individual-level data available).

b) Report causal effect estimate between exposure and outcome, and the measures of uncertainty from the MR analysis. Use an intuitive scale, such as odds ratio, or relative risk, per standard deviation difference.

c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time-period.

d) Consider any plots to visualize results (e.g. forest plot, scatterplot of associations between genetic variants and outcome versus between genetic variants and exposure).

Results

12. Assessment of assumptions

a) Assess the validity of the assumptions.

b) Report any additional statistics (e.g., assessments of heterogeneity, such as I2, Q statistic).

Results and Discussion

13. Sensitivity and additional analyses

a) Use sensitivity analyses to assess the robustness of the main results to violations of the assumptions.

b) Report results from other sensitivity analyses (e.g., replication study with different dataset, analyses of subgroups, validation of instrument(s), simulations, etc.).

c) Report any assessment of direction of causality (e.g., bidirectional MR).

d) When relevant, report and compare with estimates from non-MR analyses.

e) Consider any additional plots to visualize results (e.g., leave-one-out analyses).

Results and Discussion

DISCUSSION

14. Key results

Summarize key results with reference to study objectives.

Discussion

15. Limitations

Discuss limitations of the study, taking into account the validity of the MR assumptions, other sources of potential bias, and imprecision. Discuss both direction and magnitude of any potential bias, and any efforts to address them.

Discussion

16. Interpretation

a) Give a cautious overall interpretation of results considering objectives and limitations.

Compare with results from other relevant studies.

b) Discuss underlying biological mechanisms that could be modelled by using the genetic variants to assess the relationship between the exposure and the outcome.

c) Discuss whether the results have clinical or policy relevance, and whether interventions could have the same size effect.

Discussion

17. Generalizability

Discuss the generalizability of the study results (a) to other populations (i.e. external validity),

(b) across other exposure periods/timings, and (c) across other levels of exposure.

Discussion

OTHER INFORMATION

18. Funding

Give the source of funding and the role of the funders for the present study and, if applicable, for the original study or studies on which the present article is based.

Funding

19. Data and data sharing

Present data used to perform all analyses or report where and how the data can be accessed. State whether statistical code is publicly accessible and if so, where.

Methods

20. Conflicts of Interest

All authors should declare all potential conflicts of interest.

Conflicts of interest

Table S1. Baseline characteristics for the UK Biobank participants included in the genome-wide association study analyses of mean arterial pressure (MAP) ≤55 years, MAP >55years, and coronary artery disease (CAD) >55 years.

Variable	MAP ≤55 N=163,147	MAP >55 N=245,749	CAD > 55 Cases (N=8,788)	CAD > 55 Controls (N=184,201)
Age, mean (SD), y	48.5 (4.4)	62.5 (3.8)	62.2 (5.0)	58.2 (6.6)
Sex, N (%)				
Male	72,657 (44.5)	115,229 (46.9)	5,791 (65.9)	79,391 (43.1)
Female	90,490 (55.5)	130,520 (53.1)	2,997 (34.1)	104,810 (56.9)
Systolic blood pressure, mmHg (SD)	132.0 (16.7)	142.6 (18.7)	145.9 (19.1)	139.6 (18.6)
Diastolic blood pressure, mmHg (SD)	81.9 (10.3)	82.6 (9.9)	83.8 (10.6)	82.8 (10.0)
BMI,kg/m^2 (SD)	27.2 (5.0)	27.6 (4.6)	28.9 (4.9)	27.4 (4.7)
Current smokers, N (%)	20,440 (12.5)	20,880 (8.5)	1,024 (11.6)	14,486 (7.9)
Antihypertensive medication, N (%)	15,336 (9.4)	70,038 (28.5)	3,612 (41.1)	36,840 (20.0)

Table S2. Instruments and genetic association estimates for Model 1 of the univariable Mendelian randomization analysis. GX: genetic association estimate with MAP ≤55 years (mmHg); GY: genetic association estimate with coronary artery disease (log odds ratio); SE: standard error; SNP: single-nucleotide polymorphism.

SNP	Effect Allele	GX	GX_SE	GX_P	GY	GY_SE	GY_P
rs1057040	G	0.256	0.043	2.36E-09	0.008	0.009	3.90E-01
rs10993958	A	-0.652	0.081	6.02E-16	-0.041	0.028	1.42E-01
rs10995311	G	-0.290	0.043	2.39E-11	0.011	0.010	2.37E-01
rs11039144	A	-0.385	0.059	7.93E-11	0.003	0.012	7.75E-01
rs11070245	T	-0.237	0.043	3.73E-08	0.005	0.009	5.89E-01
rs11072508	C	0.517	0.046	2.94E-29	0.020	0.010	4.99E-02
rs11187838	A	-0.367	0.043	2.28E-17	0.024	0.009	9.21E-03
rs113397083	A	-0.616	0.084	1.68E-13	-0.048	0.017	4.30E-03
rs115262049	T	-0.433	0.076	1.28E-08	-0.032	0.020	1.08E-01
rs11642015	T	0.324	0.044	1.39E-13	0.030	0.010	1.78E-03
rs11669915	G	0.334	0.049	1.16E-11	0.038	0.011	5.53E-04
rs11721038	C	-0.487	0.082	2.95E-09	-0.046	0.015	2.53E-03
rs12137438	C	0.251	0.044	1.02E-08	0.008	0.009	3.95E-01
rs1216743	G	-0.605	0.048	2.31E-36	-0.031	0.010	2.34E-03
rs12185567	A	-0.276	0.048	7.88E-09	0.005	0.011	6.47E-01
rs12258967	G	-0.539	0.047	2.89E-30	-0.026	0.011	2.15E-02
rs12363520	A	0.293	0.052	1.75E-08	-0.023	0.013	8.61E-02
rs12627514	G	0.288	0.048	1.42E-09	0.007	0.011	5.39E-01
rs12644723	G	0.262	0.044	3.01E-09	0.021	0.009	2.49E-02
rs12656497	T	-0.504	0.044	7.43E-31	-0.011	0.009	2.39E-01
rs12693302	G	0.324	0.045	5.22E-13	0.035	0.010	3.73E-04
rs12716338	A	-0.363	0.045	7.15E-16	-0.024	0.010	1.47E-02
rs1275988	C	0.387	0.044	1.82E-18	0.003	0.009	7.50E-01
rs13112725	G	-0.385	0.050	1.69E-14	-0.001	0.011	9.48E-01
rs13121442	T	-0.280	0.043	7.16E-11	-0.037	0.009	9.18E-05
rs13125101	A	0.831	0.047	3.36E-69	0.048	0.010	3.02E-06
rs13163533	G	0.447	0.080	1.92E-08	0.015	0.019	4.26E-01
rs14235	A	-0.244	0.045	4.77E-08	-0.008	0.010	4.13E-01
rs145339349	A	1.225	0.162	4.19E-14	0.036	0.043	4.08E-01
rs167479	T	-0.533	0.043	2.61E-35	-0.015	0.014	2.79E-01
rs17173238	G	0.269	0.048	1.58E-08	0.015	0.011	1.72E-01
rs17257695	G	-0.325	0.059	4.60E-08	-0.010	0.014	4.60E-01
rs17637472	A	0.285	0.044	1.08E-10	0.041	0.010	5.64E-05
rs17677603	G	0.250	0.044	1.56E-08	0.028	0.010	3.25E-03
rs17732246	A	0.384	0.064	2.37E-09	0.019	0.014	1.67E-01
rs1801253	G	-0.442	0.049	1.82E-19	-0.015	0.011	1.70E-01
rs1887320	A	0.362	0.043	4.20E-17	0.023	0.009	1.30E-02
rs1896326	A	-0.283	0.052	5.00E-08	-0.004	0.012	7.23E-01
rs1966697	C	0.320	0.053	1.49E-09	0.008	0.011	4.91E-01
rs1980235	G	-0.447	0.046	1.64E-22	0.032	0.010	1.49E-03
rs200538	C	-0.320	0.048	3.66E-11	-0.003	0.010	7.92E-01
rs2032451	T	0.523	0.060	1.89E-18	0.008	0.014	5.95E-01
rs2163379	A	0.369	0.045	1.33E-16	0.008	0.010	4.00E-01
rs2246832	A	-0.291	0.043	1.11E-11	-0.030	0.009	1.74E-03
rs2294239	G	-0.240	0.043	3.45E-08	-0.019	0.009	4.62E-02
rs2301597	T	0.352	0.044	5.78E-16	0.000	0.009	9.82E-01
rs2306363	T	-0.344	0.053	9.90E-11	-0.050	0.012	1.96E-05
rs2443708	T	-0.283	0.046	9.15E-10	-0.013	0.010	1.97E-01
rs2478531	C	0.329	0.044	5.54E-14	0.018	0.025	4.72E-01
rs2644128	C	-0.244	0.043	1.51E-08	-0.021	0.009	2.29E-02
rs2645158	A	0.251	0.044	1.24E-08	0.016	0.010	8.53E-02
rs268263	T	-0.526	0.050	1.15E-25	-0.042	0.011	1.16E-04
rs2724486	C	-0.272	0.049	2.31E-08	-0.029	0.011	6.93E-03
rs28416181	G	-0.356	0.050	6.62E-13	-0.020	0.011	6.31E-02
rs28866311	G	0.334	0.043	7.01E-15	0.014	0.009	1.34E-01

rs2947411	A	-0.349	0.057	7.20E-10	-0.035	0.012	4.09E-03
rs2969072	A	0.329	0.046	6.77E-13	-0.006	0.011	6.10E-01
rs2978098	C	-0.237	0.043	4.02E-08	-0.004	0.009	7.01E-01
rs3096009	G	0.261	0.046	1.16E-08	0.011	0.010	2.85E-01
rs3118905	A	0.284	0.048	2.71E-09	0.014	0.011	2.09E-01
rs34394882	T	0.276	0.047	4.32E-09	-0.006	0.011	5.70E-01
rs35213536	T	0.328	0.050	5.83E-11	0.019	0.012	1.03E-01
rs35429	G	-0.281	0.044	2.01E-10	0.002	0.010	8.74E-01
rs360153	T	-0.328	0.043	4.73E-14	-0.051	0.009	5.16E-08
rs3790604	A	0.490	0.082	2.60E-09	0.014	0.016	3.93E-01
rs389883	G	-0.344	0.046	5.20E-14	-0.027	0.012	2.22E-02
rs3936510	T	0.328	0.053	8.78E-10	0.042	0.012	4.73E-04
rs4076877	T	-0.590	0.097	1.33E-09	-0.067	0.033	4.41E-02
rs4077158	T	-0.265	0.043	7.37E-10	-0.012	0.009	1.96E-01
rs4147111	C	-0.498	0.084	3.09E-09	-0.067	0.019	3.61E-04
rs419076	T	0.341	0.043	2.17E-15	0.017	0.009	6.69E-02
rs4362428	A	-0.269	0.044	6.26E-10	-0.003	0.010	7.59E-01
rs4428270	C	0.259	0.044	3.42E-09	0.022	0.010	2.34E-02
rs45475403	T	-0.536	0.094	1.09E-08	-0.053	0.023	1.83E-02
rs4588930	A	-0.244	0.043	1.91E-08	-0.006	0.009	5.37E-01
rs4712656	C	0.270	0.043	4.23E-10	0.008	0.009	3.95E-01
rs4766578	T	0.522	0.043	6.07E-34	0.066	0.011	2.83E-10
rs4980379	T	0.310	0.045	4.14E-12	0.013	0.010	2.00E-01
rs5068	G	-1.091	0.094	3.70E-31	-0.005	0.022	8.30E-01
rs56179563	A	-0.303	0.044	8.97E-12	-0.067	0.011	7.46E-10
rs56256623	A	-0.357	0.055	1.05E-10	-0.063	0.012	1.32E-07
rs56313611	T	-0.388	0.062	3.27E-10	-0.061	0.014	1.10E-05
rs568546	C	0.261	0.043	1.48E-09	0.019	0.009	3.85E-02
rs57786342	A	0.335	0.053	3.56E-10	0.015	0.012	2.10E-01
rs6026739	T	0.592	0.067	9.28E-19	0.052	0.015	3.67E-04
rs6039212	C	-0.290	0.051	1.51E-08	-0.003	0.011	7.57E-01
rs62036942	C	-0.388	0.062	4.32E-10	0.003	0.013	7.96E-01
rs62052380	T	0.363	0.066	3.18E-08	0.012	0.020	5.47E-01
rs62104477	T	0.274	0.046	2.09E-09	-0.023	0.010	2.51E-02
rs62445396	T	0.715	0.127	1.96E-08	0.018	0.031	5.53E-01
rs6438857	C	-0.251	0.044	8.15E-09	-0.011	0.009	2.47E-01
rs6798940	A	-0.248	0.043	8.44E-09	0.002	0.009	8.46E-01
rs6923947	A	0.347	0.043	1.05E-15	0.007	0.009	4.58E-01
rs6990531	G	-0.352	0.050	2.62E-12	-0.001	0.010	9.06E-01
rs7067916	A	0.288	0.050	8.13E-09	0.017	0.011	1.07E-01
rs7070797	A	-0.562	0.062	7.76E-20	-0.013	0.015	4.03E-01
rs7121365	A	0.444	0.065	8.81E-12	0.025	0.014	8.53E-02
rs7125196	C	-0.447	0.067	3.15E-11	-0.017	0.013	1.77E-01
rs71508634	T	-0.256	0.047	3.96E-08	0.005	0.010	6.40E-01
rs71654213	T	-0.299	0.044	1.57E-11	0.023	0.011	3.75E-02
rs7171632	C	0.246	0.043	1.30E-08	0.012	0.010	2.35E-01
rs72654647	A	0.328	0.050	5.70E-11	0.026	0.011	1.56E-02
rs72677850	A	-1.216	0.162	5.08E-14	-0.072	0.040	7.31E-02
rs72812818	C	-0.276	0.047	3.37E-09	-0.011	0.011	3.13E-01
rs72854462	G	0.288	0.050	7.20E-09	-0.025	0.011	2.55E-02
rs7302981	A	0.374	0.044	3.21E-17	0.000	0.010	9.76E-01
rs73046792	A	-0.352	0.058	1.13E-09	-0.016	0.016	3.17E-01
rs73075659	G	-0.411	0.045	1.10E-19	-0.006	0.011	5.56E-01
rs73234219	T	0.244	0.044	2.40E-08	-0.013	0.010	1.68E-01
rs741066	T	0.266	0.047	1.50E-08	0.036	0.011	7.22E-04
rs74233809	C	-0.771	0.080	4.48E-22	-0.072	0.014	4.09E-07
rs74661587	G	0.525	0.063	1.07E-16	0.017	0.013	1.75E-01
rs748676	A	0.543	0.082	3.26E-11	0.007	0.013	5.90E-01
rs75034121	C	-0.413	0.074	2.33E-08	0.007	0.017	6.53E-01
rs7604588	A	0.265	0.047	2.30E-08	0.024	0.010	2.26E-02
rs7753358	A	0.292	0.044	2.16E-11	0.028	0.009	3.57E-03
rs7845053	A	-0.256	0.044	5.44E-09	0.010	0.010	3.12E-01
rs79780963	T	-0.766	0.080	1.51E-21	-0.077	0.014	7.54E-08

rs79997166	C	0.537	0.090	2.62E-09	0.011	0.025	6.64E-01
rs8027450	T	0.487	0.046	4.74E-26	0.057	0.011	1.35E-07
rs8070460	C	-0.268	0.043	4.89E-10	-0.040	0.009	2.06E-05
rs891511	A	-0.437	0.047	5.35E-21	-0.021	0.011	4.92E-02
rs9667542	A	-0.310	0.054	8.13E-09	0.001	0.014	9.58E-01
rs9719973	A	0.327	0.044	8.66E-14	0.011	0.010	2.44E-01

Table S3. Instruments and genetic association estimates for Model 2 of the univariable Mendelian randomization analysis. GX: genetic association estimate with MAP ≤55 years (mmHg); GY: genetic association estimate with coronary artery disease (log odds ratio); SE: standard error; SNP: single-nucleotide polymorphism.

SNP	Effect Allele	GX	GX_SE	GX_P	GY	GY_SE	GY_P
rs1057040	G	-0.455	0.115	7.76E-05	-0.016	0.034	6.45E-01
rs10993958	A	-0.493	0.084	5.30E-09	-0.016	0.025	5.17E-01
rs10995311	G	-0.296	0.059	5.86E-07	0.016	0.017	3.62E-01
rs11039144	A	-0.425	0.059	6.66E-13	0.024	0.017	1.61E-01
rs11070245	T	-0.824	0.109	4.53E-14	-0.001	0.032	9.74E-01
rs11072508	C	-0.819	0.110	8.92E-14	0.001	0.032	9.87E-01
rs11187838	A	-0.531	0.067	2.44E-15	-0.038	0.020	5.27E-02
rs113397083	A	0.271	0.068	7.42E-05	0.027	0.020	1.77E-01
rs115262049	T	-0.523	0.064	4.62E-16	-0.014	0.019	4.58E-01
rs11642015	T	0.285	0.061	3.19E-06	0.033	0.018	6.54E-02
rs11669915	G	-0.394	0.092	1.94E-05	-0.034	0.027	2.12E-01
rs11721038	C	-0.322	0.072	9.05E-06	-0.024	0.021	2.69E-01
rs12137438	C	-0.600	0.066	8.17E-20	-0.050	0.019	9.94E-03
rs1216743	G	0.247	0.059	2.87E-05	0.035	0.017	4.30E-02
rs12185567	A	0.374	0.089	2.54E-05	0.075	0.026	3.34E-03
rs12258967	G	-0.304	0.060	3.41E-07	-0.050	0.017	4.18E-03
rs12363520	A	0.256	0.071	3.06E-04	-0.011	0.021	5.94E-01
rs12627514	G	0.322	0.072	8.84E-06	0.009	0.021	6.88E-01
rs12644723	G	-0.350	0.081	1.52E-05	0.015	0.024	5.21E-01
rs12656497	T	-0.420	0.073	1.12E-08	-0.050	0.022	2.07E-02
rs12693302	G	-0.497	0.063	2.03E-15	0.006	0.018	7.30E-01
rs12716338	A	0.488	0.059	1.21E-16	0.085	0.017	6.31E-07
rs1275988	C	-0.318	0.071	7.76E-06	-0.038	0.021	6.76E-02
rs13112725	G	-0.260	0.060	1.73E-05	0.019	0.018	2.69E-01
rs13121442	T	-0.411	0.062	3.26E-11	-0.017	0.018	3.60E-01
rs13125101	A	0.417	0.061	5.55E-12	-0.012	0.018	4.85E-01
rs13163533	G	0.280	0.065	1.87E-05	0.026	0.019	1.77E-01
rs14235	A	0.539	0.112	1.44E-06	0.019	0.033	5.57E-01
rs145339349	A	-1.000	0.222	6.50E-06	-0.063	0.066	3.44E-01
rs167479	T	0.251	0.073	5.84E-04	0.004	0.021	8.69E-01
rs17173238	G	0.482	0.063	2.44E-14	0.074	0.018	5.33E-05
rs17257695	G	0.416	0.088	2.41E-06	0.004	0.026	8.72E-01
rs17637472	A	-0.212	0.059	3.26E-04	-0.036	0.017	3.88E-02
rs17677603	G	0.333	0.059	1.44E-08	0.017	0.017	3.13E-01
rs17732246	A	0.523	0.063	1.00E-16	0.019	0.018	2.98E-01
rs1801253	G	0.222	0.059	1.79E-04	0.010	0.017	5.77E-01
rs1887320	A	-0.471	0.085	2.62E-08	-0.022	0.025	3.80E-01
rs1896326	A	-0.335	0.066	4.20E-07	0.005	0.019	7.90E-01
rs1966697	C	-0.307	0.061	5.30E-07	0.009	0.018	6.12E-01
rs1980235	G	0.311	0.060	2.15E-07	0.020	0.017	2.63E-01
rs200538	C	0.336	0.090	1.81E-04	-0.036	0.027	1.73E-01
rs2032451	T	-0.246	0.060	3.78E-05	0.000	0.017	9.85E-01
rs2163379	A	0.262	0.059	8.18E-06	0.028	0.017	1.07E-01
rs2246832	A	0.391	0.060	5.19E-11	0.007	0.017	7.00E-01
rs2294239	G	0.236	0.060	8.73E-05	0.033	0.018	6.05E-02
rs2301597	T	-0.287	0.059	1.16E-06	-0.016	0.017	3.42E-01
rs2306363	T	0.376	0.064	5.69E-09	-0.003	0.019	8.68E-01
rs2443708	T	-0.547	0.059	1.18E-20	-0.051	0.017	2.83E-03
rs2478531	C	0.245	0.063	9.14E-05	0.025	0.018	1.78E-01
rs2644128	C	0.265	0.060	1.09E-05	-0.020	0.018	2.52E-01
rs2645158	A	0.329	0.067	1.01E-06	0.053	0.019	6.90E-03
rs268263	T	-0.383	0.079	1.25E-06	0.000	0.023	9.95E-01
rs2724486	C	0.538	0.112	1.70E-06	0.004	0.033	8.99E-01
rs28416181	G	1.433	0.217	4.05E-11	0.123	0.063	5.06E-02
rs28866311	G	-0.331	0.129	1.00E-02	0.024	0.037	5.08E-01

rs2947411	A	-1.193	0.129	2.93E-20	-0.035	0.038	3.65E-01
rs2969072	A	0.234	0.060	9.21E-05	0.017	0.017	3.40E-01
rs2978098	C	-0.293	0.059	6.54E-07	-0.001	0.017	9.61E-01
rs3096009	G	0.358	0.060	2.31E-09	0.027	0.017	1.24E-01
rs3118905	A	0.321	0.068	2.69E-06	-0.009	0.020	6.53E-01
rs34394882	T	-0.318	0.061	1.67E-07	0.018	0.018	3.03E-01
rs35213536	T	-0.293	0.070	3.09E-05	-0.021	0.021	2.95E-01
rs35429	G	0.374	0.059	2.23E-10	0.007	0.017	6.65E-01
rs360153	T	-0.439	0.085	2.16E-07	-0.047	0.025	6.20E-02
rs3790604	A	0.728	0.091	1.63E-15	0.060	0.026	2.25E-02
rs389883	G	0.345	0.069	4.73E-07	0.012	0.020	5.50E-01
rs3936510	T	0.362	0.065	2.80E-08	0.020	0.019	2.84E-01
rs4076877	T	-0.282	0.059	2.07E-06	-0.017	0.017	3.19E-01
rs4077158	T	-0.400	0.077	2.44E-07	0.031	0.022	1.70E-01
rs4147111	C	0.262	0.065	5.19E-05	-0.024	0.019	2.12E-01
rs419076	T	0.362	0.068	1.02E-07	-0.023	0.020	2.45E-01
rs4362428	A	0.429	0.124	5.28E-04	0.020	0.036	5.66E-01
rs4428270	C	-0.454	0.069	3.86E-11	-0.028	0.020	1.70E-01
rs45475403	T	-0.300	0.065	4.52E-06	0.022	0.019	2.49E-01
rs4588930	A	0.328	0.061	9.75E-08	0.019	0.018	2.82E-01
rs4712656	C	-0.444	0.081	4.77E-08	-0.007	0.024	7.63E-01
rs4766578	T	-0.327	0.101	1.27E-03	-0.022	0.030	4.67E-01
rs4980379	T	0.455	0.060	5.18E-14	0.016	0.018	3.58E-01
rs5068	G	-0.405	0.105	1.13E-04	0.024	0.030	4.28E-01
rs56179563	A	-0.286	0.059	1.58E-06	-0.020	0.018	2.53E-01
rs56256623	A	-0.280	0.059	2.03E-06	-0.015	0.017	3.81E-01
rs56313611	T	-0.354	0.059	1.93E-09	-0.012	0.017	4.93E-01
rs568546	C	-0.420	0.112	1.85E-04	-0.001	0.033	9.81E-01
rs57786342	A	0.380	0.059	1.07E-10	0.012	0.017	4.94E-01
rs6026739	T	-0.335	0.063	1.15E-07	-0.055	0.019	3.18E-03
rs6039212	C	-0.282	0.059	1.58E-06	-0.024	0.017	1.56E-01
rs62036942	C	0.799	0.065	7.11E-35	0.063	0.019	8.00E-04
rs62052380	T	0.279	0.060	4.08E-06	0.021	0.018	2.31E-01
rs62104477	T	-0.398	0.069	6.41E-09	-0.017	0.020	4.03E-01
rs62445396	T	-0.321	0.059	4.88E-08	-0.025	0.017	1.42E-01
rs6438857	C	-0.385	0.076	3.60E-07	-0.071	0.022	1.71E-03
rs6798940	A	-0.351	0.067	1.45E-07	-0.020	0.020	2.98E-01
rs6923947	A	0.205	0.060	6.25E-04	0.010	0.017	5.53E-01
rs6990531	G	0.296	0.060	7.60E-07	0.027	0.017	1.14E-01
rs7067916	A	0.557	0.109	3.22E-07	0.008	0.032	7.92E-01
rs7070797	A	0.470	0.087	5.49E-08	0.013	0.025	6.00E-01
rs7121365	A	0.235	0.061	1.03E-04	0.016	0.018	3.69E-01
rs7125196	C	0.235	0.063	1.72E-04	0.010	0.018	5.90E-01
rs71508634	T	-0.416	0.061	1.25E-11	-0.011	0.018	5.38E-01
rs71654213	T	-0.208	0.064	1.13E-03	-0.039	0.019	3.79E-02
rs7171632	C	-0.474	0.060	2.08E-15	0.000	0.017	9.77E-01
rs72654647	A	0.339	0.073	3.66E-06	0.022	0.021	3.09E-01
rs72677850	A	0.351	0.060	4.31E-09	0.012	0.017	4.91E-01
rs72812818	C	0.399	0.059	1.63E-11	-0.026	0.017	1.37E-01
rs72854462	G	-0.719	0.115	3.86E-10	-0.049	0.034	1.44E-01
rs7302981	A	0.207	0.059	4.49E-04	-0.001	0.017	9.31E-01
rs73046792	A	0.475	0.082	6.53E-09	-0.018	0.024	4.41E-01
rs73075659	G	-0.339	0.063	5.83E-08	-0.023	0.018	2.15E-01
rs73234219	T	0.302	0.063	1.52E-06	0.019	0.018	3.04E-01
rs741066	T	-0.310	0.061	3.50E-07	-0.030	0.018	8.84E-02
rs74233809	C	0.270	0.060	6.59E-06	0.034	0.017	5.16E-02
rs74661587	G	0.259	0.064	5.71E-05	0.028	0.019	1.27E-01
rs748676	A	-0.516	0.064	6.00E-16	-0.004	0.019	8.41E-01
rs75034121	C	0.267	0.065	3.82E-05	0.008	0.019	6.86E-01
rs7604588	A	0.913	0.174	1.60E-07	0.053	0.050	2.95E-01
rs7753358	A	-0.275	0.069	6.58E-05	-0.022	0.020	2.73E-01
rs7845053	A	-0.259	0.059	1.16E-05	0.013	0.017	4.46E-01
rs79780963	T	-0.266	0.060	9.65E-06	-0.025	0.018	1.57E-01

rs79997166	C	-0.588	0.133	1.02E-05	0.012	0.039	7.65E-01
rs8027450	T	0.385	0.061	3.08E-10	0.037	0.018	3.90E-02
rs8070460	C	-0.303	0.068	7.78E-06	-0.014	0.020	4.95E-01
rs891511	A	-0.284	0.059	1.64E-06	0.005	0.017	7.64E-01
rs9667542	A	-0.624	0.111	1.80E-08	-0.071	0.033	3.19E-02
rs9719973	A	-0.280	0.064	1.12E-05	-0.011	0.019	5.62E-01

Table S4. Instruments and genetic association estimates for Models 1 and 3 of the multivariable Mendelian randomization analysis. GX: genetic association estimate with MAP ≤55 years (mmHg); GY: genetic association estimate with coronary artery disease (log odds ratio); GZ: genetic association estimates with MAP >55 years (mmHg); SE: standard error; SNP: single-nucleotide polymorphism.

SNP	Effect Allele	GX	GX_SE	GX_P	GZ	GZ_SE	GZ_P	GY	GY_SE	GY_P	GX and GZ mean	GX and GZ difference	Included in Model 3
rs1000423	C	-0.15	0.05	2.1E-03	-0.33	0.04	9.0E-15	-0.04	0.01	1.4E-04	-0.24	0.18	No
rs1010064	C	-0.22	0.06	9.5E-05	-0.27	0.05	1.9E-08	-0.04	0.01	4.1E-04	-0.24	0.05	No
rs10119435	A	0.42	0.13	8.1E-04	0.62	0.11	1.7E-08	0.03	0.03	2.3E-01	0.52	-0.20	Yes
rs10158537	G	0.23	0.05	9.5E-07	0.30	0.04	7.9E-14	0.00	0.01	7.6E-01	0.27	-0.07	No
rs10226118	C	-0.06	0.04	1.7E-01	-0.25	0.04	6.8E-11	0.00	0.01	7.0E-01	-0.15	0.19	No
rs10248237	A	0.26	0.10	5.9E-03	0.46	0.08	2.7E-08	0.03	0.02	1.8E-01	0.36	-0.20	Yes
rs10265221	C	0.28	0.05	4.3E-09	0.29	0.04	1.0E-12	0.01	0.01	3.8E-01	0.29	-0.02	No
rs10409243	C	0.11	0.04	1.3E-02	0.21	0.04	3.7E-08	0.01	0.01	1.6E-01	0.16	-0.10	No
rs10468291	C	0.09	0.04	4.0E-02	0.22	0.04	6.5E-09	0.00	0.01	6.1E-01	0.15	-0.13	No
rs10777213	G	0.26	0.04	7.1E-10	0.15	0.04	5.6E-05	0.00	0.01	7.0E-01	0.21	0.11	No
rs10852034	T	-0.16	0.04	2.2E-04	-0.23	0.04	1.2E-09	0.00	0.01	6.9E-01	-0.20	0.07	No
rs10858071	A	1.09	0.15	2.7E-13	0.65	0.13	8.2E-07	0.01	0.04	8.1E-01	0.87	0.45	Yes
rs10876531	C	-0.21	0.05	1.2E-05	-0.27	0.04	4.9E-11	-0.02	0.01	6.5E-02	-0.24	0.07	No
rs10900127	C	0.08	0.04	7.8E-02	0.22	0.04	6.5E-09	-0.01	0.01	1.9E-01	0.15	-0.14	No
rs10993958	A	-0.65	0.08	6.0E-16	-0.42	0.07	2.7E-09	-0.04	0.03	1.4E-01	-0.54	-0.23	Yes
rs10995307	T	0.28	0.04	4.7E-11	-0.31	0.04	1.1E-16	0.00	0.01	8.6E-01	-0.01	0.59	Yes
rs11070245	T	-0.24	0.04	3.7E-08	-0.20	0.04	1.0E-07	0.01	0.01	5.9E-01	-0.22	-0.04	No
rs11072508	C	0.52	0.05	2.9E-29	0.32	0.04	9.8E-16	0.02	0.01	5.0E-02	0.42	0.20	Yes
rs1114348	A	0.22	0.04	4.2E-07	0.25	0.04	1.3E-11	0.03	0.01	5.5E-03	0.23	-0.04	No
rs11187838	A	-0.37	0.04	2.3E-17	-0.40	0.04	6.1E-26	0.02	0.01	9.2E-03	-0.38	0.03	No
rs113044050	T	-0.24	0.06	1.3E-04	-0.37	0.05	8.1E-12	-0.02	0.01	7.4E-02	-0.30	0.13	No
rs113230003	A	-0.29	0.05	2.6E-09	-0.19	0.04	1.1E-05	-0.02	0.01	1.5E-01	-0.24	-0.10	No
rs1133400	G	0.17	0.05	9.3E-04	0.29	0.05	1.3E-10	0.01	0.01	3.7E-01	0.23	-0.12	No
rs113458760	G	-0.15	0.04	1.2E-03	-0.24	0.04	1.5E-09	-0.02	0.01	2.3E-01	-0.19	0.09	No
rs113695818	T	-0.14	0.05	2.5E-03	-0.29	0.04	1.2E-12	-0.01	0.01	5.3E-01	-0.21	0.15	No
rs115262049	T	-0.43	0.08	1.3E-08	-0.48	0.07	3.2E-13	-0.03	0.02	1.1E-01	-0.46	0.05	No
rs11642015	T	0.32	0.04	1.4E-13	0.09	0.04	1.9E-02	0.03	0.01	1.8E-03	0.21	0.23	Yes
rs11669915	G	0.33	0.05	1.2E-11	0.23	0.04	1.4E-07	0.04	0.01	5.5E-04	0.28	0.11	No
rs11676040	C	0.09	0.05	6.6E-02	0.25	0.04	7.9E-10	0.02	0.01	3.8E-02	0.17	-0.17	No
rs11749673	G	-0.13	0.05	7.0E-03	-0.25	0.04	5.7E-09	-0.02	0.01	4.3E-02	-0.19	0.12	No
rs1175651	T	0.24	0.05	3.8E-06	0.26	0.05	2.6E-08	0.00	0.01	7.9E-01	0.25	-0.01	No
rs11760498	A	0.23	0.06	7.2E-05	0.28	0.05	1.1E-08	0.01	0.01	4.0E-01	0.26	-0.06	No
rs11774829	A	-0.28	0.07	8.0E-05	-0.38	0.06	9.4E-10	-0.02	0.02	2.3E-01	-0.33	0.10	No
rs11821781	G	0.25	0.05	5.8E-07	0.32	0.04	1.4E-13	0.00	0.01	7.2E-01	0.28	-0.07	No
rs11915142	A	0.20	0.04	3.7E-06	0.25	0.04	9.3E-11	0.01	0.01	1.4E-01	0.23	-0.04	No
rs12057453	T	0.22	0.04	7.6E-07	0.24	0.04	2.4E-10	0.01	0.01	1.7E-01	0.23	-0.03	No
rs12137438	C	0.25	0.04	1.0E-08	0.10	0.04	9.2E-03	0.01	0.01	4.0E-01	0.18	0.15	No
rs12194642	A	0.25	0.04	1.5E-08	0.26	0.04	2.0E-11	0.02	0.01	2.3E-02	0.25	-0.01	No
rs12216886	G	-0.08	0.06	1.3E-01	-0.27	0.05	1.5E-08	0.00	0.01	7.1E-01	-0.18	0.19	No
rs12258967	G	-0.54	0.05	2.9E-30	-0.39	0.04	7.4E-22	-0.03	0.01	2.2E-02	-0.47	-0.15	No
rs1229984	T	-0.83	0.15	1.7E-08	-0.61	0.12	1.2E-06	-0.03	0.02	7.5E-02	-0.72	-0.22	Yes
rs12567136	T	-0.67	0.06	8.9E-31	-0.65	0.05	2.4E-38	-0.02	0.01	7.0E-02	-0.66	-0.01	No
rs12627514	G	0.29	0.05	1.4E-09	0.17	0.04	5.8E-05	0.01	0.01	5.4E-01	0.23	0.12	No
rs12643599	G	-0.27	0.04	2.9E-09	-0.27	0.04	3.1E-12	-0.05	0.01	7.1E-08	-0.27	0.01	No
rs12656497	T	-0.50	0.04	7.4E-31	-0.47	0.04	4.5E-35	-0.01	0.01	2.4E-01	-0.49	-0.03	No
rs12693302	G	0.32	0.04	5.2E-13	0.22	0.04	1.0E-08	0.03	0.01	3.7E-04	0.27	0.10	No
rs1275978	C	0.38	0.04	4.6E-18	0.48	0.04	4.4E-35	0.00	0.01	9.1E-01	0.43	-0.09	No
rs12978472	G	-0.56	0.06	8.1E-18	-0.72	0.06	8.4E-38	-0.02	0.02	2.2E-01	-0.64	0.16	No
rs12983032	A	-0.13	0.05	2.9E-03	-0.23	0.04	8.1E-09	-0.03	0.01	3.3E-03	-0.18	0.09	No
rs13107325	T	-0.48	0.08	5.7E-09	-0.64	0.07	2.7E-19	-0.01	0.02	7.7E-01	-0.56	0.16	No
rs13121442	T	-0.28	0.04	7.2E-11	-0.20	0.04	6.5E-08	-0.04	0.01	9.2E-05	-0.24	-0.08	No
rs13125101	A	0.83	0.05	3.4E-69	0.57	0.04	2.0E-44	0.05	0.01	3.0E-06	0.70	0.26	Yes

rs13227860	A	0.14	0.05	3.8E-03	0.25	0.04	1.1E-09	0.02	0.01	1.0E-01	0.19	-0.11	No
rs13324341	T	0.14	0.06	1.9E-02	0.28	0.05	4.5E-08	0.07	0.01	4.3E-09	0.21	-0.14	No
rs1436049	G	-0.13	0.05	7.1E-03	-0.24	0.04	1.4E-08	-0.01	0.01	3.6E-01	-0.19	0.11	No
rs1436138	G	-0.18	0.04	3.8E-05	-0.28	0.04	1.0E-12	-0.01	0.01	4.1E-01	-0.23	0.10	No
rs1472467	G	-0.14	0.04	1.2E-03	-0.21	0.04	3.4E-08	0.02	0.01	1.3E-02	-0.17	0.07	No
rs1487629	A	0.17	0.04	5.1E-05	0.25	0.04	2.9E-11	0.00	0.01	6.2E-01	0.21	-0.08	No
rs1492027	G	0.14	0.05	8.7E-03	0.29	0.05	2.0E-10	0.00	0.01	7.7E-01	0.21	-0.15	No
rs150857355	C	0.54	0.15	2.6E-04	0.80	0.13	8.3E-10	0.08	0.04	7.8E-02	0.67	-0.26	Yes
rs1544861	T	0.32	0.05	3.9E-12	0.16	0.04	4.0E-05	-0.01	0.01	2.7E-01	0.24	0.15	No
rs164101	G	-0.27	0.05	9.5E-09	-0.19	0.04	5.7E-06	-0.01	0.01	4.0E-01	-0.23	-0.08	No
rs1687318	T	0.25	0.05	2.6E-07	0.28	0.04	1.7E-11	0.01	0.01	2.6E-01	0.27	-0.03	No
rs16895971	C	0.30	0.06	1.7E-06	0.35	0.05	1.6E-10	0.02	0.01	1.0E-01	0.32	-0.05	No
rs17249754	A	-0.48	0.06	1.8E-17	-0.52	0.05	9.2E-26	0.07	0.01	2.1E-10	-0.50	0.04	No
rs17257695	G	-0.32	0.06	4.6E-08	-0.11	0.05	3.8E-02	-0.01	0.01	4.6E-01	-0.22	-0.22	Yes
rs17517959	C	0.13	0.04	4.8E-03	0.22	0.04	8.9E-09	0.00	0.01	8.7E-01	0.17	-0.10	No
rs17637472	A	0.28	0.04	1.1E-10	0.23	0.04	4.4E-09	0.04	0.01	5.6E-05	0.26	0.06	No
rs17717829	C	-0.18	0.04	4.5E-05	-0.27	0.04	3.0E-13	-0.01	0.01	4.9E-01	-0.23	0.10	No
rs17762	A	0.34	0.08	5.3E-05	0.41	0.07	2.4E-08	0.01	0.01	3.3E-01	0.38	-0.07	No
rs1801253	G	-0.44	0.05	1.8E-19	-0.35	0.04	5.5E-16	-0.01	0.01	1.7E-01	-0.39	-0.10	No
rs187680068	G	-0.21	0.04	1.4E-06	-0.24	0.04	3.6E-10	0.04	0.04	3.8E-01	-0.23	0.03	No
rs1896326	A	-0.28	0.05	5.0E-08	-0.17	0.05	1.8E-04	0.00	0.01	7.2E-01	-0.23	-0.11	No
rs1958603	A	-0.35	0.04	1.9E-15	-0.33	0.04	4.3E-17	-0.02	0.01	1.4E-02	-0.34	-0.03	No
rs2014590	T	-0.31	0.04	3.5E-13	-0.33	0.04	7.3E-19	-0.02	0.01	3.3E-02	-0.32	0.02	No
rs2032451	T	0.52	0.06	1.9E-18	0.44	0.05	3.8E-17	0.01	0.01	5.9E-01	0.48	0.08	No
rs2050905	G	0.11	0.04	1.3E-02	0.23	0.04	2.4E-09	0.00	0.01	9.8E-01	0.17	-0.12	No
rs2067832	G	0.08	0.04	6.4E-02	0.24	0.04	3.1E-10	-0.02	0.01	1.3E-02	0.16	-0.16	No
rs2071265	C	-0.37	0.08	5.8E-06	-0.79	0.07	3.3E-28	0.01	0.02	5.6E-01	-0.58	0.41	Yes
rs2073641	A	0.16	0.08	3.0E-02	0.38	0.07	7.6E-09	0.01	0.02	7.9E-01	0.27	-0.22	Yes
rs2087319	A	-0.12	0.05	1.8E-02	-0.27	0.04	1.2E-09	-0.02	0.01	3.1E-02	-0.19	0.15	No
rs2165301	C	0.15	0.04	7.0E-04	0.26	0.04	2.4E-11	0.02	0.01	1.5E-02	0.20	-0.11	No
rs2178270	C	-0.23	0.06	4.8E-05	-0.29	0.05	2.0E-09	-0.03	0.01	3.0E-02	-0.26	0.06	No
rs2242338	C	-0.48	0.08	9.4E-09	-0.38	0.07	1.6E-07	-0.04	0.02	7.4E-03	-0.43	-0.10	No
rs2294239	G	-0.24	0.04	3.5E-08	-0.17	0.04	4.4E-06	-0.02	0.01	4.6E-02	-0.21	-0.07	No
rs2301597	T	0.35	0.04	5.8E-16	0.29	0.04	4.9E-14	0.00	0.01	9.8E-01	0.32	0.07	No
rs2306363	T	-0.34	0.05	9.9E-11	-0.38	0.05	1.2E-16	-0.05	0.01	2.0E-05	-0.36	0.04	No
rs2311411	A	-0.13	0.04	2.1E-03	-0.23	0.04	3.0E-09	-0.03	0.01	8.7E-03	-0.18	0.09	No
rs2478531	C	0.33	0.04	5.5E-14	0.24	0.04	1.4E-10	0.02	0.03	4.7E-01	0.29	0.08	No
rs2478981	T	0.19	0.05	3.7E-05	0.29	0.04	2.6E-13	0.01	0.01	4.1E-01	0.24	-0.10	No
rs2493296	T	0.33	0.06	2.0E-07	0.39	0.05	4.7E-13	0.06	0.01	1.4E-04	0.36	-0.07	No
rs2521501	T	0.48	0.05	8.6E-25	0.50	0.04	3.2E-36	0.06	0.01	5.0E-08	0.49	-0.03	No
rs2627308	A	0.23	0.04	1.1E-07	0.32	0.04	1.3E-17	0.00	0.01	6.6E-01	0.27	-0.09	No
rs262986	A	-0.15	0.04	3.4E-04	-0.23	0.04	2.3E-09	0.00	0.01	8.7E-01	-0.19	0.07	No
rs2644128	C	-0.24	0.04	1.5E-08	-0.11	0.04	4.4E-03	-0.02	0.01	2.3E-02	-0.18	-0.14	No
rs268263	T	-0.53	0.05	1.2E-25	-0.33	0.04	4.3E-14	-0.04	0.01	1.2E-04	-0.43	-0.19	No
rs2760061	A	0.23	0.04	1.5E-07	0.26	0.04	1.1E-11	0.00	0.01	9.2E-01	0.24	-0.03	No
rs2823139	A	0.05	0.05	2.4E-01	0.24	0.04	1.3E-09	0.03	0.01	6.4E-04	0.15	-0.19	No
rs28416181	G	-0.36	0.05	6.6E-13	-0.24	0.04	4.3E-08	-0.02	0.01	6.3E-02	-0.30	-0.12	No
rs28572357	C	0.23	0.04	1.5E-07	0.23	0.04	2.7E-09	0.01	0.01	1.2E-01	0.23	0.00	No
rs286749	T	-0.12	0.06	3.1E-02	-0.29	0.05	6.7E-09	-0.04	0.01	3.6E-04	-0.21	0.17	No
rs28866311	G	0.33	0.04	7.0E-15	0.24	0.04	2.3E-10	0.01	0.01	1.3E-01	0.29	0.10	No
rs2947411	A	-0.35	0.06	7.2E-10	-0.18	0.05	1.8E-04	-0.03	0.01	4.1E-03	-0.27	-0.16	No
rs311443	G	-0.11	0.05	2.7E-02	-0.24	0.04	1.2E-08	-0.01	0.01	2.7E-01	-0.17	0.13	No
rs3118905	A	0.28	0.05	2.7E-09	0.13	0.04	1.3E-03	0.01	0.01	2.1E-01	0.21	0.15	No
rs3218036	A	0.24	0.05	1.3E-07	0.26	0.04	1.5E-10	-0.02	0.01	4.0E-02	0.25	-0.01	No
rs34148132	T	-0.24	0.05	2.8E-07	-0.24	0.04	7.5E-09	-0.05	0.01	3.8E-06	-0.24	0.00	No
rs34394882	T	0.28	0.05	4.3E-09	0.16	0.04	9.1E-05	-0.01	0.01	5.7E-01	0.22	0.12	No
rs351365	T	-0.31	0.05	3.9E-10	-0.40	0.04	1.4E-20	0.00	0.01	9.4E-01	-0.36	0.09	No
rs35444	G	-0.27	0.04	4.4E-10	-0.43	0.04	2.3E-29	0.00	0.01	8.5E-01	-0.35	0.16	No
rs35681682	C	-0.14	0.04	1.4E-03	-0.22	0.04	2.7E-09	-0.02	0.01	1.6E-02	-0.18	0.09	No
rs35942721	T	-0.27	0.05	1.7E-08	-0.27	0.04	1.0E-10	-0.03	0.01	1.7E-02	-0.27	0.00	No
rs3746038	T	-0.17	0.05	1.7E-03	-0.28	0.05	1.6E-09	0.00	0.01	9.6E-01	-0.23	0.11	No
rs3764769	T	-0.13	0.05	7.8E-03	-0.35	0.04	9.0E-17	0.00	0.01	9.6E-01	-0.24	0.22	Yes
rs3803266	G	0.19	0.05	1.3E-04	0.27	0.04	1.5E-09	-0.01	0.01	5.5E-01	0.23	-0.07	No

rs3821843	G	-0.17	0.05	2.0E-04	-0.34	0.04	5.3E-17	-0.01	0.01	4.6E-01	-0.26	0.17	No
rs389883	G	-0.34	0.05	5.2E-14	-0.26	0.04	6.6E-11	-0.03	0.01	2.2E-02	-0.30	-0.08	No
rs3918226	T	0.68	0.08	2.2E-17	0.65	0.07	4.9E-21	0.13	0.02	1.7E-09	0.66	0.02	No
rs3936510	T	0.33	0.05	8.8E-10	0.13	0.05	7.0E-03	0.04	0.01	4.7E-04	0.23	0.20	Yes
rs4076877	T	-0.59	0.10	1.3E-09	-0.19	0.09	2.6E-02	-0.07	0.03	4.4E-02	-0.39	-0.40	Yes
rs4147111	C	-0.50	0.08	3.1E-09	-0.24	0.07	1.2E-03	-0.07	0.02	3.6E-04	-0.37	-0.26	Yes
rs4362428	A	-0.27	0.04	6.3E-10	-0.25	0.04	4.6E-11	0.00	0.01	7.6E-01	-0.26	-0.02	No
rs4428270	C	0.26	0.04	3.4E-09	0.20	0.04	1.2E-07	0.02	0.01	2.3E-02	0.23	0.06	No
rs4473575	G	-0.11	0.08	1.7E-01	-0.39	0.07	3.3E-08	0.03	0.02	1.6E-01	-0.25	0.28	Yes
rs4588930	A	-0.24	0.04	1.9E-08	-0.06	0.04	9.2E-02	-0.01	0.01	5.4E-01	-0.15	-0.18	No
rs4712656	C	0.27	0.04	4.2E-10	0.18	0.04	2.0E-06	0.01	0.01	3.9E-01	0.22	0.09	No
rs483071	C	-0.21	0.04	3.8E-06	-0.24	0.04	5.9E-10	0.00	0.01	6.8E-01	-0.22	0.03	No
rs4873492	T	0.27	0.06	3.8E-06	0.33	0.05	2.7E-11	0.01	0.01	2.5E-01	0.30	-0.07	No
rs488834	C	0.26	0.05	2.0E-07	0.36	0.04	2.9E-16	0.01	0.01	4.4E-01	0.31	-0.10	No
rs4899396	T	0.04	0.04	3.6E-01	0.22	0.04	7.6E-09	0.01	0.01	6.0E-01	0.13	-0.18	No
rs4923914	T	0.16	0.05	3.6E-04	0.27	0.04	2.5E-11	-0.02	0.01	8.2E-02	0.21	-0.10	No
rs507666	A	-0.20	0.06	2.4E-04	-0.26	0.05	3.6E-08	0.08	0.01	1.6E-11	-0.23	0.06	No
rs5418	G	-0.21	0.04	1.1E-06	-0.29	0.04	2.2E-14	0.01	0.01	1.4E-01	-0.25	0.08	No
rs55646464	T	-0.27	0.05	1.0E-08	-0.32	0.04	2.9E-15	-0.01	0.01	3.9E-01	-0.30	0.05	No
rs55733296	A	0.04	0.11	7.1E-01	0.60	0.10	6.5E-10	0.07	0.04	1.4E-01	0.32	-0.56	Yes
rs56179563	A	-0.30	0.04	9.0E-12	-0.17	0.04	8.2E-06	-0.07	0.01	7.5E-10	-0.24	-0.13	No
rs56313611	T	-0.39	0.06	3.3E-10	-0.22	0.05	3.1E-05	-0.06	0.01	1.1E-05	-0.31	-0.16	No
rs56352102	T	0.39	0.06	1.8E-12	0.41	0.05	1.2E-17	0.03	0.01	1.4E-02	0.40	-0.02	No
rs569550	G	0.31	0.04	4.7E-12	0.45	0.04	3.1E-32	0.02	0.01	1.4E-01	0.38	-0.15	No
rs57139556	G	-0.59	0.08	8.6E-13	-0.60	0.07	1.6E-16	-0.05	0.02	3.5E-03	-0.60	0.00	No
rs57786342	A	0.33	0.05	3.6E-10	0.11	0.05	2.3E-02	0.02	0.01	2.1E-01	0.22	0.23	Yes
rs6031431	G	0.13	0.04	2.1E-03	0.24	0.04	3.1E-10	0.00	0.01	8.1E-01	0.19	-0.10	No
rs604723	T	-0.60	0.05	5.2E-36	-0.55	0.04	2.4E-39	-0.03	0.01	1.2E-03	-0.58	-0.05	No
rs6108171	T	-0.25	0.05	3.5E-07	-0.26	0.04	1.6E-09	0.00	0.01	7.8E-01	-0.26	0.01	No
rs6108787	G	0.36	0.04	7.4E-17	0.40	0.04	9.8E-27	0.02	0.01	1.6E-02	0.38	-0.04	No
rs62036942	C	-0.39	0.06	4.3E-10	-0.23	0.05	2.7E-05	0.00	0.01	8.0E-01	-0.31	-0.16	No
rs62390667	G	0.24	0.04	3.8E-08	0.32	0.04	1.0E-16	0.03	0.01	2.7E-03	0.28	-0.08	No
rs62447769	A	0.70	0.13	4.6E-08	0.24	0.11	2.9E-02	0.02	0.03	3.6E-01	0.47	0.45	Yes
rs6433891	G	-0.11	0.05	2.1E-02	-0.27	0.04	5.9E-11	-0.02	0.01	6.8E-02	-0.19	0.16	No
rs6438857	C	-0.25	0.04	8.2E-09	-0.19	0.04	4.1E-07	-0.01	0.01	2.5E-01	-0.22	-0.06	No
rs645040	G	-0.12	0.05	1.5E-02	-0.25	0.04	2.0E-08	-0.04	0.01	6.0E-04	-0.19	0.13	No
rs6490019	A	-0.18	0.04	5.8E-05	-0.28	0.04	6.4E-13	-0.01	0.01	5.1E-01	-0.23	0.10	No
rs66682451	G	-0.21	0.05	1.5E-05	-0.31	0.04	1.0E-13	-0.02	0.01	3.3E-02	-0.26	0.10	No
rs6697193	T	-0.14	0.06	1.5E-02	-0.34	0.05	2.2E-11	0.01	0.02	4.4E-01	-0.24	0.20	Yes
rs6777317	A	0.09	0.05	7.2E-02	0.23	0.04	3.7E-08	0.00	0.01	9.6E-01	0.16	-0.14	No
rs6798940	A	-0.25	0.04	8.4E-09	-0.13	0.04	6.0E-04	0.00	0.01	8.5E-01	-0.19	-0.12	No
rs6815273	A	-0.16	0.04	3.1E-04	-0.23	0.04	1.8E-09	-0.01	0.01	2.2E-01	-0.19	0.07	No
rs6827655	G	0.11	0.05	2.5E-02	0.24	0.04	1.8E-08	0.03	0.01	3.4E-03	0.17	-0.13	No
rs6928622	C	0.11	0.04	9.4E-03	0.21	0.04	3.6E-08	0.00	0.01	5.9E-01	0.16	-0.09	No
rs6961048	G	0.22	0.07	2.4E-03	0.41	0.06	3.7E-11	0.01	0.02	3.9E-01	0.31	-0.20	No
rs6963105	A	-0.19	0.04	7.1E-06	-0.22	0.04	3.5E-09	-0.02	0.01	1.3E-01	-0.21	0.03	No
rs6990531	G	-0.35	0.05	2.6E-12	-0.19	0.04	1.8E-05	0.00	0.01	9.1E-01	-0.27	-0.16	No
rs7107356	A	-0.25	0.04	4.4E-09	-0.31	0.04	4.0E-17	-0.01	0.01	5.0E-01	-0.28	0.06	No
rs7116280	C	0.20	0.05	2.9E-05	0.24	0.04	7.7E-09	0.02	0.01	1.2E-01	0.22	-0.04	No
rs7121365	A	0.44	0.07	8.8E-12	0.20	0.06	4.4E-04	0.02	0.01	8.5E-02	0.32	0.24	Yes
rs71326977	A	-0.06	0.06	2.9E-01	-0.31	0.05	7.8E-10	-0.03	0.01	4.5E-03	-0.18	0.25	Yes
rs71508634	T	-0.26	0.05	4.0E-08	-0.06	0.04	1.4E-01	0.00	0.01	6.4E-01	-0.16	-0.20	No
rs71654213	T	-0.30	0.04	1.6E-11	-0.13	0.04	1.1E-03	0.02	0.01	3.8E-02	-0.21	-0.17	No
rs7223364	T	0.29	0.07	7.1E-06	0.37	0.06	7.3E-11	0.01	0.01	3.2E-01	0.33	-0.08	No
rs72654647	A	0.33	0.05	5.7E-11	0.20	0.04	3.3E-06	0.03	0.01	1.6E-02	0.27	0.12	No
rs72677850	A	-1.22	0.16	5.1E-14	-0.80	0.14	9.8E-09	-0.07	0.04	7.3E-02	-1.01	-0.41	Yes
rs72792829	T	-0.21	0.05	6.4E-05	-0.27	0.05	3.8E-09	-0.01	0.01	2.1E-01	-0.24	0.06	No
rs72811742	T	-0.07	0.04	1.3E-01	-0.22	0.04	2.0E-08	-0.01	0.01	2.8E-01	-0.14	0.15	No
rs72831343	G	-0.55	0.06	1.1E-19	-0.61	0.05	3.6E-31	-0.02	0.02	2.8E-01	-0.58	0.06	No
rs72844588	A	0.21	0.06	5.0E-04	0.29	0.05	1.8E-08	0.01	0.02	3.2E-01	0.25	-0.09	No
rs72854462	G	0.29	0.05	7.2E-09	0.25	0.04	1.0E-08	-0.03	0.01	2.6E-02	0.27	0.04	No
rs72936986	C	-0.24	0.05	4.3E-07	-0.25	0.04	2.0E-09	0.01	0.01	5.3E-01	-0.25	0.01	No
rs72976751	T	0.36	0.06	7.1E-09	0.29	0.05	8.6E-08	0.01	0.01	5.3E-01	0.32	0.07	No

rs7302981	A	0.37	0.04	3.2E-17	0.30	0.04	1.5E-14	0.00	0.01	9.8E-01	0.34	0.08	No
rs73030267	C	-0.26	0.09	2.8E-03	-0.47	0.08	3.1E-10	-0.02	0.02	1.4E-01	-0.37	0.21	Yes
rs73033340	G	-0.58	0.12	2.1E-06	-0.82	0.11	1.4E-14	0.01	0.03	7.6E-01	-0.70	0.24	Yes
rs73046792	A	-0.35	0.06	1.1E-09	-0.33	0.05	3.0E-11	-0.02	0.02	3.2E-01	-0.34	-0.02	No
rs7306710	T	-0.07	0.04	1.3E-01	-0.22	0.04	8.4E-09	-0.02	0.01	3.0E-02	-0.14	0.15	No
rs73075659	G	-0.41	0.05	1.1E-19	-0.30	0.04	4.6E-14	-0.01	0.01	5.6E-01	-0.35	-0.11	No
rs7310615	C	0.52	0.04	9.8E-33	0.53	0.04	1.5E-45	0.06	0.01	1.7E-09	0.52	-0.02	No
rs73234219	T	0.24	0.04	2.4E-08	0.07	0.04	7.9E-02	-0.01	0.01	1.7E-01	0.16	0.18	No
rs73306860	A	0.60	0.07	4.7E-18	0.61	0.06	1.2E-23	0.04	0.02	4.7E-03	0.60	0.00	No
rs7340705	C	0.19	0.05	3.7E-05	0.24	0.04	1.4E-09	0.01	0.01	5.6E-01	0.22	-0.05	No
rs74233809	C	-0.77	0.08	4.5E-22	-0.56	0.07	1.4E-15	-0.07	0.01	4.1E-07	-0.67	-0.21	Yes
rs743509	C	0.09	0.05	5.8E-02	0.23	0.04	1.2E-08	0.00	0.01	8.1E-01	0.16	-0.14	No
rs7463212	T	0.17	0.04	1.1E-04	0.29	0.04	4.1E-15	0.00	0.01	6.1E-01	0.23	-0.13	No
rs74661587	G	0.53	0.06	1.1E-16	0.25	0.06	4.2E-06	0.02	0.01	1.8E-01	0.39	0.27	Yes
rs747423	T	0.27	0.05	2.4E-08	0.18	0.04	4.6E-05	0.01	0.01	6.0E-01	0.22	0.10	No
rs7484151	A	-0.34	0.06	3.4E-08	-0.34	0.05	2.2E-10	0.03	0.01	3.8E-02	-0.34	0.00	No
rs748676	A	0.54	0.08	3.3E-11	0.19	0.07	7.6E-03	0.01	0.01	5.9E-01	0.37	0.35	Yes
rs751984	C	-0.44	0.07	4.9E-11	-0.48	0.06	4.0E-16	-0.02	0.01	9.9E-02	-0.46	0.04	No
rs76452347	T	-0.25	0.06	6.9E-06	-0.30	0.05	3.7E-10	0.01	0.01	6.6E-01	-0.27	0.05	No
rs7675258	G	0.11	0.04	9.2E-03	0.22	0.04	4.3E-09	0.01	0.01	2.2E-01	0.17	-0.11	No
rs7763581	G	-0.08	0.04	6.5E-02	-0.22	0.04	6.2E-09	0.01	0.01	2.6E-01	-0.15	0.14	No
rs778124	A	0.06	0.04	1.6E-01	0.23	0.04	2.0E-09	0.02	0.01	1.7E-02	0.15	-0.17	No
rs77924615	A	-0.35	0.05	1.9E-10	-0.45	0.05	1.7E-21	0.00	0.01	7.0E-01	-0.40	0.11	No
rs7810386	A	0.14	0.04	1.3E-03	0.26	0.04	1.3E-11	0.02	0.01	1.2E-02	0.20	-0.12	No
rs78203196	C	-0.30	0.07	1.1E-05	-0.37	0.06	4.0E-10	0.01	0.01	5.0E-01	-0.33	0.07	No
rs7831859	C	-0.21	0.04	1.6E-06	-0.21	0.04	3.6E-08	-0.01	0.01	5.4E-01	-0.21	0.00	No
rs7838131	G	0.30	0.04	3.7E-12	0.34	0.04	1.9E-19	-0.01	0.01	6.1E-01	0.32	-0.04	No
rs7845053	A	-0.26	0.04	5.4E-09	-0.01	0.04	7.0E-01	0.01	0.01	3.1E-01	-0.14	-0.24	Yes
rs79023617	T	-0.11	0.04	1.3E-02	-0.33	0.04	1.5E-17	0.00	0.01	8.5E-01	-0.22	0.22	Yes
rs7911644	T	0.23	0.05	5.8E-07	0.33	0.04	1.2E-16	0.01	0.01	1.8E-01	0.28	-0.10	No
rs7938856	C	0.09	0.05	5.9E-02	0.23	0.04	2.9E-08	-0.01	0.01	3.9E-01	0.16	-0.14	No
rs79780963	T	-0.77	0.08	1.5E-21	-0.59	0.07	7.4E-17	-0.08	0.01	7.5E-08	-0.68	-0.18	No
rs7989142	G	0.18	0.05	2.9E-04	0.32	0.04	2.3E-13	0.01	0.01	5.8E-01	0.25	-0.14	No
rs79997166	C	0.54	0.09	2.6E-09	0.12	0.08	1.3E-01	0.01	0.03	6.6E-01	0.33	0.42	Yes
rs8044992	C	-0.29	0.05	1.9E-09	-0.16	0.04	6.7E-05	-0.01	0.01	2.3E-01	-0.22	-0.12	No
rs8059962	T	-0.18	0.04	4.1E-05	-0.21	0.04	1.8E-08	0.00	0.01	9.5E-01	-0.20	0.04	No
rs8070460	C	-0.27	0.04	4.9E-10	-0.11	0.04	2.4E-03	-0.04	0.01	2.1E-05	-0.19	-0.15	No
rs8112983	T	-0.13	0.04	3.1E-03	-0.20	0.04	5.0E-08	0.00	0.01	7.4E-01	-0.17	0.08	No
rs897264	T	0.00	0.05	9.4E-01	-0.27	0.05	1.1E-09	-0.01	0.01	5.9E-01	-0.14	0.28	Yes
rs9314268	C	0.14	0.05	4.0E-03	0.25	0.04	8.9E-09	-0.01	0.01	5.5E-01	0.20	-0.11	No
rs9375463	C	0.33	0.04	1.9E-14	0.48	0.04	1.4E-37	0.01	0.01	4.6E-01	0.41	-0.15	No
rs9394951	C	0.22	0.04	2.7E-07	0.21	0.04	4.5E-08	0.01	0.01	1.6E-01	0.21	0.02	No
rs9482120	C	-0.14	0.04	1.2E-03	-0.25	0.04	7.9E-11	0.00	0.01	6.1E-01	-0.20	0.11	No
rs966791	T	-0.12	0.04	5.8E-03	-0.27	0.04	3.9E-13	-0.01	0.01	3.2E-01	-0.20	0.15	No
rs9719973	A	0.33	0.04	8.7E-14	0.16	0.04	3.6E-05	0.01	0.01	2.4E-01	0.24	0.17	No
rs990902	C	-0.10	0.04	2.4E-02	-0.21	0.04	2.4E-08	-0.01	0.01	3.8E-01	-0.16	0.11	No
rs9927137	G	0.19	0.04	1.2E-05	0.24	0.04	1.1E-10	0.00	0.01	9.8E-01	0.22	-0.05	No

Table S5. Instruments and genetic association estimates for Model 2 of the multivariable Mendelian randomization analysis. GX: genetic association estimate with MAP ≤55 years (mmHg); GY: genetic association estimate with coronary artery disease (log odds ratio); GZ: genetic association estimates with MAP >55 years (mmHg); SE: standard error; SNP: single-nucleotide polymorphism.

SNP	Effect Allele	GX	GX_SE	GX_P	GZ	GZ_SE	GZ_P	GY	GY_SE	GY_P
rs1000423	C	-0.455	0.115	7.76E-05	-0.228	0.100	2.28E-02	-0.016	0.034	6.45E-01
rs1010064	C	-0.501	0.083	1.65E-09	-0.632	0.072	2.18E-18	-0.017	0.024	4.91E-01
rs10119435	A	0.267	0.059	5.28E-06	0.309	0.051	1.38E-09	0.010	0.017	5.76E-01
rs10158537	G	-0.425	0.059	6.66E-13	-0.443	0.052	9.88E-18	0.024	0.017	1.61E-01
rs10226118	C	-0.824	0.109	4.53E-14	-0.496	0.096	2.20E-07	-0.001	0.032	9.74E-01
rs10248237	A	-0.819	0.110	8.92E-14	-0.531	0.096	3.58E-08	0.001	0.032	9.87E-01
rs10265221	C	0.122	0.059	3.74E-02	0.239	0.051	2.89E-06	-0.021	0.017	2.13E-01
rs10409243	C	-0.531	0.067	2.44E-15	-0.368	0.058	2.51E-10	-0.038	0.020	5.27E-02
rs10468291	C	0.193	0.071	6.23E-03	0.269	0.061	1.17E-05	-0.003	0.021	8.77E-01
rs10777213	G	0.149	0.062	1.68E-02	0.325	0.054	2.55E-09	0.015	0.018	4.18E-01
rs10852034	T	-0.523	0.064	4.62E-16	-0.459	0.056	1.68E-16	-0.014	0.019	4.58E-01
rs10858071	A	0.124	0.061	4.21E-02	0.222	0.053	2.46E-05	-0.049	0.018	5.98E-03
rs10876531	C	0.030	0.060	6.16E-01	0.194	0.052	1.89E-04	-0.021	0.017	2.22E-01
rs10900127	C	0.098	0.062	1.13E-01	0.229	0.054	2.24E-05	0.007	0.018	6.91E-01
rs10993958	A	0.301	0.060	6.63E-07	0.519	0.053	5.25E-23	0.034	0.018	5.67E-02
rs10995307	T	-0.385	0.093	3.19E-05	-0.407	0.080	4.17E-07	-0.036	0.027	1.91E-01
rs11070245	T	-0.322	0.072	9.05E-06	-0.387	0.063	8.80E-10	-0.024	0.021	2.69E-01
rs11072508	C	0.077	0.067	2.45E-01	0.272	0.058	2.41E-06	-0.003	0.019	8.73E-01
rs1114348	A	-0.598	0.066	1.53E-19	-0.616	0.057	7.98E-27	-0.057	0.020	3.79E-03
rs11187838	A	-0.138	0.066	3.60E-02	-0.336	0.057	3.36E-09	-0.039	0.019	4.53E-02
rs113044050	T	0.178	0.065	6.41E-03	0.183	0.057	1.29E-03	0.011	0.019	5.78E-01
rs113230003	A	0.374	0.089	2.54E-05	0.281	0.078	3.14E-04	0.075	0.026	3.34E-03
rs1133400	G	0.386	0.076	3.65E-07	0.393	0.066	2.30E-09	0.045	0.022	3.99E-02
rs113458760	G	0.340	0.062	4.76E-08	0.190	0.054	4.28E-04	0.009	0.018	6.11E-01
rs113695818	T	-0.235	0.065	2.91E-04	-0.198	0.056	4.19E-04	-0.034	0.019	7.68E-02
rs115262049	T	0.263	0.067	9.75E-05	0.291	0.059	6.50E-07	0.006	0.020	7.55E-01
rs11642015	T	0.411	0.115	3.36E-04	0.452	0.101	6.97E-06	0.075	0.033	2.31E-02
rs11669915	G	-0.043	0.153	7.76E-01	0.521	0.134	9.88E-05	0.043	0.044	3.35E-01
rs11676040	C	-0.287	0.059	9.57E-07	-0.304	0.051	2.48E-09	0.014	0.017	4.27E-01
rs11749673	G	-0.363	0.084	1.50E-05	-0.364	0.073	5.16E-07	-0.026	0.025	2.95E-01
rs1175651	T	-0.106	0.059	7.22E-02	-0.208	0.051	5.03E-05	0.002	0.017	8.91E-01
rs11760498	A	-0.547	0.078	2.20E-12	-0.585	0.068	8.85E-18	0.024	0.023	3.00E-01
rs11774829	A	0.337	0.059	9.76E-09	0.122	0.051	1.70E-02	0.005	0.017	7.51E-01
rs11821781	G	0.497	0.059	4.94E-17	0.466	0.051	1.22E-19	0.088	0.017	3.13E-07
rs11915142	A	-0.318	0.071	7.76E-06	-0.165	0.062	7.39E-03	-0.038	0.021	6.76E-02
rs12057453	T	-0.255	0.060	2.35E-05	-0.439	0.052	4.83E-17	0.020	0.018	2.60E-01
rs12137438	C	-0.155	0.060	1.04E-02	-0.316	0.053	2.31E-09	0.007	0.018	7.10E-01
rs12194642	A	-0.097	0.064	1.27E-01	-0.338	0.055	1.02E-09	-0.012	0.019	5.31E-01
rs12216886	G	-0.244	0.076	1.43E-03	-0.319	0.066	1.26E-06	0.002	0.022	9.11E-01
rs12258967	G	-0.411	0.062	3.26E-11	-0.385	0.054	8.87E-13	-0.017	0.018	3.60E-01
rs1229984	T	0.429	0.202	3.32E-02	0.936	0.178	1.44E-07	-0.028	0.060	6.43E-01
rs12567136	T	0.417	0.061	5.55E-12	0.307	0.053	6.60E-09	-0.012	0.018	4.85E-01
rs12627514	G	-0.159	0.065	1.41E-02	-0.244	0.057	1.57E-05	-0.015	0.019	4.46E-01
rs12643599	G	-0.220	0.061	3.30E-04	-0.279	0.053	1.64E-07	0.000	0.018	9.92E-01
rs12656497	T	0.216	0.069	1.78E-03	0.339	0.060	1.67E-08	-0.018	0.020	3.77E-01
rs12693302	G	0.133	0.070	5.55E-02	0.239	0.060	7.65E-05	0.010	0.020	6.16E-01
rs1275978	C	0.280	0.065	1.87E-05	0.120	0.057	3.56E-02	0.026	0.019	1.77E-01
rs12978472	G	0.539	0.112	1.44E-06	0.191	0.097	4.92E-02	0.019	0.033	5.57E-01
rs12983032	A	-0.272	0.085	1.39E-03	-0.368	0.074	6.00E-07	-0.041	0.025	1.06E-01
rs13107325	T	-1.000	0.222	6.50E-06	-0.939	0.190	7.83E-07	-0.063	0.066	3.44E-01
rs13121442	T	0.251	0.073	5.84E-04	0.101	0.064	1.12E-01	0.004	0.021	8.69E-01
rs13125101	A	-0.007	0.059	9.08E-01	0.186	0.052	3.25E-04	-0.013	0.017	4.47E-01
rs13227860	A	0.472	0.064	1.05E-13	0.483	0.055	1.13E-18	0.072	0.018	8.38E-05
rs13324341	T	-0.141	0.060	1.79E-02	-0.198	0.052	1.36E-04	-0.019	0.017	2.85E-01
rs1436049	G	-0.212	0.059	3.26E-04	-0.209	0.051	4.61E-05	-0.036	0.017	3.88E-02

rs1436138	G	0.333	0.059	1.44E-08	0.242	0.051	2.13E-06	0.017	0.017	3.13E-01
rs1472467	G	0.174	0.062	5.21E-03	0.298	0.054	4.25E-08	0.037	0.018	4.10E-02
rs1487629	A	0.523	0.063	1.00E-16	0.232	0.055	2.06E-05	0.019	0.018	2.98E-01
rs1492027	G	0.231	0.059	8.78E-05	0.261	0.051	3.57E-07	0.009	0.017	5.91E-01
rs150857355	C	0.179	0.103	8.39E-02	0.426	0.090	2.27E-06	-0.016	0.030	6.00E-01
rs1544861	T	-0.471	0.085	2.62E-08	-0.263	0.074	3.62E-04	-0.022	0.025	3.80E-01
rs164101	G	-0.189	0.060	1.58E-03	-0.207	0.052	6.88E-05	-0.014	0.018	4.33E-01
rs1687318	T	-0.421	0.074	1.33E-08	-0.481	0.065	8.71E-14	-0.010	0.022	6.62E-01
rs16895971	C	-0.339	0.065	1.83E-07	-0.167	0.056	3.07E-03	0.012	0.019	5.33E-01
rs17249754	A	0.212	0.059	3.35E-04	0.312	0.051	1.12E-09	0.015	0.017	3.71E-01
rs17257695	G	0.080	0.060	1.80E-01	0.168	0.052	1.13E-03	-0.012	0.017	4.91E-01
rs17517959	C	0.311	0.060	2.15E-07	0.061	0.052	2.42E-01	0.020	0.017	2.63E-01
rs17637472	A	-0.100	0.067	1.36E-01	-0.252	0.058	1.43E-05	-0.001	0.020	9.54E-01
rs17717829	C	-0.246	0.060	3.78E-05	-0.182	0.052	4.64E-04	0.000	0.017	9.85E-01
rs17762	A	-0.125	0.061	4.10E-02	-0.276	0.053	2.33E-07	-0.048	0.018	8.72E-03
rs1801253	G	0.342	0.067	3.63E-07	0.130	0.059	2.76E-02	0.032	0.020	9.84E-02
rs187680068	G	-0.214	0.062	5.06E-04	-0.199	0.054	1.96E-04	-0.011	0.018	5.40E-01
rs1896326	A	-0.190	0.059	1.33E-03	-0.244	0.052	2.29E-06	-0.007	0.017	6.79E-01
rs1958603	A	0.262	0.090	3.43E-03	0.334	0.078	1.96E-05	0.007	0.026	8.00E-01
rs2014590	T	0.391	0.060	5.19E-11	0.324	0.052	3.99E-10	0.007	0.017	7.00E-01
rs2032451	T	0.236	0.060	8.73E-05	0.169	0.053	1.26E-03	0.033	0.018	6.05E-02
rs2050905	G	-0.155	0.066	1.96E-02	-0.304	0.058	1.46E-07	-0.015	0.020	4.32E-01
rs2067832	G	-0.287	0.059	1.16E-06	-0.158	0.051	2.06E-03	-0.016	0.017	3.42E-01
rs2071265	C	0.376	0.064	5.69E-09	0.139	0.056	1.28E-02	-0.003	0.019	8.68E-01
rs2073641	A	-0.097	0.074	1.88E-01	-0.263	0.064	3.80E-05	-0.008	0.021	6.99E-01
rs2087319	A	-0.230	0.062	1.99E-04	-0.189	0.054	4.33E-04	0.008	0.018	6.68E-01
rs2165301	C	-0.662	0.089	7.35E-14	-0.675	0.076	7.51E-19	0.009	0.026	7.38E-01
rs2178270	C	0.165	0.061	6.80E-03	0.212	0.053	5.82E-05	0.002	0.018	9.02E-01
rs2242338	C	-0.291	0.067	1.61E-05	-0.216	0.058	2.22E-04	-0.042	0.020	3.28E-02
rs2294239	G	0.221	0.063	4.20E-04	0.254	0.054	2.95E-06	0.018	0.018	3.17E-01
rs2301597	T	0.250	0.060	3.17E-05	0.259	0.052	6.92E-07	-0.023	0.018	1.89E-01
rs2306363	T	0.329	0.067	1.01E-06	0.200	0.059	6.45E-04	0.053	0.019	6.90E-03
rs2311411	A	-0.140	0.059	1.77E-02	-0.215	0.051	2.67E-05	-0.010	0.017	5.48E-01
rs2478531	C	-0.383	0.079	1.25E-06	-0.314	0.069	4.95E-06	0.000	0.023	9.95E-01
rs2478981	T	0.328	0.086	1.32E-04	0.406	0.074	4.64E-08	0.023	0.025	3.49E-01
rs2493296	T	0.177	0.060	3.37E-03	0.278	0.053	1.29E-07	0.005	0.018	7.94E-01
rs2521501	T	0.259	0.072	3.28E-04	0.287	0.063	4.70E-06	0.023	0.021	2.68E-01
rs2627308	A	-0.337	0.068	6.47E-07	-0.461	0.059	5.60E-15	0.004	0.020	8.32E-01
rs262986	A	1.266	0.201	3.30E-10	0.520	0.178	3.41E-03	0.086	0.059	1.45E-01
rs2644128	C	0.298	0.069	1.63E-05	0.322	0.060	1.01E-07	0.047	0.020	1.94E-02
rs268263	T	-0.599	0.080	5.24E-14	-0.670	0.069	3.03E-22	-0.018	0.023	4.46E-01
rs2760061	A	0.234	0.060	9.21E-05	0.113	0.052	3.00E-02	0.017	0.017	3.40E-01
rs2823139	A	-0.293	0.059	6.54E-07	-0.206	0.051	6.28E-05	-0.001	0.017	9.61E-01
rs28416181	G	0.147	0.061	1.55E-02	0.259	0.053	9.01E-07	0.009	0.018	5.99E-01
rs28572357	C	0.180	0.059	2.46E-03	0.308	0.052	2.51E-09	-0.017	0.017	3.18E-01
rs286749	T	0.358	0.060	2.31E-09	0.164	0.052	1.60E-03	0.027	0.017	1.24E-01
rs28866311	G	0.250	0.064	9.41E-05	0.289	0.056	1.98E-07	-0.053	0.019	4.95E-03
rs2947411	A	-0.158	0.081	5.10E-02	-0.349	0.070	6.71E-07	0.033	0.023	1.63E-01
rs311443	G	0.321	0.068	2.69E-06	0.262	0.059	1.01E-05	-0.009	0.020	6.53E-01
rs3118905	A	-0.109	0.066	1.00E-01	-0.224	0.058	1.03E-04	-0.001	0.019	9.45E-01
rs3218036	A	-0.318	0.061	1.67E-07	-0.178	0.053	8.00E-04	0.018	0.018	3.03E-01
rs34148132	T	-0.001	0.061	9.93E-01	0.187	0.053	4.14E-04	0.006	0.018	7.46E-01
rs34394882	T	-0.280	0.069	4.31E-05	-0.164	0.059	5.47E-03	-0.030	0.020	1.32E-01
rs351365	T	0.370	0.059	3.23E-10	0.328	0.051	1.60E-10	0.008	0.017	6.52E-01
rs35444	G	0.140	0.059	1.84E-02	0.264	0.051	2.76E-07	0.029	0.017	9.42E-02
rs35681682	C	-0.439	0.085	2.16E-07	-0.216	0.074	3.42E-03	-0.047	0.025	6.20E-02
rs35942721	T	0.745	0.095	3.25E-15	0.625	0.083	3.71E-14	0.054	0.027	4.61E-02
rs3746038	T	0.184	0.062	2.89E-03	0.321	0.054	2.35E-09	0.040	0.018	2.73E-02
rs3764769	T	0.023	0.062	7.11E-01	0.223	0.054	4.05E-05	0.033	0.018	6.63E-02
rs3803266	G	-0.080	0.078	3.09E-01	-0.279	0.068	4.09E-05	-0.029	0.023	2.10E-01
rs3821843	G	0.362	0.065	2.80E-08	0.229	0.057	5.11E-05	0.020	0.019	2.84E-01
rs389883	G	-0.282	0.059	2.07E-06	-0.245	0.052	2.41E-06	-0.017	0.017	3.19E-01
rs3918226	T	-0.400	0.077	2.44E-07	-0.169	0.067	1.18E-02	0.031	0.022	1.70E-01

rs3936510	T	-0.028	0.061	6.52E-01	-0.205	0.053	1.15E-04	-0.003	0.018	8.72E-01
rs4076877	T	-0.081	0.060	1.75E-01	-0.204	0.052	8.36E-05	-0.045	0.017	1.02E-02
rs4147111	C	-0.100	0.058	8.80E-02	-0.268	0.051	1.41E-07	-0.007	0.017	6.65E-01
rs4362428	A	0.123	0.064	5.46E-02	0.353	0.056	2.35E-10	0.018	0.019	3.49E-01
rs4428270	C	0.250	0.082	2.16E-03	0.334	0.071	2.75E-06	0.014	0.024	5.61E-01
rs4473575	G	0.362	0.068	1.02E-07	0.291	0.059	8.27E-07	-0.023	0.020	2.45E-01
rs4588930	A	-0.251	0.066	1.30E-04	-0.245	0.057	1.65E-05	-0.014	0.019	4.70E-01
rs4712656	C	0.429	0.124	5.28E-04	0.128	0.107	2.31E-01	0.020	0.036	5.66E-01
rs483071	C	-0.454	0.069	3.86E-11	-0.263	0.060	1.15E-05	-0.028	0.020	1.70E-01
rs4873492	T	-0.110	0.064	8.67E-02	-0.276	0.056	8.15E-07	-0.028	0.019	1.37E-01
rs488834	C	0.328	0.061	9.75E-08	0.181	0.053	7.32E-04	0.019	0.018	2.82E-01
rs4899396	T	-0.444	0.081	4.77E-08	-0.057	0.071	4.27E-01	-0.007	0.024	7.63E-01
rs4923914	T	-0.217	0.093	1.91E-02	-0.360	0.080	7.70E-06	-0.027	0.027	3.24E-01
rs507666	A	0.452	0.060	7.43E-14	0.520	0.052	3.69E-23	0.016	0.018	3.63E-01
rs5418	G	-0.236	0.071	9.04E-04	-0.206	0.062	8.84E-04	-0.014	0.021	4.92E-01
rs55646464	T	-0.405	0.105	1.13E-04	-0.485	0.090	6.50E-08	0.024	0.030	4.28E-01
rs55733296	A	-0.126	0.067	6.08E-02	-0.378	0.058	6.87E-11	-0.022	0.020	2.69E-01
rs56179563	A	-0.286	0.059	1.58E-06	-0.190	0.052	2.60E-04	-0.020	0.018	2.53E-01
rs56313611	T	0.187	0.060	1.94E-03	0.250	0.052	1.85E-06	0.012	0.018	4.92E-01
rs56352102	T	-0.153	0.070	2.89E-02	-0.265	0.061	1.32E-05	-0.048	0.021	2.08E-02
rs569550	G	0.148	0.080	6.40E-02	0.269	0.069	1.06E-04	0.016	0.023	4.84E-01
rs57139556	G	-0.354	0.059	1.93E-09	-0.148	0.051	3.81E-03	-0.012	0.017	4.93E-01
rs57786342	A	0.062	0.071	3.78E-01	0.272	0.062	1.00E-05	0.025	0.021	2.26E-01
rs6031431	G	-0.429	0.114	1.77E-04	-0.413	0.099	3.15E-05	-0.003	0.034	9.17E-01
rs604723	T	-0.349	0.059	2.81E-09	-0.360	0.051	1.82E-12	0.003	0.017	8.65E-01
rs6108171	T	-0.160	0.059	6.65E-03	-0.241	0.051	2.74E-06	-0.011	0.017	5.26E-01
rs6108787	G	0.049	0.066	4.60E-01	0.208	0.057	2.69E-04	-0.033	0.019	8.55E-02
rs62036942	C	-0.291	0.064	5.72E-06	-0.170	0.056	2.40E-03	-0.059	0.019	1.98E-03
rs62390667	G	0.241	0.066	2.71E-04	0.288	0.058	5.55E-07	0.034	0.019	7.55E-02
rs62447769	A	-0.094	0.110	3.95E-01	-0.538	0.095	1.58E-08	-0.049	0.033	1.37E-01
rs6433891	G	-0.118	0.061	5.25E-02	-0.295	0.053	2.65E-08	-0.019	0.018	2.77E-01
rs6438857	C	-0.270	0.065	3.00E-05	-0.321	0.056	1.20E-08	0.006	0.019	7.60E-01
rs645040	G	-0.139	0.064	2.98E-02	-0.363	0.055	5.70E-11	-0.031	0.019	9.56E-02
rs6490019	A	0.225	0.063	3.70E-04	0.260	0.055	2.32E-06	0.007	0.018	7.02E-01
rs66682451	G	-0.050	0.068	4.62E-01	-0.267	0.059	6.67E-06	-0.003	0.020	8.96E-01
rs6697193	T	0.086	0.059	1.45E-01	0.187	0.051	2.67E-04	0.016	0.017	3.40E-01
rs6777317	A	0.799	0.065	7.11E-35	0.550	0.056	1.21E-22	0.063	0.019	8.00E-04
rs6798940	A	0.328	0.085	1.07E-04	0.335	0.074	5.23E-06	0.027	0.025	2.79E-01
rs6815273	A	-0.874	0.201	1.33E-05	-0.745	0.168	9.46E-06	-0.065	0.060	2.76E-01
rs6827655	G	-0.494	0.113	1.26E-05	-0.521	0.096	6.69E-08	0.004	0.033	8.95E-01
rs6928622	C	-0.107	0.060	7.50E-02	-0.275	0.052	1.27E-07	-0.017	0.017	3.30E-01
rs6961048	G	0.214	0.060	3.46E-04	0.172	0.052	9.72E-04	0.029	0.017	9.59E-02
rs6963105	A	0.090	0.066	1.69E-01	0.185	0.057	1.24E-03	0.014	0.019	4.57E-01
rs6990531	G	-0.321	0.059	4.88E-08	-0.158	0.051	2.01E-03	-0.025	0.017	1.42E-01
rs7107356	A	-0.272	0.061	9.15E-06	-0.360	0.053	1.05E-11	-0.040	0.018	2.45E-02
rs7116280	C	0.440	0.085	2.52E-07	0.365	0.074	9.21E-07	0.008	0.025	7.48E-01
rs7121365	A	0.205	0.060	6.25E-04	0.162	0.052	1.85E-03	0.010	0.017	5.53E-01
rs71326977	A	0.210	0.059	3.40E-04	0.279	0.051	4.76E-08	0.020	0.017	2.56E-01
rs71508634	T	0.296	0.060	7.60E-07	0.075	0.052	1.50E-01	0.027	0.017	1.14E-01
rs71654213	T	-0.220	0.077	4.35E-03	-0.258	0.066	9.94E-05	-0.041	0.023	7.20E-02
rs7223364	T	-0.111	0.078	1.51E-01	-0.188	0.068	5.50E-03	-0.003	0.023	9.08E-01
rs72654647	A	-0.093	0.059	1.14E-01	-0.276	0.051	7.47E-08	0.004	0.017	8.31E-01
rs72677850	A	0.470	0.087	5.49E-08	0.253	0.076	7.97E-04	0.013	0.025	6.00E-01
rs72792829	T	-0.096	0.068	1.54E-01	-0.224	0.059	1.38E-04	-0.039	0.020	4.95E-02
rs72811742	T	0.228	0.061	1.65E-04	0.294	0.053	2.24E-08	0.020	0.018	2.62E-01
rs72831343	G	-0.390	0.061	1.42E-10	-0.316	0.053	2.17E-09	-0.007	0.018	7.06E-01
rs72844588	A	-0.198	0.059	7.85E-04	-0.269	0.051	1.63E-07	-0.040	0.017	1.95E-02
rs72854462	G	-0.213	0.064	8.67E-04	-0.259	0.056	3.45E-06	-0.038	0.019	4.50E-02
rs72936986	C	-0.474	0.060	2.08E-15	-0.469	0.052	2.51E-19	0.000	0.017	9.77E-01
rs72976751	T	0.339	0.073	3.66E-06	0.116	0.064	6.86E-02	0.022	0.021	3.09E-01
rs7302981	A	0.005	0.071	9.48E-01	-0.197	0.062	1.40E-03	0.017	0.021	4.18E-01
rs73030267	C	-0.131	0.059	2.59E-02	-0.183	0.051	3.50E-04	0.008	0.017	6.30E-01
rs73033340	G	0.221	0.059	1.69E-04	0.294	0.051	8.22E-09	0.031	0.017	7.34E-02

rs73046792	A	0.278	0.061	4.48E-06	0.297	0.053	1.80E-08	0.030	0.018	8.61E-02
rs7306710	T	-0.150	0.060	1.26E-02	-0.300	0.052	1.07E-08	-0.012	0.018	5.10E-01
rs73075659	G	0.065	0.059	2.68E-01	0.191	0.051	1.92E-04	0.008	0.017	6.36E-01
rs7310615	C	0.374	0.059	2.55E-10	0.465	0.051	1.28E-19	-0.021	0.017	2.36E-01
rs73234219	T	-0.677	0.114	2.84E-09	-0.611	0.099	7.78E-10	-0.048	0.034	1.57E-01
rs73306860	A	-0.256	0.118	2.92E-02	-0.568	0.103	3.94E-08	-0.063	0.035	7.23E-02
rs7340705	C	0.207	0.059	4.49E-04	0.213	0.051	3.42E-05	-0.001	0.017	9.31E-01
rs74233809	C	0.475	0.082	6.53E-09	0.400	0.071	1.82E-08	-0.018	0.024	4.41E-01
rs743509	C	-0.339	0.063	5.83E-08	-0.247	0.055	5.92E-06	-0.023	0.018	2.15E-01
rs7463212	T	0.213	0.059	3.19E-04	0.250	0.051	1.15E-06	-0.008	0.017	6.30E-01
rs74661587	G	-0.610	0.168	2.77E-04	-0.803	0.146	4.02E-08	0.030	0.049	5.38E-01
rs747423	T	0.177	0.061	3.51E-03	0.267	0.053	3.87E-07	0.020	0.018	2.48E-01
rs7484151	A	0.331	0.130	1.12E-02	0.428	0.114	1.80E-04	0.030	0.038	4.31E-01
rs748676	A	-0.276	0.059	3.17E-06	-0.220	0.051	1.86E-05	0.009	0.017	6.00E-01
rs751984	C	-0.088	0.060	1.43E-01	-0.298	0.052	1.02E-08	0.004	0.017	8.04E-01
rs76452347	T	0.252	0.078	1.30E-03	0.255	0.068	1.71E-04	0.025	0.023	2.65E-01
rs7675258	G	-0.310	0.061	3.50E-07	-0.152	0.053	4.01E-03	-0.030	0.018	8.84E-02
rs7763581	G	0.270	0.060	6.59E-06	0.149	0.052	4.30E-03	0.034	0.017	5.16E-02
rs778124	A	0.616	0.109	1.68E-08	0.661	0.095	3.14E-12	0.078	0.031	1.16E-02
rs77924615	A	0.289	0.065	8.05E-06	0.304	0.056	6.95E-08	0.018	0.019	3.31E-01
rs7810386	A	-0.058	0.060	3.30E-01	-0.306	0.052	4.53E-09	-0.029	0.018	9.61E-02
rs78203196	C	0.215	0.064	8.09E-04	0.289	0.056	1.89E-07	0.040	0.019	3.37E-02
rs7831859	C	-0.245	0.114	3.13E-02	-0.717	0.097	1.58E-13	-0.008	0.033	8.08E-01
rs7838131	G	0.174	0.098	7.61E-02	0.422	0.085	7.48E-07	0.016	0.028	5.82E-01
rs7845053	A	0.887	0.174	3.30E-07	0.224	0.152	1.40E-01	0.069	0.050	1.67E-01
rs79023617	T	-0.275	0.069	6.58E-05	-0.211	0.060	4.23E-04	-0.022	0.020	2.73E-01
rs7911644	T	-0.229	0.059	1.15E-04	-0.206	0.052	6.94E-05	0.008	0.017	6.50E-01
rs7938856	C	-0.220	0.098	2.54E-02	-0.443	0.085	2.16E-07	-0.030	0.029	2.99E-01
rs79780963	T	-0.266	0.060	9.65E-06	0.033	0.052	5.31E-01	-0.025	0.018	1.57E-01
rs7989142	G	0.137	0.059	2.06E-02	0.289	0.051	1.60E-08	0.018	0.017	2.88E-01
rs79997166	C	-0.588	0.133	1.02E-05	-0.203	0.117	8.39E-02	0.012	0.039	7.65E-01
rs8044992	C	0.299	0.060	5.00E-07	0.311	0.052	1.91E-09	0.005	0.017	7.72E-01
rs8059962	T	-0.186	0.060	1.94E-03	-0.249	0.052	1.67E-06	-0.029	0.018	1.01E-01
rs8070460	C	0.090	0.069	1.93E-01	0.286	0.060	1.86E-06	-0.011	0.020	5.79E-01
rs8112983	T	-0.303	0.068	7.78E-06	-0.239	0.059	5.37E-05	-0.014	0.020	4.95E-01
rs897264	T	0.263	0.079	8.75E-04	0.339	0.068	7.07E-07	0.001	0.023	9.54E-01
rs9314268	C	-0.143	0.076	5.84E-02	-0.211	0.065	1.26E-03	-0.022	0.022	3.19E-01
rs9375463	C	0.784	0.173	5.97E-06	0.705	0.150	2.70E-06	0.050	0.050	3.14E-01
rs9394951	C	-0.284	0.059	1.64E-06	-0.055	0.052	2.88E-01	0.005	0.017	7.64E-01
rs9482120	C	-0.138	0.059	1.98E-02	-0.149	0.052	4.00E-03	-0.002	0.017	9.26E-01
rs966791	T	-0.111	0.076	1.41E-01	-0.166	0.066	1.15E-02	0.011	0.022	6.04E-01
rs9719973	A	-0.624	0.111	1.80E-08	-0.403	0.097	2.94E-05	-0.071	0.033	3.19E-02
rs990902	C	-0.280	0.064	1.12E-05	-0.112	0.055	4.40E-02	-0.011	0.019	5.62E-01
rs9927137	G	-0.140	0.076	6.33E-02	-0.370	0.065	1.55E-08	0.009	0.022	6.75E-01