

---

## Supplementary information

---

# The power of genetic diversity in genome-wide association studies of lipids

---

In the format provided by the  
authors and unedited

# **Supplementary Information for “The power of genetic diversity in genome-wide association studies of lipids”**

Sarah Graham *et al.* for the Global Lipids Genetics Consortium 2021

## **Contents**

|                                                                                                                                                 |    |
|-------------------------------------------------------------------------------------------------------------------------------------------------|----|
| Supplementary Acknowledgements by Cohort: .....                                                                                                 | 3  |
| Consortium Authors: VA Million Veteran Program .....                                                                                            | 30 |
| Consortium Authors: Global Lipids Genetics Consortium .....                                                                                     | 38 |
| List of Supplementary Tables.....                                                                                                               | 53 |
| Supplementary Table 2: Lambda GC values by minor allele frequency for ancestry-specific meta-analysis with RAREMETAL .....                      | 54 |
| Supplementary Table 4: Lambda GC values by minor allele frequency for multi-ancestry meta-analysis (as performed in MR-MEGA) .....              | 55 |
| Supplementary Table 8: Genetic correlation results calculated from bivariate GREML analysis in UK Biobank and the Million Veteran Program ..... | 56 |
| Supplementary Table 13: Number of individuals by ancestry group included in the GWAS used to generate each set of PRS weights.....              | 57 |
| Supplementary Table 21: Correlation of multi-ancestry polygenic score with principal components in 1KGP3 individuals.....                       | 58 |
| Supplementary Table 22: Correlation of mean LDL-C value with PCs in European and African American MGI participants .....                        | 59 |
| Supplementary Table 23: Prediction of LDL-C in MGI individuals based on varying numbers of PCs included in the model .....                      | 60 |
| List of Supplementary Figures.....                                                                                                              | 62 |
| Supplementary Figure 1: Ancestral diversity of contributing cohorts.....                                                                        | 63 |
| Supplementary Figure 2: QQ Plots from each single-ancestry meta-analysis.....                                                                   | 64 |
| Supplementary Figure 3: Effect sizes and allele frequencies of identified index variants from ancestry-specific meta-analysis .....             | 71 |
| Supplementary Figure 4: QQ plots from multi-ancestry meta-analysis .....                                                                        | 82 |
| Supplementary Figure 5: Comparison of association results for ancestry-specific and multi-ancestry analysis.....                                | 84 |
| Supplementary Figure 6: Effect sizes by ancestry for unique index variants from ancestry-specific meta-analysis.....                            | 85 |
| Supplementary Figure 7: Genetic impact correlation estimates between ancestries for each trait analyzed .....                                   | 89 |

|                                                                                                                                              |    |
|----------------------------------------------------------------------------------------------------------------------------------------------|----|
| Supplementary Figure 8: Genetic effect correlation estimates between ancestries for each trait analyzed .....                                | 90 |
| Supplementary Figure 9: Comparison of PRS source ancestry and sample size with prediction in European and African American individuals ..... | 91 |
| Supplementary Figure 10: Comparison of original and conditional effect sizes .....                                                           | 93 |
| Supplementary Notes .....                                                                                                                    | 94 |
| Supplementary Methods: Derivation of approximate Bayes factors .....                                                                         | 98 |

## **Supplementary Acknowledgements by Cohort:**

### Africa America Diabetes Mellitus

The authors would like to gratefully acknowledge the AADM collaborators, including Olufemi Fasanmade, Thomas Johnson, Johnnie Oli, Godfrey Okafor, Benjamin A. Eghan Jr., Kofi Agyenim-Boateng, Clement Adebamowo, Albert Amoah, Joseph Acheampong, and Duncan Ngare (deceased). This project was supported by the Intramural Research Program of the National Human Genome Research Institute of the National Institutes of Health (NIH) through the Center for Research on Genomics and Global Health (CRGGH). The CRGGH is also supported by the National Institute of Diabetes and Digestive and Kidney Diseases and the Office of the Director at the NIH (Z01HG200362). Support for participant recruitment and initial genetic studies of the AADM study was provided by NIH grant No. 3T37TW00041-03S2 from the Office of Research on Minority Health. This work utilized the computational resources of the NIH HPC Biowulf cluster. (<http://hpc.nih.gov>)

### Africa Wits-INDEPTH partnership for Genomic Studies

The AWI-Gen Collaborative Centre is funded by the National Human Genome Research Institute (NHGRI), Office of the Director (OD), Eunice Kennedy Shriver National Institute Of Child Health & Human Development (NICHD), the National Institute of Environmental Health Sciences (NIEHS), the Office of AIDS research (OAR) and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), of the National Institutes of Health (NIH) under award number U54HG006938 and its supplements, as part of the H3Africa Consortium. Additional funding came from the Department of Science and Technology, South Africa, award number DST/CON 0056/2014.

### Age-related diseases: Understanding Genetic and non-genetic influences - a study at the University of Regensburg

Cohort recruiting and management was funded by the Federal Ministry of Education and Research (BMBF-01ER1206, BMBF-01ER1507, to Iris M. Heid) and by the German Research Foundation (DFG HE 3690/7-1, to Iris M. Heid). Genome-wide genotyping and lipid concentrations phenotyping was funded by the University of Regensburg for the Department of Genetic Epidemiology. The computational work supervised by Iris M. Heid was funded by the German Research Foundation (DFG) – Project-ID 387509280 – SFB 1350 (to Iris M. Heid).

### Anglo-Scandinavian Cardiac Outcomes Trial

This work was funded by the National Institutes for Health Research (NIHR) as part of the portfolio of translational research of the NIHR Barts Biomedical Research Unit and the NIHR Biomedical Research Centre at Imperial College, the International Centre for Circulatory Health Charity and the Medical Research Council through G952010. We thank all ASCOT trial participants, physicians, nurses, and practices in the participating countries for their important contribution to the study. The study was investigator-led and was conducted, analyzed, and reported independently of Pfizer who funded the

trial. JR acknowledges support by the People Programme of the European Union's Seventh Framework Programme grant n° 608765 and Marie Skłodowska-Curie grant n° 786833.

#### Atherosclerosis Risk in Communities Study

The Atherosclerosis Risk in Communities study has been funded in whole or in part with Federal funds from the National Heart, Lung, and Blood Institute, National Institutes of Health, Department of Health and Human Services (contract numbers HHSN268201700001I, HHSN268201700002I, HHSN268201700003I, HHSN268201700004I and HHSN268201700005I), R01HL087641, R01HL059367 and R01HL086694; National Human Genome Research Institute contract U01HG004402; and National Institutes of Health contract HHSN268200625226C. The authors thank the staff and participants of the ARIC study for their important contributions. Infrastructure was partly supported by Grant Number UL1RR025005, a component of the National Institutes of Health and NIH Roadmap for Medical Research. Paul S. de Vries was supported by American Heart Association grant number 18CDA34110116.

#### Austrian Stroke Prevention Study/Austrian Stroke Prevention Family Study

The authors thank the staff and the participants for their valuable contributions. We thank Birgit Reinhart for her long-term administrative commitment, Elfi Hofer for the technical assistance at creating the DNA bank, Ing. Johann Semmler and Anita Harb for DNA sequencing and DNA analyses by TaqMan assays and Irmgard Poelzl for supervising the quality management processes after ISO9001 at the biobanking and DNA analyses.

The Medical University of Graz and the Steiermärkische Krankenanstaltengesellschaft support the databank of the ASPS/ASPS-Fam. The research reported in this article was funded by the Austrian Science Fund (FWF) grant numbers P1904, P20545-P05 and P13180 and supported by the Austrian National Bank Anniversary Fund, P15435 and the Austrian Ministry of Science under the aegis of the EU Joint Programme-Neurodegenerative Disease Research (JPND)-[www.jpnd.eu](http://www.jpnd.eu).

#### Avon Longitudinal Study of Parents and Children

NJT is a Wellcome Trust Investigator (202802/Z/16/Z), is the PI of the Avon Longitudinal Study of Parents and Children (MRC & WT 217065/Z/19/Z), is supported by the University of Bristol NIHR Biomedical Research Centre (BRC-1215-2001), the MRC Integrative Epidemiology Unit (MC\_UU\_00011) and works within the CRUK Integrative Cancer Epidemiology Programme (C18281/A19169). SH is supported by the UK National Institute for Health Research Academic Clinical Fellowship. REM is a member of programme 1 at the MRC Integrative Epidemiology Unit at the University of Bristol funded by the MRC (MC\_UU\_00011/1)

#### the Beijing Atherosclerosis Study

This work was supported by the CAMS Innovation Fund for Medical Sciences (grants 2019-I2M-2-003, 2016-I2M-1-009, 2017-I2M-1-004, and 2016-I2M-1-011).

#### BioBank Japan

We acknowledge the staff of the BBJ for their outstanding assistance. This research was supported by the Tailor-Made Medical Treatment Program (BBJ) of the Ministry of Education, Culture, Sports, Science and Technology (MEXT), the Japan Agency for Medical Research and Development (AMED) under grant number JP17km0305002.

#### British 1958 birth cohort

We acknowledge use of phenotype and genotype data from the British 1958 Birth Cohort DNA collection, funded by the Medical Research Council grant G0000934 and the Wellcome Trust grant 068545/Z/02. Genotyping for the B58C-WTCCC subset was funded by the Wellcome Trust grant 076113/B/04/Z. The B58C-T1DGC genotyping utilized resources provided by the Type 1 Diabetes Genetics Consortium, a collaborative clinical study sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Allergy and Infectious Diseases (NIAID), National Human Genome Research Institute (NHGRI), National Institute of Child Health and Human Development (NICHD), and Juvenile Diabetes Research Foundation International (JDRF) and supported by U01 DK062418. B58C-T1DGC GWAS data were deposited by the Diabetes and Inflammation Laboratory, Cambridge Institute for Medical Research (CIMR), University of Cambridge, which is funded by Juvenile Diabetes Research Foundation International, the Wellcome Trust and the National Institute for Health Research Cambridge Biomedical Research Centre; the CIMR is in receipt of a Wellcome Trust Strategic Award (079895). The B58C-GABRIEL genotyping was supported by a contract from the European Commission Framework Programme 6 (018996) and grants from the French Ministry of Research.

#### British Genetics of Hypertension Trial

This work was funded by the Medical Research Council of Great Britain (grant number: G9521010D). The BRIGHT study is extremely grateful to all the patients who participated in the study and the BRIGHT nursing team. This work forms part of the research themes contributing to the translational research portfolio for the NIHR Barts Cardiovascular Biomedical Research Unit. The funders had no role in study design, data collection and analysis.

#### CAGE-KING

The KING Study was supported in part by Grants-in-Aid from MEXT (nos. 24390169, 16H05250, 25293144, 15K19242, 16H06277, 19K19434, 20K10514) as well as by a grant from the Funding Program for Next-Generation World-Leading Researchers (NEXT Program, no. LS056)

## CARDIOGENICS

The main sponsor of Cardiogenics was the EU (LSHM-CT-2006-037593). This work was supported by the British Heart Foundation (BHF) grant RG/14/5/30893 (P.D.) and forms part of the research themes contributing to the translational research portfolios of the Barts Biomedical Research Centre funded by the UK National Institute for Health Research (NIHR)

## Cardiovascular Health Study

This CHS research was supported by NHLBI contracts HSN268201200036C, HHSN268200800007C, HHSN268201800001C, N01HC55222, N01HC85079, N01HC85080, N01HC85081, N01HC85082, N01HC85083, N01HC85086, 75N92021D00006; and NHLBI grants U01HL080295, R01HL087652, R01HL105756, R01HL103612, R01HL120393, R01HL085251, and U01HL130114 with additional contribution from the National Institute of Neurological Disorders and Stroke (NINDS). Additional support was provided through R01AG023629 from the National Institute on Aging (NIA). A full list of principal CHS investigators and institutions can be found at CHS-NHLBI.org. The provision of genotyping data was supported in part by the National Center for Advancing Translational Sciences, CTSI grant UL1TR001881, and the National Institute of Diabetes and Digestive and Kidney Disease Diabetes Research Center (DRC) grant DK063491 to the Southern California Diabetes Endocrinology Research Center. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

## the China Atherosclerosis Study

This work was supported by the National Key R&D Program of China (2018YFE0115300, 2017YFC0908401, 2017YFC0211703 and 2016YFC0206503) and the National Science Foundation of China (grants 81773537, 91857118, and 91439202).

## China Kadoorie Biobank

China Kadoorie Biobank particularly acknowledges the participants, project staff in Beijing and Oxford and at the 10 regional CKB centers, and the China National Centre for Disease Control and Prevention (CDC) and its regional offices for assisting with the fieldwork. The CKB baseline survey and first re-survey were supported by the Kadoorie Charitable Foundation, Hong Kong. Long-term follow-up and data collection were supported by the Wellcome Trust, UK (212946/Z/18/Z, 202922/Z/16/Z, 104085/Z/14/Z, 088158/Z/09/Z), the National Key Research and Development Program of China (2016YFC0900500, 2016YFC0900501, 2016YFC0900504, 2016YFC1303904) and the National Natural Science Foundation of China (91846303, 81941018, 91843302, 81390540). DNA extraction and genotyping was supported by GlaxoSmithKline and the UK Medical Research Council (MC-PC-13049, MC-PC-14135). The project is supported by core funding to the Clinical Trial Service Unit and Epidemiological Studies Unit at Oxford University from the UK Medical Research Council (MC\_UU\_00017/1, MC\_UU\_12026/2, MC\_U137686851), Cancer Research UK (C16077/A29186, C500/A16896) and the British Heart

Foundation (CH/1996001/9454). Dr Holmes is supported by a British Heart Foundation Intermediate Clinical Research Fellowship (FS/18/23/33512).

#### China Health and Nutrition Survey

This research uses data from China Health and Nutrition Survey (CHNS). We are grateful to research grant funding from the National Institute for Health (NIH), the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) for R01 HD30880, National Institute on Aging (NIA) for R01 AG065357, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) for R01DK104371 and R01HL108427, the NIH Fogarty grant D43 TW009077 since 1989, and the China-Japan Friendship Hospital, Ministry of Health for support for CHNS 2009, Chinese National Human Genome Center at Shanghai since 2009, and Beijing Municipal Center for Disease Prevention and Control since 2011. We thank the National Institute for Nutrition and Health, China Center for Disease Control and Prevention, Beijing Municipal Center for Disease Control and Prevention, and the Chinese National Human Genome Center at Shanghai. Additional support for data analysis was provided by US NIH R01DK072193.

#### Cleveland Family Study

The CFS was supported by the National Institutes of Health, the National Heart, Lung, Blood Institute grants HL113338, R35HL13588, HL46380. BEC is supported by the NHLBI grant K01HL135405.

#### Cebu Longitudinal Health and Nutrition Survey

The Cebu Longitudinal Health and Nutrition Survey (CLHNS) was supported by US National Institutes of Health grants DK078150, TW005596, HL085144; pilot funds from RR020649, ES010126, and DK056350; and the Office of Population Studies Foundation in Cebu. Additional support for data analysis was provided by US NIH R01DK072193. Cassandra N Spracklen was supported by American Heart Association Postdoctoral Fellowships 15POST24470131 and 17POST33650016.

#### CoLaus study

The CoLaus study was and is supported by research grants from GlaxoSmithKline, the Faculty of Biology and Medicine of Lausanne, and the Swiss National Science Foundation (grants 33CSGO-122661, 33CS30-139468, 33CS30-148401 and 33CS30\_177535/1).

#### Cooperative Health Research in South Tyrol

Full acknowledgements for the CHRIS study are reported at <http://translational-medicine.biomedcentral.com/articles/10.1186/s12967-015-0704-9#Declarations>. The CHRIS study was

funded by the Department of Innovation, Research, and University of the Autonomous Province of Bolzano-South Tyrol.

#### CROATIA-Via and CROATIA-Korcula

The CROATIA\_Vis and CROATIA\_Korcula studies were funded by grants from the Medical Research Council (UK), European Commission Framework 6 project EUROSPAN (Contract No. LSHG-CT-2006-018947) and Republic of Croatia Ministry of Science, Education and Sports research grants. (108-1080315-0302). We would like to acknowledge the staff of several institutions in Croatia that supported the field work, including but not limited to The University of Split and Zagreb Medical Schools, Institute for Anthropological Research in Zagreb and Croatian Institute for Public Health. CH and VV are supported by an MRC University Unit Programme Grant MC\_UU\_00007/10 (QTL in Health and Disease)

#### The Danish study of Functional Disorders

This study was supported by TrygFonden (7-11-0213), the Lundbeck Foundation (R155-2013-14070), Novo Nordisk Foundation (NNF15OC0015896).

#### Diabetes Genetics Initiative of Broad Institute of Harvard and MIT, Lund University, and Novartis Institutes of BioMedical Research

The Botnia (DGI) study have been supported by grants from Folkhälsan Research Foundation, Sigrid Juselius Foundation, Ministry of Education, Nordic Center of Excellence in Disease Genetics, Gyllenberg Foundation, Swedish Cultural Foundation in Finland, Finnish Diabetes Research Foundation, Foundation for Life and Health in Finland, Finnish Medical Society, Paavo Nurmi Foundation, Perklén Foundation, Ollqvist Foundation, Närpes Health Care Foundation, the Municipal Health Care Center and Hospital in Jakobstad, Health Care Centers in Vasa, Närpes and Korsholm. This work was also partially supported by NIH grant R01-DK075787 to JNH. The skillful assistance of the Botnia Study Group is gratefully acknowledged

#### DIACORE

Cohort recruiting and management was funded by the KfH Stiftung Präventivmedizin e.V. (Carsten A. Böger). Genome-wide genotyping was funded the Else Kröner-Fresenius-Stiftung (2012\_A147), the KfH Stiftung Präventivmedizin and the University Hospital Regensburg. The Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) supported this work – Project-ID 387509280 – SFB 1350 (Subproject C6 to I.M.H.) and Iris Heid and Carsten Böger received funding by DFG BO 3815/4-1.

#### East London Genes and Health

Genes & Health ([www.genesandhealth.org](http://www.genesandhealth.org)) is/has recently been core-funded by Wellcome (WT102627, WT210561), the Medical Research Council (UK) (M009017), Higher Education Funding Council for England Catalyst, Barts Charity (845/1796), Health Data Research UK (for London substantive site), and research delivery support from the NHS National Institute for Health Research Clinical Research Network (North Thames). We thank Social Action for Health, Centre of The Cell, members of our Community Advisory Group, and staff who have recruited and collected data from volunteers. We thank the NIHR National Biosample Centre (UK Biocentre), the Social Genetic & Developmental Psychiatry Centre (King's College London), Wellcome Sanger Institute, and Broad Institute for sample processing, genotyping, sequencing and variant annotation. Most of all we thank all of the volunteers participating in Genes & Health.

The Genes & Health Research Team (in alphabetical order by surname) is Shaheen Akhtar, Mohammad Anwar, Elena Arciero, Samina Ashraf, Gerome Breen, Raymond Chung, Charles J Curtis, Maharun Chowdhury, Grainne Colligan, Panos Deloukas, Ceri Durham, Sarah Finer, Chris Griffiths, Qin Qin Huang, Matt Hurles, Karen A Hunt, Shapna Hussain, Kamrul Islam, Ahsan Khan, Amara Khan, Cath Lavery, Sang Hyuck Lee, Robin Lerner, Daniel MacArthur, Bev MacLaughlin, Hilary Martin, Dan Mason, Shefa Miah, Bill Newman, Nishat Safa, Farah Tahmasebi, Richard C Trembath, Bhavi Trivedi, David A van Heel, John Wright

#### Electronic Medical Records and Genomics

eMERGE Network (Phase III): This phase of the eMERGE Network was initiated and funded by the NHGRI through the following grants: U01HG8657 (Group Health Cooperative/University of Washington); U01HG8685 (Brigham and Women's Hospital); U01HG8672 (Vanderbilt University Medical Center); U01HG8666 (Cincinnati Children's Hospital Medical Center); U01HG6379 (Mayo Clinic); U01HG8679 (Geisinger Clinic); U01HG8680 (Columbia University Health Sciences); U01HG8684 (Children's Hospital of Philadelphia); U01HG8673 (Northwestern University); U01HG8701 (Vanderbilt University Medical Center serving as the Coordinating Center); U01HG8676 (Partners Healthcare/Broad Institute); and U01HG8664 (Baylor College of Medicine). We would also like to acknowledge the following eMERGE members who contributed to the eMERGE data for this manuscript: D. Crosslin, J. Denny, I. Kullo, M. Palmer, and I. Stanaway.

#### European Investigation into Cancer and Nutrition, Potsdam study

The recruitment phase of the EPIC-Potsdam Study was supported by the Federal Ministry of Science, Germany (01 EA 9401) and the European Union (SOC 95201408 05F02). The follow-up of the EPIC-Potsdam Study was supported by German Cancer Aid (70-2488-Ha I) and the European Community (SOC 98200769 05F02). This work was supported by a grant from the German Ministry of Education and Research (BMBF) and the State of Brandenburg (DZD grant 82DZD00302).

### Family Heart Study

This work has been funded by the NIDDK grant R01-DK-089256, and the NHLBI grant R01HL117078

### Fenland Study

The Fenland Study (10.22025/2017.10.101.00001) is funded by the Medical Research Council (MC\_UU\_12015/1). We are grateful to all the volunteers and to the General Practitioners and practice staff for assistance with recruitment. We thank the Fenland Study Investigators, Fenland Study Co-ordination team and the Epidemiology Field, Data and Laboratory teams. We further acknowledge support for genomics from the Medical Research Council (MC\_PC\_13046).

### Finland-United States Investigation of NIDDM Genetics

Support for FUSION was provided by NIH grants R01-DK062370, R01-DK072193, and intramural project number 1Z01-HG000024. Genome-wide genotyping was conducted by the Johns Hopkins University Genetic Resources Core Facility SNP Center at the Center for Inherited Disease Research (CIDR), with support from CIDR NIH contract no. N01-HG-65403.

### Finnish Twin Cohort

Phenotype and genotype data collection in the twin cohort has been supported by the Wellcome Trust Sanger Institute, the Broad Institute, ENGAGE – European Network for Genetic and Genomic Epidemiology, FP7-HEALTH-F4-2007, grant agreement number 201413, National Institute of Alcohol Abuse and Alcoholism (grants AA-12502, AA-00145, and AA-09203 to Richard J Rose and AA15416 and K02AA018755 to Danielle M Dick) and the Academy of Finland (grants 100499, 205585, 118555, 141054, 264146, 308248, and 312073 to JKaprio). JKaprio acknowledges support by the Academy of Finland (grants 265240, 263278).

### FINRISK

FINRISK has been mainly funded from budgetary funds of the Finnish Institute for Health and Welfare. Additional funds have been obtained from domestic foundations. VS has been supported by the Finnish Foundation for Cardiovascular Research.

### Framingham Heart Study

This research was conducted in part using data and resources from the Framingham Heart Study of the National Heart Lung and Blood Institute of the National Institutes of Health and Boston University School of Medicine. The analyses reflect intellectual input and resource development from the Framingham Heart Study investigators participating in the SNP Health Association Resource (SHARe) project. This

work was partially supported by the National Heart, Lung and Blood Institute's Framingham Heart Study (Contract Nos. N01-HC-25195, HHSN268201500001I and 75N92019D00031) and its contract with Affymetrix, Inc for genotyping services (Contract No. N02-HL-6-4278).

#### Genetic Park of Cilento and Vallo di Diano Project

This work was supported by IDF SHARID grant from the Italian Ministry of Universities and Research

#### GENIE UK

Original genotype data was generated as part of the GENetics of Nephropathy an International Effort (GENIE) consortium through the Medical Research Council (MC\_PC\_15025) and the Public Health Agency R&D Division (STL/4760/13), Science Foundation Ireland (SFI15/US/B3130) and NIH R01\_DK081923 and R01\_DK105154. Science Foundation Ireland and the Department for the Economy, Northern Ireland US partnership award 15/IA/3152. The GENIE\_UK data includes samples recruited as part of the Warren3/U.K. GoKinD Study Group, jointly funded by Diabetes UK and the Juvenile Diabetes Research Foundation and includes the following individuals: Professor A.P. Maxwell, Prof A.J. McKnight, Dr. D.A. Savage (Belfast); Dr. J. Walker (Edinburgh); Dr. S. Thomas, Professor G.C. Viberti (London); Professor A.J.M. Boulton (Manchester); Professor S. Marshall (Newcastle); Professor A.G. Demaine and Dr. B.A. Millward (Plymouth); and Professor S.C. Bain (Swansea).

#### German Chronic Kidney Disease Study

The GCKD study is supported by the German Ministry of Education and Research (Bundesministerium für Bildung und Forschung, FKZ 01ER 0804, 01ER 0818, 01ER 0819, 01ER 0820, and 01ER 0821) and the KfH Foundation for Preventive Medicine (Kuratorium für Heimdialyse und Nierentransplantation e.V.–Stiftung Präventiv-medizin) and corporate sponsors ([www.gckd.org](http://www.gckd.org)). Furthermore, this study was partially funded by the H2020-IMI2 consortium BEAt-DKD (Biomarker Enterprise to Attack Diabetic Kidney Disease; grant number: 115974). Whole-genome SNP microarray genotyping in the GCKD study was supported by Bayer Pharma Aktiengesellschaft (AG).

#### Genetic Epidemiology Network of Arteriopathy

Support for the Genetic Epidemiology Network of Arteriopathy (GENOA) was provided by the National Heart, Lung and Blood Institute (HL054464, HL054457, HL054481, HL100185, and HL119443) of the National Institutes of Health. We would also like to thank the families that participated in the GENOA study.

### German MI Family Study

Funding was received from the German Federal Ministry of Education and Research (BMBF) in the context of the e:Med program (e:AtheroSysMed and sysINFLAME), the FP7 European Union project CVgenes@target (261123) and a grant from the Fondation Leducq (CADgenomics: Understanding Coronary Artery Disease Genes, 12CVD02).

### Gene-Lifestyle Interactions and Complex Traits Involved in Elevated Disease Risk-V2

European Research Council: CoG-2015\_681742\_NASCENT; Swedish Research Council; Novo Nordisk Foundation; European Diabetes Research Foundation; Swedish Heart Lung Foundation

### Generation Scotland

Generation Scotland received core support from the Chief Scientist Office of the Scottish Government Health Directorates [CZD/16/6] and the Scottish Funding Council [HR03006] and is currently supported by the Wellcome Trust [216767/Z/19/Z]. Genotyping of the GS:SFHS samples was carried out by the Genetics Core Laboratory at the Edinburgh Clinical Research Facility, University of Edinburgh, Scotland and was funded by the Medical Research Council UK and the Wellcome Trust (Wellcome Trust Strategic Award “STratifying Resilience and Depression Longitudinally” (STRADL) Reference 104036/Z/14/Z).

### Genetic Overlap between Metabolic and Psychiatric traits/TEENAGE

This research has been co-financed by the European Union (European Social Fund—ESF) and Greek national funds through the Operational Program “Education and Lifelong Learning” of the National Strategic Reference Framework (NSRF)—Research Funding Program: Heracleitus II. Investing in knowledge society through the European Social Fund. This work was funded by the Wellcome Trust (098051). We thank all study participants and their families as well as all volunteers for their contribution in this study. We thank the Sample Management and Genotyping Facilities staff at the Wellcome Trust Sanger Institute for sample preparation, quality control and genotyping. We are grateful to Georgia Markou, Laiko General Hospital Diabetes Centre, Maria Emetsidou and Panagiota Fotinopoulou, Hippokratio General Hospital Diabetes Centre, Athina Karabela, Dafni Psychiatric Hospital, Eirini Glezou and Marios Mangioros, Dromokaiteio Psychiatric Hospital, Angela Rentari, Harokopio University of Athens, and Danielle Walker, Wellcome Trust Sanger Institute.

### Genetic Regulation of Arterial Pressure In humans in the Community

NJS holds an NIHR Senior Investigator award.

#### Genomic Research Cohorts for CCMB Diabetes Study

The work was supported by funding from Council of Scientific Industrial Research (CSIR), Ministry of Science and Technology, Government of India, New Delhi, INDIA and forms part of Network Project funds. We acknowledge the contribution of all the participants under the study and also of the members of GRC-Group at CSIR-Centre for Cellular and Molecular Biology, Hyderabad. INDIA. MA was supported by funds from Council of Scientific Industrial Research (CSIR), Ministry of Science and Technology, Government of India, New Delhi, INDIA.

#### GoDARTS

We are grateful to all the participants in this study, the general practitioners, the Scottish School of Primary Care for their help in recruiting the participants, and to the whole team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists, and nurses. The study complies with the Declaration of Helsinki. We acknowledge the support of the Health Informatics Centre, University of Dundee for managing and supplying the anonymised data and NHS Tayside, the original data owner. The Wellcome Trust United Kingdom Type 2 Diabetes Case Control Collection (GoDARTS) was funded by The Wellcome Trust (072960/Z/03/Z, 084726/Z/08/Z, 084727/Z/08/Z, 085475/Z/08/Z, 085475/B/08/Z). MMcC was a Wellcome Investigator and NIHR Senior Investigator. This work was supported by: NIDDK (U01-DK105535) and Wellcome (090532, 098381, 106130, 203141, 212259)

#### Genetics of Lipid Lowering and Diet Network (GOLDN)

GOLDN biospecimens, baseline phenotype data, and intervention phenotype data were collected with funding from National Heart, Lung and Blood Institute (NHLBI) grant U01 HL072524. Whole-genome sequencing in GOLDN was funded by NHLBI grant R01 HL104135-04S1.

#### Greek Recurrent Myocardial Infarction Cohort /NAFLD Study

Work was supported by the British Heart Foundation (BHF) grant RG/14/5/30893 (P.D.) and forms part of the research themes contributing to the translational research portfolios of the Barts Biomedical Research Centre funded by the UK National Institute for Health Research (NIHR). O.G. has received funding from the British Heart Foundation (BHF) (FS/14/66/3129)

#### Healthy Aging in Neighborhoods of Diversity across the Life Span

National Institute on Aging NIH AG-000513

### Health 2006,2008,2010

The Health2006 was financially supported by grants from the Velux Foundation; The Danish Medical Research Council, Danish Agency for Science, Technology and Innovation; The Aase and Ejner Danielsens Foundation; ALK-Abello A/S, Hørsholm, Denmark, and Research Centre for Prevention and Health, the Capital Region of Denmark. Health2008 was supported by the Timber Merchant Vilhelm Bang's Foundation, the Danish Heart Foundation (Grant number 07-10-R61-A1754-B838-22392F), and the Health Insurance Foundation (Helsefonden) (Grant number 2012B233).

### Hellenic Isolated Cohorts MANOLIS and POMAK

This work was funded by the Wellcome Trust (098051) and the European Research Council (ERC-2011-StG 280559-SEPI). The MANOLIS cohort is named in honour of Manolis Giannakakis, 1978-2010. We thank the residents of the Mylopotamos villages for taking part.

### Hein Nixdorf Recall Study

This work was supported by the Heinz Nixdorf Foundation; the German Research Council [projects SI 236/8-1, SI 236/9-1, ER 155/6-1, ER 155/6-2].

### Health and Retirement Study

HRS is supported by the National Institute on Aging (NIA U01AG009740). The genotyping was funded separately by the National Institute on Aging (RC2 AG036495, RC4 AG039029). Our genotyping was conducted by the NIH Center for Inherited Disease Research (CIDR) at Johns Hopkins University. Genotyping quality control and final preparation of the data were performed by the Genetics Coordinating Center at the University of Washington and the School of Public Health at the University of Michigan.

### Hispanic Community Health Study/Study of Latinos

The baseline examination of HCHS/SOL was carried out as a collaborative study supported by contracts from the NHLBI to the University of North Carolina (N01-HC65233), University of Miami (N01-HC65234), Albert Einstein College of Medicine (N01-HC65235), Northwestern University (N01-HC65236), and San Diego State University (N01-HC65237). The following institutes, centers, and offices contributed to the first phase of HCHS/SOL through a transfer of funds to the NHLBI: National Institute on Minority Health and Health Disparities, National Institute on Deafness and Other Communication Disorders, National Institute of Dental and Craniofacial Research (NIDCR), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Neurological Disorders and Stroke, and NIH Office of Dietary Supplements. The Genetic Analysis Center at the University of Washington was supported by NHLBI and NIDCR contracts (HHSN268201300005C AM03 and MOD03). Additional analysis support was

provided by NIDDK grant 1R01DK101855-01, NHLBI grant N01HC65233, and AHA grant 13GRNT16490017. Genotyping efforts were supported by the NIH Department of Health and Human Services (HSN26220/20054C), National Center for Advancing Translational Science Clinical Translational Science Institute (UL1TR000124), and NIDDK Diabetes Research Center (DK063491). Kristin L. Young was supported by R21 HL140419. Heather M Highland was funded by NHLBI training grant T32 HL007055, T32 HL129982, ADA Grant #1-19-PDF-045, and R01HL142825.

#### Hunter Community Study

The authors would like to thank the men and women participating in the HCS as well as all the staff, investigators and collaborators who have supported or been involved in the project to date. The cohort was supported by grants from the University of Newcastle Strategic Initiatives Fund, the Gladys M Brawn Senior Research Fellowship scheme; and the Vincent Fairfax Family Foundation, a private philanthropic trust. The Hunter Medical Research Institute provided media support during the initial recruitment of participants; and Dr Anne Crotty and Prof. Levi provided financial support towards freezing costs for the long-term storage of participant blood samples.

#### HUNT Study

The HUNT Study is a collaboration between the HUNT Research Centre (Faculty of Medicine and Health Sciences, NTNU, Norwegian University of Science and Technology), Nord-Trøndelag County Council, Central Norway Regional Health Authority, and the Norwegian Institute of Public Health. The genotyping in HUNT was financed by the National Institutes of Health; University of Michigan; the Research Council of Norway; the Liaison Committee for Education, Research and Innovation in Central Norway; and the Joint Research Committee between St Olavs hospital and the Faculty of Medicine and Health Sciences, NTNU.

#### Hypertension Genetic Epidemiology Network (HyperGEN + HyperGEN LVH)

The Hypertension Genetic Epidemiology Network (HyperGEN) Study is part of the National Heart, Lung, and Blood Institute (NHLBI) Family Blood Pressure Program; collection of the data represented here was supported by grants U01 HL054472, U01 HL054473, U01 HL054495, and U01 HL054509. The HyperGEN: Genetics of Left Ventricular Hypertrophy Study was supported by NHLBI grant R01 HL055673 with whole-genome sequencing made possible by supplement -18S1.

#### Hypertension Genetic Epidemiology Network (Axiom chip)

The study was support by the National Institutes of Health, the National Heart, Lung, Blood Institute grant HL086718

### INdian DIabetes CONsortium

The study was majorly supported by Council of Scientific and Industrial Research (CSIR), Government of India through CARDIOMED project Grant Number: BSC0122 provided to CSIR-Institute of Genomics and Integrative Biology. Study was also partially funded by Department of Science and Technology-PURSE-II (DST/SR/PURSE II/11) given to Jawaharlal Nehru University. We are very much thankful to the INdian DIabetes CONsortium (INDICO) and all the study participants who have participated in the study.

### Inter99

The Inter99 was initiated by Torben Jørgensen (PI), Knut Borch-Johnsen (co-PI), Hans Ibsen and Troels F. Thomsen. The steering committee comprises the former two and Charlotta Pisinger. The study was financially supported by research grants from the Danish Research Council, the Danish Centre for Health Technology Assessment, Novo Nordisk Inc., Research Foundation of Copenhagen County, Ministry of Internal Affairs and Health, the Danish Heart Foundation, the Danish Pharmaceutical Association, the Augustinus Foundation, the Ib Henriksen Foundation, the Becket Foundation, and the Danish Diabetes Association. Novo Nordisk Foundation Center for Basic Metabolic Research is an independent Research Center, based at the University of Copenhagen, Denmark and partially funded by an unconditional donation from the Novo Nordisk Foundation ([www.cbmr.ku.dk](http://www.cbmr.ku.dk)) (Grant number NNF18CC0034900).

### Jackson Heart Study

The Jackson Heart Study (JHS) is supported and conducted in collaboration with Jackson State University (HHSN268201800013I), Tougaloo College (HHSN268201800014I), the Mississippi State Department of Health (HHSN268201800015I) and the University of Mississippi Medical Center (HHSN268201800010I, HHSN268201800011I and HHSN268201800012I) contracts from the National Heart, Lung, and Blood Institute (NHLBI) and the National Institute on Minority Health and Health Disparities (NIMHD). The authors also wish to thank the staffs and participants of the JHS.

The views expressed in this manuscript are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; the National Institutes of Health; or the U.S. Department of Health and Human Services.

### The Johnston County Osteoarthritis Project

The JoCoOA is supported in part by S043, S1734, & S3486 from the CDC/Association of Schools of Public Health; 5-P60-AR30701 & 5-P60-AR49465 from NIAMS/NIH, and U01 DP003206 from the CDC

### Japan PGx Data Science Consortium

The authors thank the Japan PGx Data Science Consortium (JPDSC) for kindly providing genotype and phenotype data. The JPDSC was comprised of six pharmaceutical companies in Japan, namely Astellas

Pharma, Inc.; Daiichi Sankyo Co., Ltd.; Mitsubishi Tanabe Pharma Corporation; Otsuka Pharmaceutical Co., Ltd.; Taisho Pharmaceutical Co., Ltd.; and Takeda Pharmaceutical Co., Ltd.

#### Kangbuk Samsung Cohort Study (KSCS)

This KSCS research was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (NRF-2020R1A2C1012931) and by the Medical Research Funds from Kangbuk Samsung Hospital. We are thankful for the computing resources provided by the Global Science experimental Data hub Center (GSDC) Project and the Korea Research Environment Open NETwork (KREONET) of the Korea Institute of Science and Technology Information (KISTI).

#### Korea Association REsource

The KARE cohort was supported by grants from Korea Centers for Disease Control and Prevention (4845–301, 4851–302, 4851–307) and an intramural grant from the Korea National Institute of Health (2019-NG-053-01).

#### Korean Genome and Epidemiology Study

Genotype data were provided by the Collaborative Genome Program for Fostering New Post-Genome Industry (3000–3031b). An intramural grant from the Korea National Institute of Health (2019-NG-053-01).

#### KORA

The KORA study was initiated and financed by the Helmholtz Zentrum München – German Research Center for Environmental Health, which is funded by the German Federal Ministry of Education and Research (BMBF) and by the State of Bavaria. KORA research has been supported within the Munich Center of Health Sciences (MC-Health), Ludwig-Maximilians-Universität, as part of LMUinnovativ and is funded by the Bavarian State Ministry of Health and Care through the research project DigiMed Bayern ([www.digimed-bayern.de](http://www.digimed-bayern.de)). The German Center for Diabetes Research (DZD) was supported by the German Federal Ministry of Education and Research (BMBF).

#### Korea National Diabetes Program

This study was supported by a grant from the Korea Healthcare Technology R&D Project, Ministry of Health and Welfare Republic of Korea (HI10C2020).

#### Kuwait Obesity Diabetes Genetic Program

Kuwait Foundation for Advancement of Sciences is acknowledged for institutional funding.

#### Leicester BIORESOURCE

CPN is funded by the British Heart Foundation. NJS holds an NIHR Senior Investigator award.

#### Long Life Family Study

This work has been funded by the NIA grants, U01AG023746, U01AG023712, U01AG023749, U01AG023755, U01AG023744, and U19AG063893

#### London Life Sciences Prespective Population Study

The LOLIPOP study is supported by the National Institute for Health Research (NIHR) Comprehensive Biomedical Research Centre Imperial College Healthcare NHS Trust, the British Heart Foundation (SP/04/002), the Medical Research Council (G0601966, G0700931), the Wellcome Trust (084723/Z/08/Z, 090532 & 098381) the NIHR (RP-PG-0407-10371), the NIHR Official Development Assistance (ODA, award 16/136/68), the European Union FP7 (EpiMigrant, 279143) and H2020 programs (iHealth-T2D, 643774). We acknowledge support of the MRC-PHE Centre for Environment and Health, and the NIHR Health Protection Research Unit on Health Impact of Environmental Hazards. The work was carried out in part at the NIHR/Wellcome Trust Imperial Clinical Research Facility. The views expressed are those of the author(s) and not necessarily those of the Imperial College Healthcare NHS Trust, the NHS, the NIHR or the Department of Health. We thank the participants and research staff who made the study possible. JC is supported by the Singapore Ministry of Health's National Medical Research Council under its Singapore Translational Research Investigator (STaR) Award (NMRC/STaR/0028/2017).

#### Ludwigshafen Risk and Cardiovascular Health Study

The LURIC study was supported by the 7th Framework Program (AtheroRemo, grant agreement number 201668 and RiskyCAD, grant agreement number 305739) of the European Union, the INTERREG IV Oberrhein Program (Project A28) with support from the European Regional Development Fund (ERDF) and the Wissenschaftsoffensive TMO, and European Union's Horizon 2020 research and innovation programme under the ERA-Net Cofund action N° 727565 (OCTOPUS project) and the German Ministry of Education and Research (grant number 01EA1801A)

#### Metabolic Syndrome in Men

The METSIM study was funded by the Academy of Finland (grants no. 77299 and 124243).

#### Mexico City Study

This study was supported in Mexico by the Fondo Sectorial de Investigación en Salud y Seguridad Social (SSA/IMSS/ISSSTECONACYT, project 150352), Temas Prioritarios de Salud Instituto Mexicano del Seguro Social (2014-FIS/IMSS/PROT/PRI0/14/34). The authors would like to thank Araceli Méndez Padrón for technical support. In Canada, this research was enabled in part by support provided by Compute Ontario ([www.computeontario.ca](http://www.computeontario.ca)), WestGrid ([www.westgrid.ca](http://www.westgrid.ca)) and Compute Canada ([www.compute.canada.ca](http://www.compute.canada.ca)).

#### Million Veteran Program (MVP)

This research is supported by funding from the Department of Veterans Affairs Office of Research and Development, Million Veteran Program Grant I01-BX003340 and I01-BX003362. This publication does not represent the views of the Department of Veterans Affairs or the United States Government. A list of MVP investigators can be found in supplementary materials.

#### Montreal Heart Institute Biobank

We thank all participants and staff of the André and France Desmarais MHI Biobank. This work was funded by the Canadian Institutes of Health Research (PJT #156248), the Canada Research Chair Program, Genome Quebec and Genome Canada, and the Montreal Heart Institute Foundation.

#### Mount Sinai BioMe Biobank

The Mount Sinai BioMe Biobank has been supported by The Andrea and Charles Bronfman Philanthropies and in part by Federal funds from the NHLBI and NHGRI (U01HG00638001; U01HG007417; X01HL134588). We thank all participants in the Mount Sinai Biobank. We also thank all our recruiters who have assisted and continue to assist in data collection and management and are grateful for the computational resources and staff expertise provided by Scientific Computing at the Icahn School of Medicine at Mount Sinai.

#### MRC National Survey of Health and Development

We thank NSHD study members who took part in the data collections for their continuing support. This work was supported by the UK Medical Research Council which provides core funding for the MRC National Survey of Health and Development (MC\_UU\_12019/06).

#### Multi-Ethnic Study of Atherosclerosis

MESA and the MESA SHARe projects are conducted and supported by the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with MESA investigators. Support for MESA is provided by

contracts 75N92020D00001, HHSN268201500003I, N01-HC-95159, 75N92020D00005, N01-HC-95160, 75N92020D00002, N01-HC-95161, 75N92020D00003, N01-HC-95162, 75N92020D00006, N01-HC-95163, 75N92020D00004, N01-HC-95164, 75N92020D00007, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168, N01-HC-95169, UL1-TR-000040, UL1-TR-001079, UL1-TR-001420. Also supported in part by the National Center for Advancing Translational Sciences, CTSI grant UL1TR001881, and the National Institute of Diabetes and Digestive and Kidney Disease Diabetes Research Center (DRC) grant DK063491 to the Southern California Diabetes Endocrinology Research Center.

#### Nutrition and Health of Aging Population in China

This work was supported by the Major Project of the Ministry of Science and Technology of China (2017YFC0909701, 2016YFC1304903), the National Natural Science Foundation of China (81970684, 81700700), the Chinese Academy of Sciences (ZDBS-SSW-DQC-02, KSCX2-EW-R-10, KJZD-EW-L14-2-2) and Shanghai Municipal Science and Technology Major Project (2017SHZDZX01)

#### the Nagahama Prospective Cohort for Comprehensive Human Bioscience (the Nagahama Study)

This work was supported by a university grant, Center of Innovation Program, Global University Project, and a Grant-in-Aid for Scientific Research (25293141, 26670313, 26293198, 17H04182, 17H04126, 17H04123, 18K18450) from the Ministry of Education, Culture, Sports, Science and Technology of Japan; Practical Research Project for Rare/Intractable Diseases (ek0109070, ek0109283, ek0109196, ek0109348), Research and Development Grants for Dementia (dk0207006, dk0207027), Program for an Integrated Database of Clinical and Genomic Information (kk0205008), Practical Research Project for Lifestyle-related Diseases including Cardiovascular Diseases and Diabetes Mellitus (ek0210066, ek0210096, ek0210116), Research Program for Health Behavior Modification by Utilizing IoT (le0110005, le0110013), and Research and Development Grants for Longevity Science (dk0110040) from the Japan Agency for Medical Research and Development (AMED); Takeda Medical Research Foundation, Mitsubishi Foundation, Daiwa Securities Health Foundation, and Sumitomo Foundation.

#### Nijmegen Biomedical Study

The Nijmegen Biomedical Study is a population-based survey conducted at the Department for Health Evidence and the Department of Laboratory Medicine of the Radboud university medical center. Principal investigators of the Nijmegen Biomedical Study are L.A.L.M. Kiemeny, A.L.M. Verbeek, D.W. Swinkels en B. Franke

#### The Netherlands Epidemiology of Obesity Study

The authors of the NEO study thank all individuals who participated in the Netherlands Epidemiology in Obesity study, all participating general practitioners for inviting eligible participants and all research nurses for collection of the data. We thank the NEO study group, Pat van Beelen, Petra Noordijk and

Ingeborg de Jonge for the coordination, lab and data management of the NEO study. The genotyping in the NEO study was supported by the Centre National de Génotypage (Paris, France), headed by Jean-Francois Deleuze. The NEO study is supported by the participating Departments, the Division and the Board of Directors of the Leiden University Medical Center, and by the Leiden University, Research Profile Area Vascular and Regenerative Medicine. Dennis Mook-Kanamori is supported by Dutch Science Organization (ZonMW-VENI Grant 916.14.023).

#### Northern Ireland Cohort for Longitudinal Study of Ageing

The analysis of molecular biomarkers for NICOLA's Wave 1 was funded by the Economic and Social Research Council, award reference ES/L008459/1. Generic analysis of data was supported by ESRC (ES/L008459/1) and the Science Foundation Ireland-Department for the Economy (SFI-DfE) Investigator Program Partnership Award (15/IA/3152). We are grateful to all the participants of the NICOLA Study, and the whole NICOLA team, which includes nursing staff, research scientists, clerical staff, computer and laboratory technicians, managers and receptionists. The Atlantic Philanthropies, the Economic and Social Research Council, the UKCRC Centre of Excellence for Public Health Northern Ireland, the Centre for Ageing Research and Development in Ireland, the Office of the First Minister and Deputy First Minister, the Health and Social Care Research and Development Division of the Public Health Agency, the Wellcome Trust/Wolfson Foundation and Queen's University Belfast provide core financial support for NICOLA. The authors alone are responsible for the interpretation of the data and any views or opinions presented are solely those of the authors and do not necessarily represent those of the NICOLA Study team.

#### Netherlands Twin Register

Funding was obtained from the Netherlands Organization for Scientific Research (NWO) and The Netherlands Organisation for Health Research and Development (ZonMW) grants 904-61-090, 985-10-002, 904-61-193, 480-04-004, 400-05-717, Addiction-31160008, 016-115-035, 400-07-080, Middelgroot-911-09-032, NWO-Groot 480-15-001/674, Center for Medical Systems Biology (CSMB, NWO Genomics), NBIC/BioAssist/RK(2008.024), Biobanking and Biomolecular Resources Research Infrastructure (BBMRI – NL, 184.021.007 and 184.033.111), X-Omics 184-034-019; Spinozapremie (NWO- 56-464-14192), KNAW Academy Professor Award (PAH/6635) and University Research Fellow grant (URF) to DIB; Amsterdam Public Health research institute (former EMGO+) , Neuroscience Amsterdam research institute (former NCA) ; the European Community's Fifth and Seventh Framework Program (FP5- LIFE QUALITY-CT-2002-2006, FP7- HEALTH-F4-2007-2013, grant 01254: GenomEUtwin, grant 01413: ENGAGE ; the European Research Council (ERC Starting 284167, ERC Consolidator 771057, ERC Advanced 230374), Rutgers University Cell and DNA Repository (NIMH U24 MH068457-06), the National Institutes of Health (NIH, R01D0042157-01A1, MH081802, DA018673, R01 DK092127-04, Grand Opportunity grants 1RC2 MH089951); the Avera Institute for Human Genetics, Sioux Falls, South Dakota (USA). Part of the genotyping and analyses were funded by the Genetic Association Information Network (GAIN) of the

Foundation for the National Institutes of Health. Computing was supported by NWO through grant 2018/EW/00408559, BiG Grid, the Dutch e-Science Grid and SURFSARA.

#### Nurses' Health Study

The Nurses' Health Study is supported by US National Institutes of Health grants UM1 CA186107 and R01 CA49449.

#### Nurses' Health Study II

The Nurses' Health Study II is supported by US National Institutes of Health grants U01 CA176726 and R01 CA67262.

#### Health Professionals Follow-up Study

The Health Professionals Follow-up Study is supported by US National Institutes of Health grant U01 CA 167552.

#### Oglistra Genetic Park

The study was supported by grant from the Italian Ministry of Education, University and Research (MIUR) n°: 5571/DSPAR/2002. We express our gratitude to all the study participants for their contributions and to the municipal administrations for their economic and logistic support.

#### Orkney Complex Disease Study

The Orkney Complex Disease Study (ORCADES) was supported by the Chief Scientist Office of the Scottish Government (CZB/4/276, CZB/4/710), a Royal Society URF to J.F.W., the MRC Human Genetics Unit quinquennial programme "QTL in Health and Disease", Arthritis Research UK and the European Union framework program 6 EUROSPAN project (contract no. LSHG-CT-2006-018947). DNA extractions were performed at the Edinburgh Clinical Research Facility, University of Edinburgh. We would like to acknowledge the invaluable contributions of the research nurses in Orkney, the administrative team in Edinburgh and the people of Orkney.

#### Osteoporosis Fractures in Men, The Gothenburg Study

MrOS in Sweden is supported by the Swedish Research Council, the Swedish Foundation for Strategic Research, the ALF/LUA research grant in Gothenburg, the Lundberg Foundation, the Knut and Alice Wallenberg Foundation, the Torsten Soderberg Foundation, and the Novo Nordisk Foundation.

#### Oxford Biobank

This work was supported by the British Heart Foundation (RG/17/1/32663)

#### Penn Medicine BioBank

We acknowledge the Penn Medicine BioBank (PMBB) for providing data and thank the patient-participants of Penn Medicine who consented to participate in this research program. We would also like to thank the Penn Medicine BioBank team and Regeneron Genetics Center for providing genetic variant data for analysis. The PMBB is approved under IRB protocol# 813913 and supported by Perelman School of Medicine at University of Pennsylvania

#### pcosN

YSC is supported by the National Research Foundation of Korea (NRF) Grant funded by the Ministry of Education (NRF-2020R11A2075302) and Hallym University Research Fund 2020 (HRF-202002-008).

#### PRecOciuous Coronary ARtery DISease

PROCARDIS was supported by the European Community Sixth Framework Program (LSHM-CT- 2007-037273), AstraZeneca, the Swedish Research Council, the Knut and Alice Wallenberg Foundation, the Swedish Heart-Lung Foundation, the Torsten and Ragnar Soderberg Foundation, the Strategic Cardiovascular Program of Karolinska Institutet and Stockholm County Council, the Foundation for Strategic Research and the Stockholm County Council (560283). HW is supported by the British Heart Foundation Centre for Research Excellence, Wellcome Trust core award (090532/Z/09/Z, 203141/Z/16/Z, 201543/B/16/Z), European Union Seventh Framework Programme FP7/2007-2013 under grant agreement no. HEALTH-F2-2013-601456 (CVGenes@Target) & the TriPartite Immunometabolism Consortium [TriC]-Novo Nordisk Foundation's Grant number NNF15CC0018486. AG acknowledge support from the Wellcome Trust (201543/B/16/Z), European Union Seventh Framework Programme FP7/2007-2013 under grant agreement no. HEALTH-F2-2013-601456 (CVGenes@Target) & the TriPartite Immunometabolism Consortium [TriC]-Novo Nordisk Foundation's Grant number NNF15CC0018486. Maria Sabater-Lleal is supported by a Miguel Servet contract from the ISCIII Spanish Health Institute (CP17/00142) and co-financed by the European Social Fund.

#### Quebec Family Study

The Quebec Family Study was funded by multiple grants from the Medical Research Council of Canada and the Canadian Institutes of Health Research. This work was supported by a team grant from the Canadian Institutes of Health Research (FRN-CCT-83028)

#### QIMR Berghofer Genetic Epidemiology Cohort

Funded by the Australian National Health and Medical Research Council (241944, 339462, 389927, 389875, 389891, 389892, 389938, 442915, 442981, 496739, 552485, 552498), the Australian Research Council (A7960034, A79906588, A79801419, DP0770096, DP0212016, DP0343921) and the U.S. National Institutes of Health (AA07535, AA10248, AA11998, AA13320, AA13321, AA13326, AA14041, AA17688, DA12854, MH66206).

#### The Raine Study

The Raine Study was supported by the National Health and Medical Research Council of Australia [grant numbers 572613, 403981, and 1059711] and the Canadian Institutes of Health Research [grant number MOP-82893]. The authors are grateful to the Raine Study participants and their families, and to the Raine Study team for cohort coordination and data collection. The authors gratefully acknowledge the NHMRC for their long term funding to the study over the last 30 years and also the following institutes for providing funding for Core Management of the Raine Study: The University of Western Australia (UWA), Curtin University, Women and Infants Research Foundation, Telethon Kids Institute, Edith Cowan University, Murdoch University, The University of Notre Dame Australia and The Raine Medical Research Foundation. This work was supported by resources provided by the Pawsey Supercomputing Centre with funding from the Australian Government and Government of Western Australia.

#### Relationship between Insulin Sensitivity and Cardiovascular Disease

The RISC Study is partly supported by EU grant QLG1-CT-2001-01252.

#### Religious Orders Study & the Rush Memory and Aging Project

P30AG10161, R01AG15819, R10AG17917, U01AG46152, U01AG61356 and the Translational Genomics Research Institute

#### Rotterdam Study 1,2,3

The generation and management of GWAS genotype data for the Rotterdam Study (RS I, RS II, RS III) was executed by the Human Genotyping Facility of the Genetic Laboratory of the Department of Internal Medicine, Erasmus MC, Rotterdam, The Netherlands. The GWAS datasets are supported by the Netherlands Organisation of Scientific Research NWO Investments (nr. 175.010.2005.011, 911-03-012), the Genetic Laboratory of the Department of Internal Medicine, Erasmus MC, the Research Institute for Diseases in the Elderly (014-93-015; RIDE2), the Netherlands Genomics Initiative (NGI)/Netherlands Organisation for Scientific Research (NWO) Netherlands Consortium for Healthy Aging (NCHA), project nr. 050-060-810. We thank Pascal Arp, Mila Jhamai, Marijn Verkerk, Lizbeth Herrera and Marjolein

Peters, PhD, and Carolina Medina-Gomez, PhD, for their help in creating the GWAS database, and Linda Broer, PhD, and Carolina Medina-Gomez, PhD, for the creation and analysis of imputed data. The Rotterdam Study is funded by Erasmus Medical Center and Erasmus University, Rotterdam, Netherlands Organization for the Health Research and Development (ZonMw), the Research Institute for Diseases in the Elderly (RIDE), the Ministry of Education, Culture and Science, the Ministry for Health, Welfare and Sports, the European Commission (DG XII), and the Municipality of Rotterdam. The authors are very grateful to the study participants, the staff from the Rotterdam Study (particularly L. Buist and J.H. van den Boogert) and the participating general practitioners and pharmacists.

### Sardinia

Supported by contracts (HHSN271201600005C, to F. Cucca) from the Intramural Research Program of the 366 National Institute on Aging, National Institutes of Health (NIH)

### Shanghai Breast Cancer Study

The generation and management of GWAS genotype data for the SBCS was supported by R01CA64277 and R01CA15847.

### Steno Diabetes Center T2D Cases

Novo Nordisk Foundation Center for Basic Metabolic Research is an independent Research Center, based at the University of Copenhagen, Denmark and partially funded by an unconditional donation from the Novo Nordisk Foundation ([www.cbmr.ku.dk](http://www.cbmr.ku.dk)) (Grant number NNF18CC0034900).

### Study of Health in Pomerania

SHIP (Study of Health in Pomerania) and SHIP-TREND both represent population-based studies. SHIP is supported by the German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung (BMBF); grants 01ZZ9603, 01ZZ0103, and 01ZZ0403) and the German Research Foundation (Deutsche Forschungsgemeinschaft (DFG); grant GR 1912/5-1). SHIP and SHIP-TREND are part of the Community Medicine Research net (CMR) of the University of Greifswald which is funded by the BMBF as well as the Ministry for Education, Science and Culture and the Ministry of Labor, Equal Opportunities, and Social Affairs of the Federal State of Mecklenburg-West Pomerania. The CMR encompasses several research projects that share data from SHIP.

### SIGMA1,2

This work was conducted as part of the Slim Initiative in Genomic Medicine for the Americas (SIGMA), a joint U.S.-Mexico project funded by the Carlos Slim Foundation. The Universidad Nacional Autónoma de

México/Instituto Nacional de Ciencias Médicas and Nutrición Salvador Zubirán (UNAM/INCMNSZ) diabetes study was supported by the Consejo Nacional de Ciencia y Tecnología (grants 138826, 128877, and CONACyT-SALUD 2009-01-115250) and a grant from Dirección General de Asuntos del Personal Académico (UNAM, IT 214711). The Diabetes in Mexico Study (DMS) was supported by the Consejo Nacional de Ciencia y Tecnología (grant 86867) and by the Carlos Slim Foundation. The Mexico City Diabetes Study (MCDS) was supported by National Institutes of Health (grant R01HL24799 from the National Heart, Lung, and Blood Institute) and by the Consejo Nacional de Ciencia y Tecnología (grants 2092, M9303, F677-M9407, 251M, 2005-C01-14502, and SALUD 2010-2- 151165). The Multiethnic Cohort Study of Diet and Cancer (MEC) was supported by National Institutes of Health (grants CA54281 and CA063464). This project was also supported by an American Diabetes Association Innovative and Clinical Translational Award 1-19-ICTS-068 and by DGAPA/UNAM Funding Project IN215219. J.M.M. is supported by American Diabetes Association Innovative and Clinical Translational Award 1-19-ICTS-068 and by NHGRI, grant FAIN# U01HG011723.

#### SORBS

This work was supported by grants from the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation – Projektnummer 209933838 – SFB 1052; B03, C01; SPP 1629 TO 718/2- 1). We thank all those who participated in the study. Sincere thanks are given to Dr. Knut Krohn (University of Leipzig) for the genotyping support.

#### Shanghai Women Health Study

The generation and management of GWAS genotype data for the SWHS was supported by UM1CA182910 and R01CA148677

#### Special Turku Coronary Risk Factor Intervention Project – Parents

STRIP has been financially supported by Academy of Finland (grants 206374, 251360 and 276861); Juho Vainio Foundation; Finnish Cardiac Research Foundation; Finnish Cultural Foundation; Finnish Ministry of Education and Culture; Sigrid Juselius Foundation; Yrjö Jahnsson Foundation; C.G. Sundell Foundation; Special Governmental Grants for Health Sciences Research, Turku University Hospital; Foundation for Pediatric Research; and Turku University Foundation.

#### The Hellenic study of Interactions between Single nucleotide polymorphisms and Eating in Atherosclerosis Susceptibility

This work was supported by the British Heart Foundation (BHF) grant RG/14/5/30893 (P.D.) and forms part of the research themes contributing to the translational research portfolios of the Barts Biomedical Research Centre funded by the UK National Institute for Health Research (NIHR)

#### Taiwan US Diabetic Retinopathy Study

This study was supported by the National Eye Institute of the National Institutes of Health (EY014684) and ARRA Supplement (EY014684-03S1, -04S1), the National Institute of Diabetes and Digestive and Kidney Disease grant DK063491 to the Southern California Diabetes Endocrinology Research Center, the Eye Birth Defects Foundation Inc., the National Science Council, Taiwan (NSC 98-2314-B-075A-002-MY3) and the Taichung Veterans General Hospital, Taichung, Taiwan (TCVGH-1003001C).

#### Taiwan Hypertension study of Rare Variants

The Rare Variants for Hypertension in Taiwan Chinese (THRV) is supported by the National Heart, Lung, and Blood Institute (NHLBI) grant (R01HL111249) and its participation in TOPMed is supported by an NHLBI supplement (R01HL111249-04S1). THRV is a collaborative study between Washington University in St. Louis, LA BioMed at Harbor UCLA, University of Texas in Houston, Taichung Veterans General Hospital, Taipei Veterans General Hospital, Tri-Service General Hospital, National Health Research Institutes, National Taiwan University, and Baylor University. THRV is based (substantially) on the parent SAPHIRE study, along with additional population-based and hospital-based cohorts. SAPHIRE was supported by NHLBI grants (U01HL54527, U01HL54498) and Taiwan funds, and the other cohorts were supported by Taiwan funds.

#### Tracking Adolescents' Individual Lives Survey - Population Cohort

TRAILS (TRacking Adolescents' Individual Lives Survey) is a collaborative project involving various departments of the University Medical Center and University of Groningen, the University of Utrecht, the Radboud Medical Center Nijmegen, and the Parnassia Group, all in the Netherlands. TRAILS has been financially supported by various grants from the Netherlands Organization for Scientific Research NWO (Medical Research Council program grant GB-MW 940-38-011; ZonMW Brainpower grant 100-001-004; ZonMw Risk Behavior and Dependence grants 60-60600-97-118; ZonMw Culture and Health grant 261-98-710; Social Sciences Council medium-sized investment grants GB-MaGW 480-01-006 and GB-MaGW 480-07-001; Social Sciences Council project grants GB-MaGW 452-04-314 and GB-MaGW 452-06-004; NWO large-sized investment grant 175.010.2003.005; NWO Longitudinal Survey and Panel Funding 481-08-013 and 481-11-001; NWO Vici 016.130.002 and 453-16-007/2735; NWO Gravitation 024.001.003), the Dutch Ministry of Justice (WODC), the European Science Foundation (EuroSTRESS project FP-006), the European Research Council (ERC-2017-STG-757364 en ERC-CoG-2015-681466), Biobanking and Biomolecular Resources Research Infrastructure BBMRI-NL (CP 32), the Gratama foundation, the Jan Dekker foundation, the participating universities, and Accare Centre for Child and Adolescent Psychiatry. Statistical analyses were carried out on the Genetic Cluster Computer (<http://www.geneticcluster.org>), which is financially supported by the Netherlands Scientific

Organization (NWO 480-05-003) along with a supplement from the Dutch Brain Foundation. We are grateful to everyone who participated in this research or worked on this project to make it possible.

#### TWINGENE:

TWINGENE is a substudy of the Swedish Twin Registry which is managed by Karolinska Institutet and receives funding through the Swedish Research Council under the grant no 2017-00641.

#### Twins UK

TwinsUK receives funding from the Wellcome Trust (212904/Z/18/Z), Medical Research Council. TwinsUK and Massimo Mangino are supported by the National Institute for Health Research (NIHR)-funded BioResource, Clinical Research Facility and Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust in partnership with King's College London. Paraskevi Christofidou is supported by SYSCID project (H2020 contract #733100)

#### The UK Household Longitudinal Study

The UK Household Longitudinal Study was funded by grants from the Economic & Social Research Council (ES/H029745/1) and the Wellcome Trust (WT098051). UKHLS is led by the Institute for Social and Economic Research at the University of Essex and funded by the Economic and Social Research Council. The survey was conducted by NatCen and the genome-wide scan data were analysed and deposited by the Wellcome Trust Sanger Institute. Information on how to access the data can be found on the Understanding Society website (<https://www.understandingsociety.ac.uk/>).

#### Vejle Diabetes Biobank

The Vejle Diabetes Biobank was supported by The Danish Research Council for Independent Research and by Region of Southern Denmark.

#### The Viking Health Study- Shetland

The Viking Health Study – Shetland (VIKING) was supported by the MRC Human Genetics Unit quinquennial programme grant “QTL in Health and Disease”. DNA extractions and genotyping were performed at the Edinburgh Clinical Research Facility, University of Edinburgh. We would like to acknowledge the invaluable contributions of the research nurses in Shetland, the administrative team in Edinburgh and the people of Shetland.

#### Whitehall II Study

The Whitehall II Study has been supported by grants from the UK Medical Research Council (K013351, R024227, S011676); the British Heart Foundation (PG/11/63/29011 and RG/13/2/30098); the British Health and Safety Executive; the British Department of Health; the National Heart, Lung, and Blood Institute (R01HL036310); the National Institute on Ageing, National Institute of Health (R01AG056477, R01AG034454); and the Economic and Social Research Council (ES/J023299/1).

#### Women's Health Initiative

The WHI program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services through contracts HHSN268201600018C, HHSN268201600001C, HHSN268201600002C, HHSN268201600003C, and HHSN268201600004C. We also acknowledge the contributions of the following individuals:

*Program Office:* (National Heart, Lung, and Blood Institute, Bethesda, Maryland) Jacques Rossouw, Shari Ludlam, Joan McGowan, Leslie Ford, and Nancy Geller

*Clinical Coordinating Center:* (Fred Hutchinson Cancer Research Center, Seattle, WA) Garnet Anderson, Ross Prentice, Andrea LaCroix, and Charles Kooperberg

*Investigators and Academic Centers:* (Brigham and Women's Hospital, Harvard Medical School, Boston, MA) JoAnn E. Manson; (MedStar Health Research Institute/Howard University, Washington, DC) Barbara V. Howard; (Stanford Prevention Research Center, Stanford, CA) Marcia L. Stefanick; (The Ohio State University, Columbus, OH) Rebecca Jackson; (University of Arizona, Tucson/Phoenix, AZ) Cynthia A. Thomson; (University at Buffalo, Buffalo, NY) Jean Wactawski-Wende; (University of Florida, Gainesville/Jacksonville, FL) Marian Limacher; (University of Iowa, Iowa City/Davenport, IA) Jennifer Robinson; (University of Pittsburgh, Pittsburgh, PA) Lewis Kuller; (Wake Forest University School of Medicine, Winston-Salem, NC) Sally Shumaker; (University of Nevada, Reno, NV) Robert Brunner

*Women's Health Initiative Memory Study:* (Wake Forest University School of Medicine, Winston-Salem, NC) Mark Espeland

#### Women's Genome Health Study

The WGHS is supported by the National Heart, Lung, and Blood Institute (HL043851 and HL080467) and the National Cancer Institute (CA047988 and UM1CA182913). Additional support and funding for genotyping was provided by Amgen.

**Consortium Authors: VA Million Veteran Program  
MVP Executive Committee**

- Co-Chair: J. Michael Gaziano, M.D., M.P.H.

VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130

- Co-Chair: Sumitra Muralidhar, Ph.D.

US Department of Veterans Affairs, 810 Vermont Avenue NW, Washington, DC 20420

- Rachel Ramoni, D.M.D., Sc.D., Chief VA Research and Development Officer

US Department of Veterans Affairs, 810 Vermont Avenue NW, Washington, DC 20420

- Jean Beckham, Ph.D.

Durham VA Medical Center, 508 Fulton Street, Durham, NC 27705

- Kyong-Mi Chang, M.D.

Philadelphia VA Medical Center, 3900 Woodland Avenue, Philadelphia, PA 19104

- Christopher J. O'Donnell, M.D., M.P.H.

VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130

- Philip S. Tsao, Ph.D.

VA Palo Alto Health Care System, 3801 Miranda Avenue, Palo Alto, CA 94304

- James Breeling, M.D., Ex-Officio

US Department of Veterans Affairs, 810 Vermont Avenue NW, Washington, DC 20420

- Grant Huang, Ph.D., Ex-Officio

US Department of Veterans Affairs, 810 Vermont Avenue NW, Washington, DC 20420

- JP Casas Romero, M.D., Ph.D., Ex-Officio

VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130

**MVP Program Office**

- Sumitra Muralidhar, Ph.D.

US Department of Veterans Affairs, 810 Vermont Avenue NW, Washington, DC 20420

- Jennifer Moser, Ph.D.

US Department of Veterans Affairs, 810 Vermont Avenue NW, Washington, DC 20420

### **MVP Recruitment/Enrollment**

- Recruitment/Enrollment Director/Deputy Director, Boston – Stacey B. Whitbourne, Ph.D.; Jessica V. Brewer, M.P.H.

VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130

- MVP Coordinating Centers
  - Clinical Epidemiology Research Center (CERC), West Haven – Mihaela Aslan, Ph.D.  
West Haven VA Medical Center, 950 Campbell Avenue, West Haven, CT 06516
  - Cooperative Studies Program Clinical Research Pharmacy Coordinating Center, Albuquerque – Todd Connor, Pharm.D.; Dean P. Argyres, B.S., M.S.  
New Mexico VA Health Care System, 1501 San Pedro Drive SE, Albuquerque, NM 87108
  - Genomics Coordinating Center, Palo Alto – Philip S. Tsao, Ph.D.  
VA Palo Alto Health Care System, 3801 Miranda Avenue, Palo Alto, CA 94304
  - MVP Boston Coordinating Center, Boston - J. Michael Gaziano, M.D., M.P.H.  
VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130
  - MVP Information Center, Canandaigua – Brady Stephens, M.S.  
Canandaigua VA Medical Center, 400 Fort Hill Avenue, Canandaigua, NY 14424
- VA Central Biorepository, Boston – Mary T. Brophy M.D., M.P.H.; Donald E. Humphries, Ph.D.; Luis E. Selva, Ph.D.

VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130

- MVP Informatics, Boston – Nhan Do, M.D.; Shahpoor Shayan

VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130

- MVP Data Operations/Analytics, Boston – Kelly Cho, Ph.D.

VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130

### **MVP Science**

- Science Operations – Christopher J. O'Donnell, M.D., M.P.H.

VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130

- Genomics Core - Christopher J. O'Donnell, M.D., M.P.H.; Saiju Pyarajan Ph.D.

VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130

Philip S. Tsao, Ph.D.

VA Palo Alto Health Care System, 3801 Miranda Avenue, Palo Alto, CA 94304

- Phenomics Core- Kelly Cho, M.P.H, Ph.D.

VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130

- Data and Computational Sciences – Saiju Pyarajan, Ph.D.

VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA 02130

- Statistical Genetics – Elizabeth Hauser, Ph.D.

Durham VA Medical Center, 508 Fulton Street, Durham, NC 27705

Yan Sun, Ph.D.

Atlanta VA Medical Center, 1670 Clairmont Road, Decatur, GA 30033

Hongyu Zhao, Ph.D.

West Haven VA Medical Center, 950 Campbell Avenue, West Haven, CT 06516

#### **Current MVP Local Site Investigators**

- Atlanta VA Medical Center (Peter Wilson, M.D.)

1670 Clairmont Road, Decatur, GA 30033

- Bay Pines VA Healthcare System (Rachel McArdle, Ph.D.)

10,000 Bay Pines Blvd Bay Pines, FL 33744

- Birmingham VA Medical Center (Louis Dellitalia, M.D.)

700 S. 19th Street, Birmingham AL 35233

- Central Western Massachusetts Healthcare System (Kristin Mattocks, Ph.D., M.P.H.)

421 North Main Street, Leeds, MA 01053

- Cincinnati VA Medical Center (John Harley, M.D., Ph.D.)

3200 Vine Street, Cincinnati, OH 45220

- Clement J. Zablocki VA Medical Center (Jeffrey Whittle, M.D., M.P.H.)

5000 West National Avenue, Milwaukee, WI 53295

- VA Northeast Ohio Healthcare System (Frank Jacono, M.D.)

10701 East Boulevard, Cleveland, OH 44106

- Durham VA Medical Center (Jean Beckham, Ph.D.)

508 Fulton Street, Durham, NC 27705

- Edith Nourse Rogers Memorial Veterans Hospital (John Wells., Ph.D.)

200 Springs Road, Bedford, MA 01730

- Edward Hines, Jr. VA Medical Center (Salvador Gutierrez, M.D.)

5000 South 5th Avenue, Hines, IL 60141

- Veterans Health Care System of the Ozarks (Gretchen Gibson, D.D.S., M.P.H.)

1100 North College Avenue, Fayetteville, AR 72703

- Fargo VA Health Care System (Kimberly Hammer, Ph.D.)

2101 N. Elm, Fargo, ND 58102

- VA Health Care Upstate New York (Laurence Kaminsky, Ph.D.)

113 Holland Avenue, Albany, NY 12208

- New Mexico VA Health Care System (Gerardo Villareal, M.D.)

1501 San Pedro Drive, S.E. Albuquerque, NM 87108

- VA Boston Healthcare System (Scott Kinlay, M.B.B.S., Ph.D.)

150 S. Huntington Avenue, Boston, MA 02130

- VA Western New York Healthcare System (Junzhe Xu, M.D.)

3495 Bailey Avenue, Buffalo, NY 14215-1199

- Ralph H. Johnson VA Medical Center (Mark Hamner, M.D.)

109 Bee Street, Mental Health Research, Charleston, SC 29401

- Columbia VA Health Care System (Roy Mathew, M.D.)

6439 Garners Ferry Road, Columbia, SC 29209

- VA North Texas Health Care System (Sujata Bhushan, M.D.)

4500 S. Lancaster Road, Dallas, TX 75216

- Hampton VA Medical Center (Pran Iruvanti, D.O., Ph.D.)

100 Emancipation Drive, Hampton, VA 23667

- Richmond VA Medical Center (Michael Godschalk, M.D.)

1201 Broad Rock Blvd., Richmond, VA 23249

- Iowa City VA Health Care System (Zuhair Ballas, M.D.)

601 Highway 6 West, Iowa City, IA 52246-2208

- Eastern Oklahoma VA Health Care System (Douglas Ivins, M.D.)

1011 Honor Heights Drive, Muskogee, OK 74401

- James A. Haley Veterans' Hospital (Stephen Mastorides, M.D.)

13000 Bruce B. Downs Blvd, Tampa, FL 33612

- James H. Quillen VA Medical Center (Jonathan Moorman, M.D., Ph.D.)

Corner of Lamont & Veterans Way, Mountain Home, TN 37684

- John D. Dingell VA Medical Center (Saib Gappy, M.D.)

4646 John R Street, Detroit, MI 48201

- Louisville VA Medical Center (Jon Klein, M.D., Ph.D.)

800 Zorn Avenue, Louisville, KY 40206

- Manchester VA Medical Center (Nora Ratcliffe, M.D.)

718 Smyth Road, Manchester, NH 03104

- Miami VA Health Care System (Hermes Florez, M.D., Ph.D.)

1201 NW 16th Street, 11 GRC, Miami FL 33125

- Michael E. DeBakey VA Medical Center (Olaoluwa Okusaga, M.D.)

2002 Holcombe Blvd, Houston, TX 77030

- Minneapolis VA Health Care System (Maureen Murdoch, M.D., M.P.H.)

One Veterans Drive, Minneapolis, MN 55417

- N. FL/S. GA Veterans Health System (Peruvemba Sriram, M.D.)

1601 SW Archer Road, Gainesville, FL 32608

- Northport VA Medical Center (Shing Shing Yeh, Ph.D., M.D.)

79 Middleville Road, Northport, NY 11768

- Overton Brooks VA Medical Center (Neeraj Tandon, M.D.)

510 East Stoner Ave, Shreveport, LA 71101

- Philadelphia VA Medical Center (Darshana Jhala, M.D.)

3900 Woodland Avenue, Philadelphia, PA 19104

- Phoenix VA Health Care System (Samuel Aguayo, M.D.)

650 E. Indian School Road, Phoenix, AZ 85012

- Portland VA Medical Center (David Cohen, M.D.)

3710 SW U.S. Veterans Hospital Road, Portland, OR 97239

- Providence VA Medical Center (Satish Sharma, M.D.)

830 Chalkstone Avenue, Providence, RI 02908

- Richard Roudebush VA Medical Center (Suthat Liangpunsakul, M.D., M.P.H.)

1481 West 10th Street, Indianapolis, IN 46202

- Salem VA Medical Center (Kris Ann Oursler, M.D.)

1970 Roanoke Blvd, Salem, VA 24153

- San Francisco VA Health Care System (Mary Whooley, M.D.)

4150 Clement Street, San Francisco, CA 94121

- South Texas Veterans Health Care System (Sunil Ahuja, M.D.)

7400 Merton Minter Boulevard, San Antonio, TX 78229

- Southeast Louisiana Veterans Health Care System (Joseph Constans, Ph.D.)

2400 Canal Street, New Orleans, LA 70119

- Southern Arizona VA Health Care System (Paul Meyer, M.D., Ph.D.)

3601 S 6th Avenue, Tucson, AZ 85723

- Sioux Falls VA Health Care System (Jennifer Greco, M.D.)

2501 W 22nd Street, Sioux Falls, SD 57105

- St. Louis VA Health Care System (Michael Rauchman, M.D.)

915 North Grand Blvd, St. Louis, MO 63106

- Syracuse VA Medical Center (Richard Servatius, Ph.D.)

800 Irving Avenue, Syracuse, NY 13210

- VA Eastern Kansas Health Care System (Melinda Gaddy, Ph.D.)

4101 S 4th Street Trafficway, Leavenworth, KS 66048

- VA Greater Los Angeles Health Care System (Agnes Wallbom, M.D., M.S.)

11301 Wilshire Blvd, Los Angeles, CA 90073

- VA Long Beach Healthcare System (Timothy Morgan, M.D.)

5901 East 7th Street Long Beach, CA 90822

- VA Maine Healthcare System (Todd Stapley, D.O.)

1 VA Center, Augusta, ME 04330

- VA New York Harbor Healthcare System (Scott Sherman, M.D., M.P.H.)

423 East 23rd Street, New York, NY 10010

- VA Pacific Islands Health Care System (George Ross, M.D.)

459 Patterson Rd, Honolulu, HI 96819

- VA Palo Alto Health Care System (Philip Tsao, Ph.D.)

3801 Miranda Avenue, Palo Alto, CA 94304-1290

- VA Pittsburgh Health Care System (Patrick Strollo, Jr., M.D.)

University Drive, Pittsburgh, PA 15240

- VA Puget Sound Health Care System (Edward Boyko, M.D.)

1660 S. Columbian Way, Seattle, WA 98108-1597

- VA Salt Lake City Health Care System (Laurence Meyer, M.D., Ph.D.)

500 Foothill Drive, Salt Lake City, UT 84148

- VA San Diego Healthcare System (Samir Gupta, M.D., M.S.C.S.)

3350 La Jolla Village Drive, San Diego, CA 92161

- VA Sierra Nevada Health Care System (Mostaqul Huq, Pharm.D., Ph.D.)

975 Kirman Avenue, Reno, NV 89502

- VA Southern Nevada Healthcare System (Joseph Fayad, M.D.)

6900 North Pecos Road, North Las Vegas, NV 89086

- VA Tennessee Valley Healthcare System (Adriana Hung, M.D., M.P.H.)

1310 24th Avenue, South Nashville, TN 37212

- Washington DC VA Medical Center (Jack Lichy, M.D., Ph.D.)

50 Irving St, Washington, D. C. 20422

- W.G. (Bill) Hefner VA Medical Center (Robin Hurley, M.D.)

1601 Brenner Ave, Salisbury, NC 28144

- White River Junction VA Medical Center (Brooks Robey, M.D.)

163 Veterans Drive, White River Junction, VT 05009

- William S. Middleton Memorial Veterans Hospital (Robert Striker, M.D., Ph.D.)

2500 Overlook Terrace, Madison, WI 53705

## Consortium Authors: Global Lipids Genetics Consortium

Sarah E Graham<sup>1</sup>, Shoa L Clarke<sup>2,3</sup>, Kuan-Han H Wu<sup>4</sup>, Stavroula Kanoni<sup>5</sup>, Greg JM Zajac<sup>6</sup>, Shweta Ramdas<sup>7</sup>, Ida Surakka<sup>1</sup>, Ioanna Ntalla<sup>8</sup>, Sailaja Vedantam<sup>9,10</sup>, Thomas W Winkler<sup>11</sup>, Adam E Locke<sup>12</sup>, Eirini Marouli<sup>5</sup>, Mi Yeong Hwang<sup>13</sup>, Sohee Han<sup>13</sup>, Akira Narita<sup>14</sup>, Ananyo Choudhury<sup>15</sup>, Amy R Bentley<sup>16</sup>, Kenneth Ekoru<sup>16</sup>, Anurag Verma<sup>17</sup>, Bhavi Trivedi<sup>18</sup>, Hilary C Martin<sup>19</sup>, Karen A Hunt<sup>18</sup>, Qin Hui<sup>20,21</sup>, Derek Klarin<sup>22,23,24</sup>, Xiang Zhu<sup>25,26,27,28</sup>, Gudmar Thorleifsson<sup>29</sup>, Anna Helgadottir<sup>29</sup>, Daniel F Gudbjartsson<sup>29,30</sup>, Hilma Holm<sup>29</sup>, Isleifur Olafsson<sup>31</sup>, Masato Akiyama<sup>32,33</sup>, Saori Sakaue<sup>34,32,35</sup>, Chikashi Terao<sup>36</sup>, Masahiro Kanai<sup>37,38,39</sup>, Wei Zhou<sup>40,41,42</sup>, Ben M Brumpton<sup>43,44,45</sup>, Humaira Rasheed<sup>43,44</sup>, Sanni E Ruotsalainen<sup>46</sup>, Aki S Havulinna<sup>46,47</sup>, Yogasudha Veturi<sup>48</sup>, QiPing Feng<sup>49</sup>, Elisabeth A Rosenthal<sup>50</sup>, Todd Lingren<sup>51</sup>, Jennifer Allen Pacheco<sup>52</sup>, Sarah A Pendergrass<sup>53</sup>, Jeffrey Haessler<sup>54</sup>, Franco Giulianini<sup>55</sup>, Yuki Bradford<sup>48</sup>, Jason E Miller<sup>48</sup>, Archie Campbell<sup>56,57</sup>, Kuang Lin<sup>58</sup>, Iona Y Millwood<sup>58,59</sup>, George Hindy<sup>60</sup>, Asif Rasheed<sup>61</sup>, Jessica D Faul<sup>62</sup>, Wei Zhao<sup>63</sup>, David R Weir<sup>62</sup>, Constance Turman<sup>64</sup>, Hongyan Huang<sup>64</sup>, Mariaelisa Graff<sup>65</sup>, Anubha Mahajan<sup>66</sup>, Michael R Brown<sup>67</sup>, Weihua Zhang<sup>68,69,70</sup>, Ketian Yu<sup>71</sup>, Ellen M Schmidt<sup>71</sup>, Anita Pandit<sup>71</sup>, Stefan Gustafsson<sup>72</sup>, Xianying Yin<sup>73</sup>, Jian'an Luan<sup>74</sup>, Jing-Hua Zhao<sup>75</sup>, Fumihiko Matsuda<sup>76</sup>, Hye-Mi Jang<sup>13</sup>, Kyunghoon Yoon<sup>13</sup>, Carolina Medina-Gomez<sup>77,78</sup>, Achilleas Pitsillides<sup>79</sup>, Jouke Jan Hottenga<sup>80,81</sup>, Gonneke Willemssen<sup>80,82</sup>, Andrew R Wood<sup>83</sup>, Yingji Ji<sup>83</sup>, Zishan Gao<sup>84,85,86</sup>, Simon Haworth<sup>87,88</sup>, Ruth E Mitchell<sup>87,89</sup>, Jin Fang Chai<sup>90</sup>, Mette Aadahl<sup>91</sup>, Jie Yao<sup>92</sup>, Ani Manichaikul<sup>93</sup>, Helen R Warren<sup>94,95</sup>, Julia Ramirez<sup>94</sup>, Jette Bork-Jensen<sup>96</sup>, Line L Kårhus<sup>91</sup>, Anuj Goel<sup>97,98</sup>, Maria Sabater-Lleal<sup>99,100</sup>, Raymond Noordam<sup>101</sup>, Carlo Sidore<sup>102</sup>, Edoardo Fiorillo<sup>103</sup>, Aaron F McDaid<sup>104,105</sup>, Pedro Marques-Vidal<sup>106</sup>, Matthias Wielscher<sup>107</sup>, Stella Trompet<sup>108,109</sup>, Naveed Sattar<sup>110</sup>, Line T Møllehave<sup>91</sup>, Betina H Thuesen<sup>91</sup>, Matthias Munz<sup>111</sup>, Lingyao Zeng<sup>112,113</sup>, Jianfeng Huang<sup>114</sup>, Bin Yang<sup>114</sup>, Alaitz Poveda<sup>115</sup>, Azra Kurbasic<sup>115</sup>, Claudia Lamina<sup>116</sup>, Lukas Forer<sup>116</sup>, Markus Scholz<sup>117,118</sup>, Tessel E. Galesloot<sup>119</sup>, Jonathan P. Bradfield<sup>120</sup>, E Warwick Daw<sup>121</sup>, Joseph M Zmuda<sup>122</sup>, Jonathan S Mitchell<sup>123</sup>, Christian Fuchsberger<sup>123</sup>, Henry Christensen<sup>124</sup>, Jennifer A Brody<sup>125</sup>, Mary F Feitosa<sup>121</sup>, Mary K Wojczynski<sup>121</sup>, Michael Preuss<sup>126</sup>, Massimo Mangino<sup>127,128</sup>, Paraskevi Christofidou<sup>127</sup>, Niek Verweij<sup>129</sup>, Jan W Benjamins<sup>129</sup>, Jorgen Engmann<sup>130,131</sup>, Rachel L Kember<sup>132</sup>, Roderick C Slieker<sup>133,134</sup>, Ken Sin Lo<sup>135</sup>, Nuno R Zilhao<sup>136</sup>, Phuong Le<sup>137</sup>, Marcus E Kleber<sup>138,139</sup>, Graciela E Delgado<sup>138</sup>, Shaofeng Huo<sup>140</sup>, Daisuke D Ikeda<sup>141</sup>, Hiroyuki Iha<sup>141</sup>, Jian Yang<sup>142,143</sup>, Jun Liu<sup>144</sup>, Hampton L Leonard<sup>145,146</sup>, Jonathan Marten<sup>147</sup>, Børge Schmidt<sup>148</sup>, Marina Arendt<sup>148,149</sup>, Laura J Smyth<sup>150</sup>, Marisa Cañadas-Garre<sup>150</sup>, Chaolong Wang<sup>151,152</sup>, Masahiro Nakatochi<sup>153</sup>, Andrew Wong<sup>154</sup>, Nina Hutri-Kähönen<sup>155,156</sup>, Xueling Sim<sup>90</sup>, Rui Xia<sup>157</sup>, Alicia Huerta-Chagoya<sup>158</sup>, Juan Carlos Fernandez-Lopez<sup>159</sup>, Valeriya Lyssenko<sup>160,161</sup>, Meraj Ahmed<sup>162</sup>, Anne U Jackson<sup>6</sup>, Marguerite R Irvin<sup>163</sup>, Christopher Oldmeadow<sup>164</sup>, Han-Na Kim<sup>165,166</sup>, Seungho Ryu<sup>167,168</sup>, Paul RHJ Timmers<sup>169,147</sup>, Liubov Arbeeveva<sup>170</sup>, Rajkumar Dorajoo<sup>152</sup>, Leslie A Lange<sup>171</sup>, Xiaoran Chai<sup>172,173</sup>, Gauri Prasad<sup>174,175</sup>, Laura Lorés-Motta<sup>176</sup>, Marc Pauper<sup>176</sup>, Jirong Long<sup>177</sup>, Xiaohui Li<sup>92</sup>, Elizabeth Theusch<sup>178</sup>, Fumihiko Takeuchi<sup>179</sup>, Cassandra N Spracklen<sup>180,181</sup>, Anu Loukola<sup>46</sup>, Sailalitha Bollepalli<sup>46</sup>, Sophie C Warner<sup>182,183</sup>, Ya Xing Wang<sup>184</sup>, Wen B. Wei<sup>185</sup>, Teresa Nutile<sup>186</sup>, Daniela Ruggiero<sup>186,187</sup>, Yun Ju Sung<sup>188</sup>, Yi-Jen Hung<sup>189</sup>, Shufeng Chen<sup>114</sup>, Fangchao Liu<sup>114</sup>, Jingyun Yang<sup>190,191</sup>, Katherine A Kentistou<sup>169</sup>, Mathias Gorski<sup>11,192</sup>, Marco Brumat<sup>193</sup>, Karina Meidtner<sup>194,195</sup>, Lawrence F Bielak<sup>196</sup>, Jennifer A Smith<sup>196,62</sup>, Prashantha Hebbar<sup>197</sup>, Aliki-Eleni Farmaki<sup>198,199</sup>, Edith Hofer<sup>200,201</sup>, Maoxuan Lin<sup>202</sup>, Chao Xue<sup>1</sup>, Jifeng Zhang<sup>1</sup>, Maria Pina Concas<sup>203</sup>, Simona Vaccargiu<sup>204</sup>, Peter J van der Most<sup>205</sup>, Niina Pitkänen<sup>206,207</sup>, Brian E Cade<sup>208,209</sup>, Jiwon Lee<sup>208</sup>, Sander W. van der Laan<sup>210</sup>, Kumaraswamy Naidu Chitralla<sup>211</sup>, Stefan Weiss<sup>212</sup>, Martina E Zimmermann<sup>11</sup>, Jong Young Lee<sup>213</sup>, Hyeok Sun Choi<sup>214</sup>, Maria Nethander<sup>215,216</sup>, Sandra Freitag-Wolf<sup>217</sup>, Lorraine Southam<sup>218,219</sup>, Nigel W Rayner<sup>220,221,222,218</sup>, Carol A

Wang<sup>223</sup>, Shih-Yi Lin<sup>224,225,226</sup>, Jun-Sing Wang<sup>227,228</sup>, Christian Couture<sup>229</sup>, Leo-Pekka Lyytikäinen<sup>230,231</sup>, Kjell Nikus<sup>232,233</sup>, Gabriel Cuellar-Partida<sup>234</sup>, Henrik Vestergaard<sup>235</sup>, Bertha Hildalgo<sup>236</sup>, Olga Giannakopoulou<sup>5</sup>, Qiuyin Cai<sup>177</sup>, Morgan O Obura<sup>237</sup>, Jessica van Setten<sup>238</sup>, Xiaoyin Li<sup>239</sup>, Karen Schwander<sup>240</sup>, Natalie Terzikhan<sup>241</sup>, Jae Hun Shin<sup>214</sup>, Rebecca D Jackson<sup>242</sup>, Alexander P Reiner<sup>243</sup>, Lisa Warsinger Martin<sup>244</sup>, Zhengming Chen<sup>245,246</sup>, Liming Li<sup>247</sup>, Heather M Highland<sup>65</sup>, Kristin L Young<sup>65</sup>, Takahisa Kawaguchi<sup>76</sup>, Joachim Thiery<sup>248,118</sup>, Joshua C Bis<sup>125</sup>, Girish N. Nadkarni<sup>126</sup>, Lenore J Launer<sup>249</sup>, Huaixing Li<sup>140</sup>, Mike A Nalls<sup>145,146</sup>, Olli T Raitakari<sup>250,251,252</sup>, Sahoko Ichihara<sup>253</sup>, Sarah H Wild<sup>254</sup>, Christopher P Nelson<sup>182,183</sup>, Harry Campbell<sup>169</sup>, Susanne Jäger<sup>194,195</sup>, Toru Nabika<sup>255</sup>, Fahd Al-Mulla<sup>256</sup>, Harri Niinikoski<sup>257,258</sup>, Peter S Braund<sup>182,183</sup>, Ivana Kolcic<sup>259</sup>, Peter Kovacs<sup>260</sup>, Tota Giardoglou<sup>261</sup>, Tomohiro Katsuya<sup>262,263</sup>, Konain Fatima Bhatti<sup>5</sup>, Dominique de Kleijn<sup>264</sup>, Gert J. de Borst<sup>264</sup>, Eung Kweon Kim<sup>265</sup>, Hieab H.H. Adams<sup>241,266</sup>, M. Arfan Ikram<sup>241</sup>, Xiaofeng Zhu<sup>239</sup>, Folkert W Asselbergs<sup>238</sup>, Adriaan O Kraaijeveld<sup>238</sup>, Joline WJ Beulens<sup>133,267</sup>, Xiao-Ou Shu<sup>177</sup>, Loukianos S Rallidis<sup>268</sup>, Oluf Pedersen<sup>96</sup>, Torben Hansen<sup>96</sup>, Paul Mitchell<sup>269</sup>, Alex W Hewitt<sup>270,271</sup>, Mika Kähönen<sup>272,273</sup>, Louis Pérusse<sup>229,274</sup>, Claude Bouchard<sup>275</sup>, Anke Tönjes<sup>276</sup>, Yii-Der Ida Chen<sup>92</sup>, Craig E Pennell<sup>223</sup>, Trevor A Mori<sup>277</sup>, Wolfgang Lieb<sup>278</sup>, Andre Franke<sup>279</sup>, Claes Ohlsson<sup>280,281</sup>, Dan Mellström<sup>280,282</sup>, Yoon Shin Cho<sup>214</sup>, Hyejin Lee<sup>283</sup>, Jian-Min Yuan<sup>284,285</sup>, Woon-Puay Koh<sup>286,287</sup>, Sang Youl Rhee<sup>288</sup>, Jeong-Taek Woo<sup>288</sup>, Iris M Heid<sup>11</sup>, Klaus J Stark<sup>11</sup>, Henry Völzke<sup>289</sup>, Georg Homuth<sup>212</sup>, Michele K Evans<sup>290</sup>, Alan B Zonderman<sup>290</sup>, Ozren Polasek<sup>259</sup>, Gerard Pasterkamp<sup>210</sup>, Imo E Hoefer<sup>210</sup>, Susan Redline<sup>208,209</sup>, Katja Pakkala<sup>206,207,291</sup>, Albertine J Oldehinkel<sup>292</sup>, Harold Snieder<sup>205</sup>, Ginevra Biino<sup>293</sup>, Reinhold Schmidt<sup>200</sup>, Helena Schmidt<sup>294</sup>, Y Eugene Chen<sup>1</sup>, Stefania Bandinelli<sup>295</sup>, George Dedoussis<sup>198</sup>, Thangavel Alphonse Thanaraj<sup>256</sup>, Sharon LR Kardia<sup>196</sup>, Norihiro Kato<sup>179</sup>, Matthias B Schulze<sup>194,195,296</sup>, Giorgia Grotto<sup>193,297</sup>, Bettina Jung<sup>298</sup>, Carsten A Böger<sup>298,299,300</sup>, Peter K Joshi<sup>169</sup>, David A Bennett<sup>190,191</sup>, Philip L De Jager<sup>301,302</sup>, Xiangfeng Lu<sup>114</sup>, Vasiliki Mamakou<sup>303,304</sup>, Morris Brown<sup>305,95</sup>, Mark J Caulfield<sup>94,95</sup>, Patricia B Munroe<sup>94,95</sup>, Xiuqing Guo<sup>92</sup>, Marina Ciullo<sup>186,187</sup>, Jost B. Jonas<sup>306,307,308</sup>, Nilesh J Samani<sup>182,183</sup>, Jaakko Kaprio<sup>46</sup>, Päivi Pajukanta<sup>309</sup>, Linda S Adair<sup>310,311</sup>, Sonny Augustin Bechayda<sup>312,313</sup>, H. Janaka de Silva<sup>314</sup>, Ananda R Wickremasinghe<sup>315</sup>, Ronald M Krauss<sup>316</sup>, Jer-Yuarn Wu<sup>317</sup>, Wei Zheng<sup>177</sup>, Anneke I den Hollander<sup>176</sup>, Dwaipayan Bharadwaj<sup>318,319</sup>, Adolfo Correa<sup>320</sup>, James G Wilson<sup>321</sup>, Lars Lind<sup>322</sup>, Chew-Kiat Heng<sup>323</sup>, Amanda E Nelson<sup>170,324</sup>, Yvonne M Golightly<sup>170,325,326,327</sup>, James F Wilson<sup>169,147</sup>, Brenda Penninx<sup>328,329</sup>, Hyung-Lae Kim<sup>330</sup>, John Attia<sup>331,164</sup>, Rodney J Scott<sup>331,164</sup>, D C Rao<sup>332</sup>, Donna K Arnett<sup>333</sup>, Mark Walker<sup>334</sup>, Heikki A Koistinen<sup>335,336,337</sup>, Giriraj R Chandak<sup>162,338</sup>, Chittaranjan S Yajnik<sup>339</sup>, Josep M Mercader<sup>340,341,342</sup>, Teresa Tusie-Luna<sup>343,344,345</sup>, Carlos Aguilar-Salinas<sup>346,347</sup>, Clicerio Gonzalez Villalpando<sup>348</sup>, Lorena Orozco<sup>349</sup>, Myriam Fornage<sup>157,350</sup>, E Shyong Tai<sup>351,90</sup>, Rob M van Dam<sup>90,351</sup>, Terho Lehtimäki<sup>230,231</sup>, Nish Chaturvedi<sup>154</sup>, Mitsuhiro Yokota<sup>352</sup>, Jianjun Liu<sup>152</sup>, Dermot F Reilly<sup>353</sup>, Amy Jayne McKnight<sup>150</sup>, Frank Kee<sup>150</sup>, Karl-Heinz Jöckel<sup>148</sup>, Mark I McCarthy<sup>66,354</sup>, Colin NA Palmer<sup>355</sup>, Veronique Vitart<sup>147</sup>, Caroline Hayward<sup>147</sup>, Eleanor Simonsick<sup>356</sup>, Cornelia M van Duijn<sup>144</sup>, Fan Lu<sup>357</sup>, Jia Qu<sup>357</sup>, Haretsugu Hishigaki<sup>141</sup>, Xu Lin<sup>140</sup>, Winfried März<sup>358,359,138</sup>, Esteban J Parra<sup>137</sup>, Miguel Cruz<sup>360</sup>, Vilmundur Gudnason<sup>136,361</sup>, Jean-Claude Tardif<sup>135,362</sup>, Guillaume Lettre<sup>135,363</sup>, Leen M t Hart<sup>134,364,237</sup>, Petra JM Elders<sup>365</sup>, Scott M Damrauer<sup>366,367</sup>, Meena Kumari<sup>368</sup>, Mika Kivimäki<sup>131</sup>, Pim van der Harst<sup>129</sup>, Tim D Spector<sup>127</sup>, Ruth J.F. Loos<sup>126,369</sup>, Michael A Province<sup>121</sup>, Bruce M Psaty<sup>370,371</sup>, Ivan Brandslund<sup>124,372</sup>, Peter P Pramstaller<sup>123</sup>, Kaare Christensen<sup>373</sup>, Samuli Ripatti<sup>46,374,375</sup>, Elisabeth Widén<sup>46</sup>, Hakon Hakonarson<sup>376,377</sup>, Struan F.A. Grant<sup>377,378,379</sup>, Lambertus ALM Kiemeny<sup>119</sup>, Jacqueline de Graaf<sup>119</sup>, Markus Loeffler<sup>117,118</sup>, Florian Kronenberg<sup>380</sup>, Dongfeng Gu<sup>114,381</sup>, Jeanette Erdmann<sup>382</sup>, Heribert Schunkert<sup>383,384</sup>, Paul W Franks<sup>115</sup>, Allan Linneberg<sup>91,385</sup>, J. Wouter Jukema<sup>108,386</sup>, Amit V Khera<sup>387,388,389,390</sup>, Minna Männikkö<sup>391</sup>, Marjo-Riitta Jarvelin<sup>107,392,393</sup>, Zoltan Kutalik<sup>394,105</sup>, Francesco Cucca<sup>395,396</sup>, Dennis O Mook-Kanamori<sup>397,398</sup>, Ko Willems van Dijk<sup>399,400,401</sup>, Hugh Watkins<sup>402,403</sup>, David P Strachan<sup>404</sup>, Niels Grarup<sup>96</sup>, Peter Sever<sup>405</sup>, Neil

Poulter<sup>406</sup>, Jerome I Rotter<sup>92</sup>, Thomas M Dantoft<sup>91</sup>, Fredrik Karpe<sup>407,408</sup>, Matt J Neville<sup>407,408</sup>, Nicholas J Timpson<sup>87,89</sup>, Ching-Yu Cheng<sup>172,409</sup>, Tien-Yin Wong<sup>172,409</sup>, Chiea Chuen Khor<sup>152</sup>, Charumathi Sabanayagam<sup>172,409</sup>, Annette Peters<sup>86,410,411</sup>, Christian Gieger<sup>85,86,411</sup>, Andrew T Hattersley<sup>412</sup>, Nancy L Pedersen<sup>413</sup>, Patrik KE Magnusson<sup>413</sup>, Dorret I Boomsma<sup>414,415,416</sup>, Eco JC de Geus<sup>417,329</sup>, L Adrienne Cupples<sup>79,418</sup>, Joyce B.J. van Meurs<sup>77,78</sup>, Mohsen Ghanbari<sup>78,419</sup>, Penny Gordon-Larsen<sup>310,311</sup>, Wei Huang<sup>420</sup>, Young Jin Kim<sup>13</sup>, Yasuharu Tabara<sup>76</sup>, Nicholas J Wareham<sup>74</sup>, Claudia Langenberg<sup>74</sup>, Eleftheria Zeggini<sup>218,219,421</sup>, Johanna Kuusisto<sup>422</sup>, Markku Laakso<sup>422</sup>, Erik Ingelsson<sup>423,424,425,426</sup>, Goncalo Abecasis<sup>427,428</sup>, John C Chambers<sup>429,68,69,430</sup>, Jaspal S Kooner<sup>69,70,431,432</sup>, Paul S de Vries<sup>67</sup>, Alanna C Morrison<sup>67</sup>, Kari E. North<sup>65</sup>, Martha Daviglus<sup>433</sup>, Peter Kraft<sup>64,434</sup>, Nicholas G Martin<sup>435</sup>, John B Whitfield<sup>435</sup>, Shahid Abbas<sup>436</sup>, Danish Saleheen<sup>61,437,438</sup>, Robin G Walters<sup>245,246,439</sup>, Michael V Holmes<sup>245,246,440</sup>, Corri Black<sup>441</sup>, Blair H Smith<sup>442</sup>, Anne E Justice<sup>443</sup>, Aris Baras<sup>428</sup>, Julie E Buring<sup>444,445</sup>, Paul M Ridker<sup>55,445</sup>, Daniel I Chasman<sup>55,445</sup>, Charles Kooperberg<sup>54</sup>, Wei-Qi Wei<sup>446</sup>, Gail P Jarvik<sup>447</sup>, Bahram Namjou<sup>448</sup>, M. Geoffrey Hayes<sup>449,450,451</sup>, Marylyn D Ritchie<sup>48</sup>, Pekka Jousilahti<sup>47</sup>, Veikko Salomaa<sup>47</sup>, Kristian Hveem<sup>43,452,453</sup>, Bjørn Olav Åsvold<sup>43,452,454</sup>, Michiaki Kubo<sup>455</sup>, Yoichiro Kamatani<sup>456,457</sup>, Yukinori Okada<sup>34,456,458,459</sup>, Yoshinori Murakami<sup>460</sup>, Unnur Thorsteinsdottir<sup>29,461</sup>, Kari Stefansson<sup>29,461</sup>, Yuk-Lam Ho<sup>462</sup>, Julie A Lynch<sup>463,464</sup>, Daniel J Rader<sup>465,466</sup>, Philip S Tsao<sup>2,3,467</sup>, Kyong-Mi Chang<sup>468,465</sup>, Kelly Cho<sup>462,469</sup>, Christopher J O'Donnell<sup>462,469</sup>, John M Gaziano<sup>462,469</sup>, Peter Wilson<sup>470,471</sup>, Charles N Rotimi<sup>16</sup>, Scott Hazelhurst<sup>472,473</sup>, Michèle Ramsay<sup>472,474</sup>, Richard C Trembath<sup>475</sup>, David A van Heel<sup>18</sup>, Gen Tamiya<sup>14</sup>, Masayuki Yamamoto<sup>14</sup>, Bong-Jo Kim<sup>13</sup>, Karen L Mohlke<sup>180</sup>, Timothy M Frayling<sup>83</sup>, Joel N Hirschhorn<sup>9,10,476</sup>, Sekar Kathiresan<sup>477,388,390</sup>, Michael Boehnke<sup>6</sup>, Pradeep Natarajan<sup>478,479,480,481</sup>, Gina M Peloso<sup>482</sup>, Christopher D Brown<sup>7</sup>, Andrew P Morris<sup>483</sup>, Themistocles L Assimes<sup>2,3,467</sup>, Panos Deloukas<sup>5,484,95</sup>, Yan V Sun<sup>20,21</sup>, Cristen J Willer<sup>1,485,486</sup>

#### Affiliations:

<sup>1</sup>Department of Internal Medicine, Division of Cardiology, University of Michigan, Ann Arbor, MI 48109, USA, <sup>2</sup>VA Palo Alto Health Care system, Palo Alto, California, USA, <sup>3</sup>Department of Medicine, Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, California, USA, <sup>4</sup>Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, MI, USA, <sup>5</sup>William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, Charterhouse square, EC1M 6BQ, UK, <sup>6</sup>Department of Biostatistics and Center for Statistics Genetics, University of Michigan, Ann Arbor, MI 48109, USA, <sup>7</sup>Department of Genetics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA, <sup>8</sup>Clinical Pharmacology, William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, EC1M 6BQ UK, <sup>9</sup>Endocrinology, Boston Childrens Hospital, Boston 02115 MA, USA, <sup>10</sup>Medical and Population Genetics, Broad Institute, 75 Ames street, Cambridge, MA 02142, USA, <sup>11</sup>Department of Genetic Epidemiology, University of Regensburg, Regensburg, Germany, <sup>12</sup>McDonnell Genome Institute and Department of Medicine, Washington University, St. Louis, MO, 63108, USA, <sup>13</sup>Division of Genome Science, Department of Precision Medicine, National Institute of Health, Chungcheongbuk-do, South Korea, <sup>14</sup>Tohoku Medical Megabank Organization, Tohoku University, Sendai 980-8573, Japan, <sup>15</sup>Sydney Brenner Institute for Molecular Bioscience, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa., <sup>16</sup>Center for Research on Genomics and Global Health, National Human Genome Research Institute, National Institutes of Health, 12 South Drive, Room 4047, Bethesda, MD, 20892, USA, <sup>17</sup>Department of Genetics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104, USA., <sup>18</sup>Blizard Institute, Barts and the

London School of Medicine and Dentistry, Queen Mary University of London, London, UK, <sup>19</sup>Wellcome Sanger Institute, Hinxton, UK, <sup>20</sup>Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, Georgia, USA, <sup>21</sup>Atlanta VA Health Care System, Decatur, Georgia, USA, <sup>22</sup>Malcolm Randall VA Medical Center, Gainesville, FL, USA, <sup>23</sup>Division of Vascular Surgery and Endovascular Therapy, University of Florida College of Medicine, Gainesville, FL, USA, <sup>24</sup>Program in Medical and Population Genetics, Broad Institute of MIT and Harvard, Cambridge, Massachusetts, USA, <sup>25</sup>Department of Statistics, The Pennsylvania State University, University Park, PA, USA, <sup>26</sup>Huck Institutes of the Life Sciences, The Pennsylvania State University, University Park, PA, USA, <sup>27</sup>VA Palo Alto Health Care System, Palo Alto, CA, USA, <sup>28</sup>Department of Statistics, Stanford University, Stanford, CA, USA, <sup>29</sup>deCODE genetics/Amgen, Inc. Sturlugata 8, Reykjavik, 102, Iceland, <sup>30</sup>School of Engineering and Natural Sciences, University of Iceland, Sæmundargötu 2, Reykjavik, 102, Iceland, <sup>31</sup>Department of Clinical Biochemistry, Landspítali - National University Hospital of Iceland, Hringbraut, Reykjavik, 101, Iceland, <sup>32</sup>Laboratory for Statistical Analysis, RIKEN Center for Integrative Medical Sciences, Japan, <sup>33</sup>Department of Ophthalmology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, <sup>34</sup>Department of Statistical Genetics, Osaka University Graduate School of Medicine, Osaka, Japan, <sup>35</sup>Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, <sup>36</sup>Laboratory for Statistical and Translational Genetics, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan., <sup>37</sup>Laboratory for Statistical Analysis, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan., <sup>38</sup>Program in Medical and Population Genetics, Broad Institute of MIT and Harvard, Cambridge, MA, USA., <sup>39</sup>Department of Biomedical Informatics, Harvard Medical School, Boston, MA, USA., <sup>40</sup>Analytic and Translational Genetics Unit, Massachusetts General Hospital, Boston, Massachusetts, USA, <sup>41</sup>Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, Michigan, USA, <sup>42</sup>Program in Medical and Population Genetics, Broad Institute of Harvard and MIT, Cambridge, Massachusetts, USA, <sup>43</sup>K.G. Jebsen Center for Genetic Epidemiology, Department of Public Health and Nursing, NTNU, Norwegian University of Science and Technology, Trondheim, Norway, <sup>44</sup>MRC Integrative Epidemiology Unit, University of Bristol, UK, <sup>45</sup>Department of Thoracic Medicine, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway, <sup>46</sup>Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Tukholmankatu 8, 00014 Helsinki, Finland, <sup>47</sup>Department of Public Health and Welfare, Finnish institute for Health and Welfare, Helsinki, Finland, <sup>48</sup>Department of Genetics, Institute for Biomedical Informatics, University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA 19104, USA, <sup>49</sup>Division of Clinical Pharmacology, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, <sup>50</sup>Department of Medicine (Medical Genetics), University of Washington, USA, <sup>51</sup>Division of Biomedical Informatics, Cincinnati Children's Hospital Medical Center, USA, <sup>52</sup>Center for Genetic Medicine, Northwestern University, USA, <sup>53</sup>Genentech, 1 DNA Way, South San Francisco, 94084, USA, <sup>54</sup>Fred Hutchinson Cancer Research Center, Division of Public Health Sciences, Seattle WA 9810, USA, <sup>55</sup>Division of Preventive Medicine, Brigham and Women's Hospital, Boston, MA 02215, USA, <sup>56</sup>Centre for Genomic and Experimental Medicine, Institute of Genetics & Molecular Medicine, University of Edinburgh, Western General Hospital, Edinburgh EH4 2XU, United Kingdom, <sup>57</sup>Usher Institute for Population Health Sciences and Informatics, The University of Edinburgh, Nine, Edinburgh Bioquarter, 9 Little France Road, Edinburgh, EH16 4UX, UK, <sup>58</sup>Clinical Trial Service Unit and Epidemiological Studies Unit, Nuffield Department of Population Health, University of Oxford, Oxford OX3 7LF, United Kingdom, <sup>59</sup>Medical Research Council Population Health Research Unit, Nuffield Department of Population Health, University of Oxford, Oxford OX3 7LF, United Kingdom, <sup>60</sup>Department of Population Medicine, Qatar University College of Medicine, QU Health, Doha, Qatar,

<sup>61</sup>Center for Non-Communicable Diseases, Karachi, Sindh, Pakistan, <sup>62</sup>Survey Research Center, Institute for Social Research, University of Michigan, Ann Arbor, MI, 48104, USA, <sup>63</sup>Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, MI, 48109, USA, <sup>64</sup>Program in Genetic Epidemiology and Statistical Genetics, Department of Epidemiology, Harvard T.H. Chan School of Public Health, 677 Huntington Avenue, Boston, MA, 02115, USA, <sup>65</sup>Department of Epidemiology, University of North Carolina, Chapel Hill, NC, USA, <sup>66</sup>Wellcome Centre for Human Genetics, University of Oxford, UK, <sup>67</sup>Human Genetics Center, Department of Epidemiology, Human Genetics, and Environmental Sciences, School of Public Health, The University of Texas Health Science Center at Houston, Houston, Texas, 77030, USA, <sup>68</sup>Department of Epidemiology and Biostatistics, Imperial College London, London W2 1PG, UK, <sup>69</sup>Department of Cardiology, Ealing Hospital, London North West University Healthcare NHS Trust, Middlesex UB1 3HW, UK, <sup>70</sup>Imperial College Healthcare NHS Trust, London W12 0HS, UK, <sup>71</sup>Department of Biostatistics, Center for Statistical Genetics, University of Michigan, Ann Arbor, USA, <sup>72</sup>Department of Medical Sciences, Molecular Epidemiology and Science for Life Laboratory, Uppsala University, Uppsala, Sweden., <sup>73</sup>Department of Biostatistics, Center for Statistical Genetics, University of Michigan, Ann Arbor, MI, 48109, USA, <sup>74</sup>MRC Epidemiology Unit, University of Cambridge School of Clinical Medicine, Cambridge, CB2 0QQ, UK, <sup>75</sup>Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, University of Cambridge Strangeways Research Laboratory, Cambridge, CB1 8RN, UK, <sup>76</sup>Center for Genomic Medicine, Kyoto University Graduate School of Medicine, Kyoto, Japan, <sup>77</sup>Department of Internal Medicine, Erasmus MC, University Medical Center Rotterdam, the Netherlands, <sup>78</sup>Department of Epidemiology, Erasmus MC, University Medical Center Rotterdam, the Netherlands, <sup>79</sup>Department of Biostatistics, Boston University School of Public Health, 801 Massachusetts Ave, Boston, MA 02118, USA, <sup>80</sup>Department of Biological Psychology, Behavioral and Movement Sciences, Vrije Universiteit Amsterdam, Netherlands, <sup>81</sup>Amsterdam Public Health, VU medical center Amsterdam, Netherlands, <sup>82</sup>Amsterdam Public Health research institute, VU medical center Amsterdam, Netherlands, <sup>83</sup>Genetics of Complex Traits, University of Exeter Medical School, University of Exeter, Exeter, EX2 5DW, UK, <sup>84</sup>Department of Clinical Acupuncture and Moxibustion, Nanjing University of Chinese Medicine, Nanjing, Jiangsu 210029, China, <sup>85</sup>Research Unit of Molecular Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany, <sup>86</sup>Institute of Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany, <sup>87</sup>MRC Integrative Epidemiology Unit at the University of Bristol, Oakfield Road, Bristol, BS8 2BN, United Kingdom, <sup>88</sup>Bristol Dental School, University of Bristol, Lower Maudlin Street, Bristol BS1 2LY, United Kingdom, <sup>89</sup>Population Health Sciences, Bristol Medical School, University of Bristol, Oakfield Grove, Bristol, BS8 2BN, United Kingdom, <sup>90</sup>Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, 117549, Singapore, <sup>91</sup>Center for Clinical Research and Prevention, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark, <sup>92</sup>The Institute for Translational Genomics and Population Sciences, Department of Pediatrics, Lundquist Institute for Biomedical Innovations (Formerly LABioMed) at Harbor-UCLA Medical Center, Torrance, CA 90502, USA, <sup>93</sup>Center for Public Health Genomics, University of Virginia, Charlottesville, VA 22903 USA, <sup>94</sup>William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, John Vane Science Centre, Charterhouse Square, London, EC1M 6BQ, UK, <sup>95</sup>NIHR Barts Cardiovascular Biomedical Research Centre, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, EC1M 6BQ, UK, <sup>96</sup>Novo Nordisk Foundation Center for Basic Metabolic Research, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark, <sup>97</sup>Division of Cardiovascular Medicine, Radcliffe Department of Medicine, John

Radcliffe Hospital, University of Oxford, Oxford. United Kingdom. OX3 9DU, <sup>98</sup>Wellcome Centre for Human Genetics, University of Oxford, Oxford. United Kingdom. OX3 7BN, <sup>99</sup>Group of Genomics of Complex Diseases. Research Institute of Hospital de la Santa Creu i Sant Pau (IIB Sant Pau), Barcelona, Spain, <sup>100</sup>Cardiovascular Medicine Unit, Department of Medicine, Karolinska Institutet, Center for Molecular Medicine, Karolinska University Hospital, Stockholm, Sweden, <sup>101</sup>Department of Internal Medicine, Section Gerontology and Geriatrics, Leiden University Medical Center, Leiden, the Netherlands, <sup>102</sup>Institute for Genetic and Biomedical Research, Italian National Council of Research (IRGB CNR), Cagliari Italy, <sup>103</sup>Institute for Genetic and Biomedical Research, Italian National Council of Research (IRGB CNR), Lanusei, Italy, <sup>104</sup>University Center for Primary Care and Public Health, University of Lausanne, Rte de la Corniche 10, Lausanne, 1010, Switzerland, <sup>105</sup>Swiss Institute of Bioinformatics, Lausanne, 1015, Switzerland, <sup>106</sup>Department of Medicine, Internal Medicine, Lausanne University Hospital and University of Lausanne, Rue du Bugnon 46, Lausanne, 1011, Switzerland, <sup>107</sup>Department of Epidemiology and Biostatistics, MRC-PHE Centre for Environment and Health, School of Public Health, Imperial College London, London, UK, <sup>108</sup>Dept of Cardiology, Leiden University Medical Center, Leiden, the Netherlands, <sup>109</sup>Dept of Internal Medicine, Section of Gerontology and Geriatrics, Leiden university Medical Center, Leiden, the Netherlands, <sup>110</sup>BHF Glasgow Cardiovascular Research Centre, Faculty of Medicine, Glasgow, United Kingdom, <sup>111</sup>Institute for Cardiogenetics, University of Lübeck, DZHK (German Research Centre for Cardiovascular Research), partner site Hamburg/Lübeck/Kiel, University Heart Center Lübeck, Lübeck and Charité – University Medicine Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Institute for Dental and Craniofacial Sciences, Department of Periodontology and Synoptic Dentistry, Berlin, Germany, <sup>112</sup>Deutsches Herzzentrum München, Klinik für Herz- und Kreislauferkrankungen, Technische Universität München, Munich, Germany., <sup>113</sup>Deutsches Zentrum für Herz-Kreislauf-Forschung (DZHK) e.V., partner site Munich Heart Alliance, Munich, Germany., <sup>114</sup>Key Laboratory of Cardiovascular Epidemiology & Department of Epidemiology, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100037, China, <sup>115</sup>Lund University Diabetes Centre, Malmö, Sweden, <sup>116</sup>Institute of Genetic Epidemiology, Department of Genetics and Pharmacology, Medical University of Innsbruck, Innsbruck, Austria and German Chronic Kidney Disease study, Austria, <sup>117</sup>Institute for Medical Informatics, Statistics and Epidemiology, University of Leipzig, Haertelstrasse 16-18, 04107 Leipzig, Germany, <sup>118</sup>LIFE Research Centre for Civilization Diseases, University of Leipzig, Philipp-Rosenthal-Straße 27, 04103 Leipzig, Germany, <sup>119</sup>Radboud university medical center, Radboud Institute for Health Sciences, Nijmegen, The Netherlands, <sup>120</sup>Quantinuum Research LLC, Wayne, PA, 19087 USA, <sup>121</sup>Division of Statistical Genomics, Department of Genetics; Washington University School of Medicine; St. Louis, MO, USA, <sup>122</sup>Department of Epidemiology; University of Pittsburgh; Pittsburgh, PA, USA, <sup>123</sup>Institute for Biomedicine, Eurac Research, Affiliated Institute of the University of Lübeck, Via Galvani 31, 39100, Bolzano, Italy, <sup>124</sup>Department of Clinical Biochemistry, Lillebaelt Hospital, Vejle, Denmark, <sup>125</sup>Cardiovascular Health Research Unit, Department of Medicine, University of Washington, Seattle, 98101, USA, <sup>126</sup>The Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, 10029, USA, <sup>127</sup>Department of Twin Research and Genetic Epidemiology, King's College London, London SE1 7EH, UK, <sup>128</sup>NIHR Biomedical Research Centre at Guy's and St Thomas' Foundation Trust, London SE1 9RT, UK, <sup>129</sup>University of Groningen, University Medical Center Groningen, Department of Cardiology, 9700RB Groningen, The Netherlands, <sup>130</sup>Institute of Cardiovascular Sciences, University College London, Gower Street, WC1E 6BT London, UK,

<sup>131</sup>Department of Epidemiology and Public Health, University College London, 1-19 Torrington Place, WC1E 6BT London, United Kingdom, <sup>132</sup>Department of Psychiatry, University of Pennsylvania, Philadelphia, PA, 19104, USA, <sup>133</sup>Amsterdam UMC, Department of Epidemiology and Biostatistics, Amsterdam Public Health Research Institute, Amsterdam, 1081HV, the Netherlands., <sup>134</sup>Leiden University Medical Center, Department of Cell and Chemical Biology, Leiden, 2333ZA, The Netherlands, <sup>135</sup>Montreal Heart Institute, 5000 Belanger Street, Montreal, Quebec, H1T 1C8, Canada, <sup>136</sup>Icelandic Heart Association, 201 Kopavogur, Iceland, <sup>137</sup>Department of Anthropology, University of Toronto at Mississauga, Mississauga, ON L5L 1C6, Canada, <sup>138</sup>Vth Department of Medicine, Medical Faculty Mannheim, Heidelberg University, 68167 Mannheim, Germany, <sup>139</sup>SYNLAB MVZ Humangenetik Mannheim GmbH, 68163 Mannheim, Germany, <sup>140</sup>Shanghai Institute of Nutrition and Health, University of Chinese Academy of Sciences, Chinese Academy of Sciences, Shanghai, China, <sup>141</sup>Biomedical Technology Research Center, Tokushima Research Institute, Otsuka Pharmaceutical Co., Ltd., Tokushima, Japan, <sup>142</sup>Institute for Molecular Bioscience, The University of Queensland, Brisbane, Queensland 4072, Australia, <sup>143</sup>Institute for Advanced Research, Wenzhou Medical University, Wenzhou, Zhejiang 325027, China, <sup>144</sup>Nuffield Department of Population Health, University of Oxford, Oxford, United Kingdom, <sup>145</sup>Laboratory of Neurogenetics, National Institute on Aging, NIH, Bethesda MD, USA, <sup>146</sup>Data Tecnica International, Glen Echo MD, USA, <sup>147</sup>MRC Human Genetics Unit, Institute of Genetics and Cancer, University of Edinburgh, Western General Hospital, Crewe Road, Edinburgh, EH4 2XU, Scotland, <sup>148</sup>Institute for Medical Informatics, Biometrie and Epidemiology, University of Duisburg-Essen, Essen, Germany, <sup>149</sup>Department of Computer Science, University of Applied Sciences and Arts Dortmund, Emil-Figge-Str. 42, 44227 Dortmund, Germany, <sup>150</sup>Centre for Public Health, Queen's University of Belfast, Northern Ireland, <sup>151</sup>Department of Epidemiology and Biostatistics, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, <sup>152</sup>Genome Institute of Singapore, Agency for Science, Technology and Research, 138672, Singapore, <sup>153</sup>Public Health Informatics Unit, Department of Integrated Health Sciences, Nagoya University Graduate School of Medicine, Nagoya, 461-8673, Japan, <sup>154</sup>MRC Unit for Lifelong Health and Ageing at UCL, 1-19 Torrington Place, London, WC1E 7HB, United Kingdom, <sup>155</sup>Department of Pediatrics, Tampere University Hospital, Tampere 33521, Finland, <sup>156</sup>Department of Pediatrics, Faculty of Medicine and Health Technology, Tampere University, Tampere 33014, Finland, <sup>157</sup>Brown Foundation Institute of Molecular Medicine, McGovern Medical School, University of Texas Health Science Center at Houston, Houston TX 77030, USA, <sup>158</sup>Departamento de Medicina Genómica y Toxicología Ambiental, Instituto de Investigaciones Biomédicas, UNAM, Ciudad de Mexico, Mexico, <sup>159</sup>Departamento de Genómica Computacional, Instituto Nacional de Medicina Genómica, Ciudad de Mexico, Mexico, <sup>160</sup>Center for diabetes research, University of Bergen, Bergen, Norway, <sup>161</sup>Lund University Diabetes Center, Lunds University, Malmö, Sweden, <sup>162</sup>Genomic Research on Complex diseases (GRC Group), CSIR-Centre for Cellular and Molecular Biology, Hyderabad, Telangana, India, <sup>163</sup>University of Alabama at Birmingham, Epidemiology, School of Public Health, Birmingham, Alabama, USA, <sup>164</sup>Hunter Medical Research Institute, Newcastle, Australia, <sup>165</sup>Medical Research Institute, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, 03181, Korea, <sup>166</sup>Department of Clinical Research Design & Evaluation, SAIHST, Sungkyunkwan University, Seoul, 06355, Korea, <sup>167</sup>Center for Cohort Studies, Total Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, 04514, Korea, <sup>168</sup>Department of Occupational and Environmental Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, 03181, Korea, <sup>169</sup>Centre for Global Health Research, Usher Institute, University of Edinburgh, Teviot Place, Edinburgh, EH8 9AG, Scotland, <sup>170</sup>Thurston Arthritis Research

Center, University of North Carolina, Chapel Hill, North Carolina, USA, <sup>171</sup>Division of Biomedical Informatics and Personalized Medicine, Department of Medicine, Anschutz Medical Campus, University of Colorado, Denver, Aurora, CO 80045, USA, <sup>172</sup>Ocular Epidemiology, Singapore Eye Research Institute, Singapore National Eye Centre, 168751, Singapore, <sup>173</sup>Department of Ophthalmology, National University of Singapore and National University Health System, 119228, Singapore, <sup>174</sup>Genomics and Molecular Medicine Unit, CSIR-Institute of Genomics and Integrative Biology, New Delhi - 110020, India., <sup>175</sup>Academy of Scientific and Innovative Research, CSIR-Institute of Genomics and Integrative Biology Campus, New Delhi 110020, India., <sup>176</sup>Departments of Ophthalmology and Human Genetics, Radboud University Nijmegen Medical Center, Philips van Leydenlaan 15, Nijmegen, 6525 EX, the Netherlands, <sup>177</sup>Vanderbilt Epidemiology Center, Division of Epidemiology, Vanderbilt University Medical Center, Nashville, TN, USA, <sup>178</sup>Department of Pediatrics, University of California San Francisco, Oakland, CA 94609 USA, <sup>179</sup>National Center for Global Health and Medicine, Tokyo, 1628655, Japan, <sup>180</sup>Department of Genetics, University of North Carolina, Chapel Hill, NC 27599 USA, <sup>181</sup>Department of Biostatistics and Epidemiology, University of Massachusetts-Amherst, Amherst, MA 01003 USA, <sup>182</sup>Department of Cardiovascular Sciences, University of Leicester, Leicester, UK, <sup>183</sup>NIHR Leicester Biomedical Research Centre, Glenfield Hospital, Leicester, UK, <sup>184</sup>Beijing Institute of Ophthalmology, Beijing Key Laboratory of Ophthalmology and Visual Sciences, Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University, 17 Hougou Lane, Chong Wen Men, Beijing, 100005, China, <sup>185</sup>Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University, 1 Dong Jiao Min Xiang, Dong Cheng District, Beijing, 100730, China, <sup>186</sup>Institute of Genetics and Biophysics "Adriano Buzzati-Traverso" - CNR, Naples, Italy, <sup>187</sup>IRCCS Neuromed, Pozzilli, Isernia, Italy, <sup>188</sup>Department of Psychiatry, Washington University, St. Louis, MO 63110, USA, <sup>189</sup>Division of Endocrinology and Metabolism, Tri-Service General Hospital Songshan Branch, Taipei, Taiwan, <sup>190</sup>Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, Illinois, USA, <sup>191</sup>Department of Neurological Sciences, Rush University Medical Center, Chicago, Illinois, USA, <sup>192</sup>Department of Nephrology, University Hospital Regensburg, Regensburg, Germany, <sup>193</sup>Department of Medicine, Surgery and Health Sciences, University of Trieste, Strada di Fiume 447, 34149, Trieste, Italy, <sup>194</sup>Department of Molecular Epidemiology, German Institute of Human Nutrition Potsdam-Rehbruecke, Nuthetal, Germany, <sup>195</sup>German Center for Diabetes Research (DZD), München-Neuherberg, Germany, <sup>196</sup>Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, MI 48109, USA, <sup>197</sup>Department of Genetics and Bioinformatics, Dasman Diabetes Institute, Kuwait City, Kuwait, <sup>198</sup>Department of Nutrition and Dietetics, School of Health Science and Education, Harokopio University of Athens, Athens, Greece, <sup>199</sup>Department of Population Science and Experimental Medicine, University College London, London, UK, <sup>200</sup>Clinical Division of Neurogeriatrics, Department of Neurology, Medical University of Graz, Graz, Austria, <sup>201</sup>Institute for Medical Informatics, Statistics and Documentation, Medical University of Graz, Graz, Austria, <sup>202</sup>Department of Bioinformatics and Genomics, University of North Carolina at Charlotte, NC 28223 USA, <sup>203</sup>Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy, <sup>204</sup>Institute of Genetic and Biomedical Research, National Research Council of Italy, UOS of Sassari, Sassari, Italy, <sup>205</sup>University of Groningen, University Medical Center Groningen, Department of Epidemiology, Groningen, 9700 RB, the Netherlands, <sup>206</sup>Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku, Turku, Finland, <sup>207</sup>Centre for Population Health Research, University of Turku and Turku University Hospital, Turku, Finland, <sup>208</sup>Sleep Medicine and Circadian Disorders, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA, <sup>209</sup>Division of Sleep Medicine, Harvard Medical School, Boston, Massachusetts 02115, USA, <sup>210</sup>Central Diagnostics Laboratory, Division Laboratories, Pharmacy, and Biomedical genetics, University

Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands, <sup>211</sup>Laboratory of Epidemiology and Population Science National Institute on Aging Intramural Research Program, NIH 251 Bayview Blvd, NIH Biomedical Research Center, NIA, Baltimore, MD 21224, USA, <sup>212</sup>Interfaculty Institute for Genetics and Functional Genomics, Department of Functional Genomics, University of Greifswald and University Medicine Greifswald, Greifswald, Germany, <sup>213</sup>Oneomics. co. ltd. 2F, Soonchunhyang Mirai Medical Center 173, Buheuyng-ro, Bucheon-si Gyeonggi-do, 14585, Korea, <sup>214</sup>Department of Biomedical Science, Hallym University, Chuncheon, Gangwon-do 24252, Korea, <sup>215</sup>Centre for Bone and Arthritis Research, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden., <sup>216</sup>Bioinformatics Core Facility, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, <sup>217</sup>Institute of Medical Informatics and Statistics, Kiel University, Kiel, Germany., <sup>218</sup>Institute of Translational Genomics, Helmholtz Zentrum München – German Research Center for Environmental Health, Neuherberg, Germany, <sup>219</sup>Wellcome Trust Sanger Institute, Hinxton, CB10 1SA, UK, <sup>220</sup>Wellcome Centre for Human Genetics, University of Oxford, Oxford, UK, <sup>221</sup>Oxford Centre for Diabetes Endocrinology and Metabolism, Oxford, UK, <sup>222</sup>Wellcome Sanger Institute, Hinxton, Cambridge, HH CB10 1 UK, <sup>223</sup>School of Medicine and Public Health, College of Health, Medicine and Wellbeing, University of Newcastle, Newcastle, New South Wales, 2308, Australia, <sup>224</sup>Center for Geriatrics and Gerontology, Division of Endocrinology and Metabolism, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan, <sup>225</sup>School of Medicine, National Yang-Ming University, Taipei, Taiwan, <sup>226</sup>School of Medicine, National Defense Medical Center, Taipei, Taiwan, <sup>227</sup>Division of Endocrinology and Metabolism, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan, <sup>228</sup>Department of Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan, <sup>229</sup>Dept of Kinesiology, Université Laval, Québec, Canada, <sup>230</sup>Department of Clinical Chemistry, Fimlab Laboratories, Tampere 33520, Finland, <sup>231</sup>Department of Clinical Chemistry, Finnish Cardiovascular Research Center - Tampere, Faculty of Medicine and Health Technology, Tampere University, Tampere 33014, Finland, <sup>232</sup>Department of Cardiology, Heart Center, Tampere University Hospital, Tampere 33521, Finland, <sup>233</sup>Department of Cardiology, Finnish Cardiovascular Research Center - Tampere, Faculty of Medicine and Health Technology, Tampere University, Tampere 33014, Finland, <sup>234</sup>University of Queensland Diamantina Institute, Translational Research Institute, Kent St, Woolloongabba, Brisbane, QLD, 4102, Australia., <sup>235</sup>Novo Nordisk Foundation Center for Basic Metabolic Research, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark, Department of Medicine, Bornholms Hospital, Rønne, Denmark, <sup>236</sup>School of Public Health, University of Alabama at Birmingham, Birmingham, Alabama, USA, <sup>237</sup>Amsterdam UMC, Department of Epidemiology and Biostatistics, Amsterdam Public Health Research Institute, Amsterdam, 1081HV, the Netherlands, <sup>238</sup>Cardiology, Division Heart & Lungs, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands, <sup>239</sup>Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, OH, 44106, USA, <sup>240</sup>Division of Statistical Genomics, Department of Genetics, Washington University School of Medicine, St. Louis, MO, USA, <sup>241</sup>Department of Epidemiology - Erasmus MC - University Medical Center Rotterdam, Rotterdam, the Netherlands, <sup>242</sup>Ohio State University, Division of Endocrinology, Columbus OH 43210, USA, <sup>243</sup>University of Washington, Department of Epidemiology, Seattle WA 98195, USA, <sup>244</sup>George Washington University, School of Medicine and Health Sciences, Washington DC 20037, USA, <sup>245</sup>Clinical Trial Service Unit and Epidemiological Studies Unit, Nuffield Department of Population Health, University of Oxford, Oxford OX3 7LF, UK, <sup>246</sup>Medical Research Council Population Health Research Unit, Nuffield Department of Population Health, University of Oxford, Oxford OX3 7LF, UK, <sup>247</sup>Department of Epidemiology, School of

Public Health, Peking University Health Science Center, Beijing, China, <sup>248</sup>Institute for Laboratory Medicine, University Hospital Leipzig, Paul-List-Strasse 13/15, 04103 Leipzig, Germany, <sup>249</sup>Laboratory of Epidemiology and Population Sciences, National Institute on Aging, NIH, Baltimore, MD, 20892-9205, USA, <sup>250</sup>Centre for Population Health Research, University of Turku and Turku University Hospital, Finland, <sup>251</sup>Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku, Finland, <sup>252</sup>Department of Clinical Physiology and Nuclear Medicine, Turku University Hospital, Turku, Finland, <sup>253</sup>Department of Environmental and Preventive Medicine, Jichi Medical University School of Medicine, Shimotsuke, 329-0498, Japan, <sup>254</sup>Centre for Population Health Sciences, Usher Institute, University of Edinburgh, Teviot Place, Edinburgh, EH8 9AG, Scotland, <sup>255</sup>Department of Functional Pathology, Shimane University School of Medicine, Izumo, 6938501, Japan, <sup>256</sup>Department of Genetics and Bioinformatics, Dasman Diabetes Institute, Kuwait, <sup>257</sup>Department of Pediatrics and Adolescent Medicine, Turku University Hospital and University of Turku, Turku, Finland, <sup>258</sup>Department of Physiology, University of Turku, Turku, Finland, <sup>259</sup>Faculty of Medicine, University of Split, Šoltanska 2, HR-21000, Split, Croatia, <sup>260</sup>Medical Department III – Endocrinology, Nephrology, Rheumatology, University of Leipzig Medical Center, Liebigstr. 21, 04103 Leipzig, Germany, <sup>261</sup>Department of Nutrition-Dietetics, Harokopio University, Eleftheriou Venizelou, Athens, 17676, Greece, <sup>262</sup>Department of Clinical Gene Therapy, Osaka University Graduate School of Medicine, Suita, 5650871, Japan, <sup>263</sup>Department of Geriatric and General Medicine, Osaka University Graduate School of Medicine, Suita, 5650871, Japan, <sup>264</sup>Department of Vascular Surgery, Division of Surgical Specialties, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands, <sup>265</sup>Corneal Dystrophy Research Institute, Department of Ophthalmology, Yonsei University College of Medicine, Seoul 03722, Korea, <sup>266</sup>Dept of Radiology and Nuclear Medicine, Erasmus MC - University Medical Center Rotterdam, Rotterdam, the Netherlands, <sup>267</sup>Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, 3584CG, the Netherlands, <sup>268</sup>Second Department of Cardiology, Medical School, National and Kapodistrian University of Athens, Attikon University Hospital, Athens, Greece, <sup>269</sup>Center for Vision Research, Department of Ophthalmology and The Westmead Institute, University of Sydney, Hawkesbury Rd, Sydney, New South Wales, 2145, Australia, <sup>270</sup>Menzies Institute for Medical Research, School of Medicine, University of Tasmania, Liverpool St, Hobart, Tasmania, 7000, Australia, <sup>271</sup>Centre for Eye Research Australia, University of Melbourne, Melbourne, Victoria, 3002, Australia, <sup>272</sup>Department of Clinical Physiology, Tampere University Hospital, Tampere 33521, Finland, <sup>273</sup>Department of Clinical Physiology, Finnish Cardiovascular Research Center - Tampere, Faculty of Medicine and Health Technology, Tampere University, Tampere 33014, Finland, <sup>274</sup>Institute of Nutrition and Functional Foods (INAF), Université Laval, Québec, Canada, <sup>275</sup>Pennington Biomedical Research Center, Baton Rouge, LA 70808, USA, <sup>276</sup>Medical Department III – Endocrinology, Nephrology, Rheumatology, University of Leipzig Medical Center, Liebigstr. 18, 04103 Leipzig, Germany, <sup>277</sup>Medical School, Faculty of Health and Medical Sciences, University of Western Australia, Perth, Western Australia, 6000, Australia, <sup>278</sup>Institute of Epidemiology, Kiel University, Kiel, Germany, <sup>279</sup>Institute of Clinical Molecular Biology, Kiel University, Kiel, Germany, <sup>280</sup>Centre for Bone and Arthritis Research, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, <sup>281</sup>Sahlgrenska University Hospital, Department of Drug Treatment, Gothenburg, Sweden, <sup>282</sup>Geriatric Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, <sup>283</sup>Department of Internal Medicine, EwhaWomans University School of Medicine, Seoul, Korea, <sup>284</sup>Division of Cancer Control and Population Sciences, UPMC Hillman Cancer Center, University of Pittsburgh, Pittsburgh, PA 15232, USA, <sup>285</sup>Department of Epidemiology, Graduate School of Public

Health, University of Pittsburgh, Pittsburgh, PA 15232, USA, <sup>286</sup>Healthy Longevity Translational Research Programme, Yong Loo Lin School of Medicine, National University of Singapore, Singapore 117545, Singapore, <sup>287</sup>Singapore Institute for Clinical Sciences, Agency for Science Technology and Research (A\*STAR), Singapore 117609, Singapore, <sup>288</sup>Department of Endocrinology and Metabolism, Kyung Hee University School of Medicine, Seoul 02447, Korea, <sup>289</sup>Institute for Community Medicine, University Medicine Greifswald, Germany, <sup>290</sup>Laboratory of Epidemiology and Population Science National Institute on Aging Intramural Research Program, NIH 251 Bayview Blvd, NIH Biomedical Research Center, Baltimore, MD 21224, USA, <sup>291</sup>Paavo Nurmi Centre, Sports and Exercise Medicine Unit, Department of Physical Activity and Health, University of Turku, Turku, Finland, <sup>292</sup>University of Groningen, University Medical Center Groningen, Interdisciplinary Center Psychopathology and Emotion Regulation (ICPE), Groningen, 9700 RB, the Netherlands, <sup>293</sup>Institute of Molecular Genetics, National Research Council of Italy, Pavia, Italy, <sup>294</sup>Gottfried Schatz Research Center for Cell Signaling, Metabolism and Aging, Medical University of Graz, Graz, Austria, <sup>295</sup>Local Health Unit Toscana Centro, Firenze, Italy, <sup>296</sup>Institute of Nutritional Science, University of Potsdam, Nuthetal, Germany, <sup>297</sup>Institute for Maternal and Child Health IRCCS "Burlo Garofolo", Via dell'Istria 65/1, 34137, Trieste, Italy, <sup>298</sup>Dept of Nephrology, University Hospital Regensburg, Regensburg, Germany, <sup>299</sup>Dept of Nephrology, Diabetology, Rheumatology; Traunstein Hospital, Traunstein, Germany, <sup>300</sup>KfH Kidney Center Traunstein, Traunstein, Germany, <sup>301</sup>Center for Translational and Systems Neuroimmunology, Department of Neurology, Columbia University Medical Center, New York, NY, USA, <sup>302</sup>Program in Medical and Population Genetics, Broad Institute, Cambridge, MA, USA, <sup>303</sup>Medical School, National and Kapodistrian University Athens, 75 M. Assias Street, 115 27 Athens, Greece, <sup>304</sup>Dromokaiteio Psychiatric Hospital, 124 61 Athens, Greece, <sup>305</sup>Clinical Pharmacology, William Harvey Research Institute, Queen Mary University of London, London, EC1M 6BQ, UK, <sup>306</sup>Department of Ophthalmology, Medical Faculty Mannheim, Heidelberg University, Kutzerufer 1, Mannheim, 68167, Germany, <sup>307</sup>Beijing Institute of Ophthalmology, Beijing Key Laboratory of Ophthalmology and Visual Sciences, Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University, 17 Hougou Lane, Chong Wen Men, Beijing, 100005, China, <sup>308</sup>Institute of Molecular and Clinical Ophthalmology Basel, Switzerland, <sup>309</sup>Department of Human Genetics, David Geffen School of Medicine at UCLA, University of California, Los Angeles, CA, USA, <sup>310</sup>Department of Nutrition, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, North Carolina, 27599 USA, <sup>311</sup>Carolina Population Center, University of North Carolina, Chapel Hill, North Carolina, 27516 USA, <sup>312</sup>USC–Office of Population Studies Foundation, University of San Carlos, Cebu City, 6000, Philippines, <sup>313</sup>Department of Anthropology, Sociology, and History, University of San Carlos, Cebu City, 6000 Philippines, <sup>314</sup>Department of Medicine, Faculty of Medicine, University of Kelaniya, Ragama, 11010, Sri Lanka, <sup>315</sup>Department of Public Health, Faculty of Medicine, University of Kelaniya, Ragama, 11010, Sri Lanka, <sup>316</sup>Departments of Pediatrics and Medicine, University of California, San Francisco, San Francisco, CA, <sup>317</sup>Institute of Biomedical Sciences, Academia Sinica, Taiwan, <sup>318</sup>Academy of Scientific and Innovative Research, CSIR-Institute of Genomics and Integrative Biology Campus, New Delhi 110020, India, <sup>319</sup>Systems Genomics Laboratory, School of Biotechnology, Jawaharlal Nehru University, New Delhi - 110067, India, <sup>320</sup>Department of Medicine, University of Mississippi Medical Center, Jackson, MS, 39216, USA, <sup>321</sup>Department of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, MS, 39216, USA, <sup>322</sup>Department of Medical Sciences, Uppsala University, Sweden, <sup>323</sup>Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore; and Khoo Teck Puat - National University Children's Medical Institute, National University Health System, Singapore, <sup>324</sup>Department of Medicine, University of North Carolina, Chapel Hill, NC, USA, <sup>325</sup>Department of

Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, North Carolina, USA, <sup>326</sup>Injury Prevention Research Center, University of North Carolina, Chapel Hill, North Carolina, USA, <sup>327</sup>Division of Physical Therapy, University of North Carolina, Chapel Hill, North Carolina, USA, <sup>328</sup>Department of Psychiatry, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands, <sup>329</sup>Amsterdam Public Health research institute, VU medical center Amsterdam, Amsterdam, the Netherlands, <sup>330</sup>Department of Biochemistry, College of Medicine, Ewha Womans University, Seoul 07804, Korea, <sup>331</sup>Faculty of Health and Medicine, University of Newcastle, Newcastle, Australia, <sup>332</sup>Washington University School of Medicine, Division of Biostatistics, St Louis, MO, USA, <sup>333</sup>University of Kentucky, College of Public Health, Lexington, KY, USA, <sup>334</sup>Institute of Cellular Medicine (Diabetes), The Medical School, Newcastle University, Framlington Place, Newcastle upon Tyne, NE2 4HH, UK, <sup>335</sup>Department of Population Health, Finnish Institute for Health and Welfare, P.O. Box 30, FI-00271 Helsinki, Finland, <sup>336</sup>University of Helsinki and Department of Medicine, Helsinki University Hospital, P.O.Box 340, Haartmaninkatu 4, Helsinki, FI-00029, Finland, <sup>337</sup>Minerva Foundation Institute for Medical Research, Biomedicum 2U, Tukholmankatu 8, Helsinki, FI-00290, Finland, <sup>338</sup>Academy of Scientific and Innovative Research (AcSIR), New Delhi, India, <sup>339</sup>Diabetology Research Centre, KEM Hospital and Research Centre, Pune, Maharashtra, India, <sup>340</sup>Programs in Metabolism and Medical and Population Genetics, Broad Institute of MIT and Harvard, Cambridge, MA, USA, <sup>341</sup>Diabetes Unit and Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, USA, <sup>342</sup>Harvard Medical School, Boston, Massachusetts, USA, <sup>343</sup>Unidad de Biología Molecular y Medicina Genómica, Instituto de Investigaciones Biomédicas UNAM/ Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, <sup>344</sup>Unidad de Biología Molecular y Medicina Genómica, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico 14080, Mexico, <sup>345</sup>Instituto de Investigaciones Biomédicas, UNAM, Ciudad de México, CDMX, Mexico, <sup>346</sup>Dirección de Nutrición and Unidad de Estudios de Enfermedades Metabólicas, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, <sup>347</sup>Departamento de Endocrinología y Metabolismo, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico 14080, Mexico, <sup>348</sup>Instituto Nacional de Salud Publica y Centro de Estudios en Diabetes, Cuernavaca, Mexico, <sup>349</sup>Instituto Nacional de Medicina Genómica, 14610 Ciudad de México, CDMX, Mexico, <sup>350</sup>Human Genetics Center, School of Public Health, University of Texas Health Science Center at Houston, Houston TX 77030, USA, <sup>351</sup>Yong Loo Lin School of Medicine, National University of Singapore and National University Health System, 119228, Singapore, <sup>352</sup>Kurume University School of Medicine, Kurume, 830-0011, Japan, <sup>353</sup>Genetics, Merck Sharp & Dohme Corp., Kenilworth, NJ, 07033, USA, <sup>354</sup>Oxford Centre for Diabetes, Endocrinology & Metabolism, University of Oxford, UK, <sup>355</sup>Population Health and Genomics, University of Dundee, Ninewells Hospital and Medical School, Dundee, DD1 9SY, UK, <sup>356</sup>Intramural Research Program, National Institute on Aging, 3001 S. Hanover St., Baltimore, MD 21225, USA, <sup>357</sup>The Eye Hospital, School of Ophthalmology & Optometry, Wenzhou Medical University, Wenzhou, Zhejiang 325027, China, <sup>358</sup>Synlab Academy, SYNLAB Holding Deutschland GmbH, Mannheim and Augsburg, Germany, <sup>359</sup>Clinical Institute of Medical and Chemical Laboratory Diagnostics, Medical University of Graz, Austria, <sup>360</sup>Unidad de Investigación Médica en Bioquímica, Hospital de Especialidades, Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Mexico City, Mexico, <sup>361</sup>Faculty of Medicine, University of Iceland, 101 Reykjavik, Iceland, <sup>362</sup>Department of Medicine, Faculty of Medicine, Université de Montréal, 2900 Edouard Montpetit Blvd, Montreal, Quebec, H3T 1J4, Canada, <sup>363</sup>Department of Medicine, Faculty of Medicine, Université de Montréal, 2900 Edouard Montpetit Blvd, Montreal, Quebec, H3T 1J4, Canada, <sup>364</sup>Leiden University Medical Center, Department of Biomedical Data Sciences, Section Molecular Epidemiology, Leiden,

2333ZA, The Netherlands, <sup>365</sup>Amsterdam UMC, Department of General Practice and Elderly Care, Amsterdam Public Health Research Institute, Amsterdam, 1081HV, The Netherlands, <sup>366</sup>Department of Surgery, University of Pennsylvania, Philadelphia, PA, 19104, USA, <sup>367</sup>Corporal Michael Crescenz VA Medical Center, Philadelphia, Pennsylvania, PA, 19104, USA, <sup>368</sup>Institute of Social and Economic Research, University of Essex, Wivenhoe Park, CO4 3SQ, United Kingdom, <sup>369</sup>The Mindich Child Health and Development Institute, Icahn School of Medicine at Mount Sinai, New York, NY, 10029, USA, <sup>370</sup>Cardiovascular Health Research Unit, Departments of Medicine, Epidemiology and Health Services, University of Washington, Seattle, 98101, WA, USA, <sup>371</sup>Kaiser Permanent Washington Health Research Institute, Seattle, 98101, WA, USA, <sup>372</sup>Institute of Regional Health Research, University of Southern Denmark, Odense, Denmark, <sup>373</sup>Danish Aging Research Center, University of Southern Denmark; Odense C, Denmark, <sup>374</sup>Public Health, Faculty of Medicine, University of Helsinki, Finland, <sup>375</sup>Broad Institute of MIT and Harvard, Cambridge, MA, USA, <sup>376</sup>Center for Applied Genomics, Children's Hospital of Philadelphia, Philadelphia, PA, 19104 USA, <sup>377</sup>Department of Pediatrics, The University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, 19104 USA, <sup>378</sup>Division of Human Genetics, Children's Hospital of Philadelphia, Philadelphia, PA, 19104 USA, <sup>379</sup>Department of Genetics, University of Pennsylvania, Philadelphia, PA, 19104 USA, <sup>380</sup>Institute of Genetic Epidemiology, Department of Genetics and Pharmacology, Medical University of Innsbruck, Innsbruck, Austria and German Chronic Kidney Disease study, <sup>381</sup>School of Medicine, Southern University of Science and Technology, Shenzhen, China, <sup>382</sup>Institute for Cardiogenetics, University of Lübeck, DZHK (German Research Centre for Cardiovascular Research), partner site Hamburg/Lübeck/Kiel, and University Heart Center Lübeck, Lübeck, Germany, <sup>383</sup>Deutsches Herzzentrum München, Klinik für Herz- und Kreislauferkrankungen, Technische Universität München, Munich, Germany, <sup>384</sup>Deutsches Zentrum für Herz-Kreislauf-Forschung (DZHK) e.V., partner site Munich Heart Alliance, Munich, Germany, <sup>385</sup>Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark, <sup>386</sup>Netherlands Heart Institute, Utrecht, the Netherlands, <sup>387</sup>Division of Cardiology, Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA, <sup>388</sup>Program of Medical and Population Genetics, Broad Institute, Cambridge, Massachusetts, USA, <sup>389</sup>Center for Genomic Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA, <sup>390</sup>Department of Medicine, Harvard Medical School, Boston, Massachusetts, USA, <sup>391</sup>Northern Finland Birth Cohorts, Infrastructure for population studies, Faculty of Medicine, University of Oulu, Oulu, Finland, <sup>392</sup>Center for Life Course Health Research, Faculty of Medicine, University of Oulu, Oulu, Finland, <sup>393</sup>Biocenter of Oulu, University of Oulu, Oulu, Finland, <sup>394</sup>University Center for Primary Care and Public Health, Rte de Berne 113, Lausanne, 1010, Switzerland, <sup>395</sup>Institute for Genetic and Biomedical Research, Italian National Council of Research (IRGB CNR), Cagliari, Italy, <sup>396</sup>University of Sassari, Sassari, Italy, <sup>397</sup>Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, the Netherlands, <sup>398</sup>Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, the Netherlands, <sup>399</sup>Department of Internal Medicine, Division of Endocrinology, Leiden University Medical Center, Leiden, the Netherlands, <sup>400</sup>Einthoven Laboratory for Experimental Vascular Medicine, Leiden University Medical Center, Leiden, the Netherlands, <sup>401</sup>Department of Human Genetics, Leiden University Medical Center, Leiden, the Netherlands, <sup>402</sup>Division of Cardiovascular Medicine, Radcliffe Department of Medicine, John Radcliffe Hospital, University of Oxford, Oxford, OX3 9DU, UK, <sup>403</sup>Wellcome Centre for Human Genetics, University of Oxford, Oxford, OX3 7BN, UK, <sup>404</sup>Population Health Research Institute, St George's, University of London, London SW17 0RE, UK, <sup>405</sup>National Heart and Lung Institute, Imperial College London, London, W2 1PG, UK, <sup>406</sup>School of Public Health, Imperial College London, London, W2 1PG, UK, <sup>407</sup>OCDEM, University of

Oxford, Churchill Hospital, Oxford OX3 7LE, UK, <sup>408</sup>NIHR Oxford Biomedical Research Centre, Churchill Hospital, Oxford, UK, <sup>409</sup>Ophthalmology & Visual Sciences Academic Clinical Program (Eye ACP), Duke-NUS Medical School, 169857, Singapore, <sup>410</sup>DZHK (German Centre for Cardiovascular Research), Munich Heart Alliance partner site, Munich, Germany, <sup>411</sup>German Center for Diabetes Research (DZD), Neuherberg, Germany, <sup>412</sup>University of Exeter Medical School, University of Exeter, Exeter, EX2 5DW, UK, <sup>413</sup>Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden, <sup>414</sup>Netherlands Twin Register, Department of Biological Psychology, Behavioral and Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands, <sup>415</sup>Amsterdam Public Health, VU medical center Amsterdam, Amsterdam, the Netherlands, <sup>416</sup>Amsterdam Reproduction & Development research institute, VU medical center Amsterdam, Amsterdam, the Netherlands, <sup>417</sup>Department of Biological Psychology, Behavioral and Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands, <sup>418</sup>Framingham Heart Study, National Heart, Lung, and Blood Institute, US National Institutes of Health, Bethesda, MD, USA, <sup>419</sup>Department of Genetics, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran, <sup>420</sup>Department of Genetics, Shanghai-MOST Key Laboratory of Health and Disease Genomics, Chinese National Human Genome Center at Shanghai, Shanghai, 201203 China, <sup>421</sup>TUM School of Medicine, Technical University of Munich and Klinikum Rechts der Isar, Munich, Germany, <sup>422</sup>Institute of Clinical Medicine, Internal Medicine, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland, <sup>423</sup>Department of Medicine, Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA 94305, USA, <sup>424</sup>Stanford Cardiovascular Institute, Stanford University, Stanford, CA 94305, USA, <sup>425</sup>Stanford Diabetes Research Center, Stanford University, Stanford, CA 94305, USA, <sup>426</sup>Department of Medical Sciences, Molecular Epidemiology and Science for Life Laboratory, Uppsala University, Uppsala, Sweden, <sup>427</sup>Department of Biostatistics, Center for Statistical Genetics, University of Michigan, Ann Arbor, <sup>428</sup>Regeneron Pharmaceuticals, Tarrytown, NY, USA, <sup>429</sup>Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore 308232, Singapore, <sup>430</sup>Imperial College Healthcare NHS Trust, Imperial College London, London W12 0HS, UK, <sup>431</sup>MRC-PHE Centre for Environment and Health, Imperial College London, London W2 1PG, UK, <sup>432</sup>National Heart and Lung Institute, Imperial College London, London W12 0NN, UK, <sup>433</sup>Institute for Minority Health Research, University of Illinois College of Medicine, Chicago, Illinois, USA, <sup>434</sup>Department of Biostatistics, Harvard T.H. Chan School of Public Health, 677 Huntington Avenue, Boston, MA, 02115, USA, <sup>435</sup>QIMR Berghofer Medical Research Institute, 300 Herston Road, Brisbane, Queensland 4006, Australia, <sup>436</sup>Center for Non-Communicable Diseases, Karachi, Sindh, Pakistan & Faisalabad Institute of Cardiology, Faisalabad, Pakistan, <sup>437</sup>Department of Medicine, Columbia University Irving Medical Center, New York, NY, USA, <sup>438</sup>Department of Cardiology, Columbia University Irving Medical Center, New York, NY, USA, <sup>439</sup>Big Data Institute, University of Oxford, Oxford OX3 7LF, UK, <sup>440</sup>National Institute for Health Research Oxford Biomedical Research Centre, Oxford University Hospitals, Oxford, UK, <sup>441</sup>Aberdeen Centre for Health Data Science, 1:042 Polwarth Building, School of Medicine, Medical Science and Nutrition, University of Aberdeen, Foresterhill, Aberdeen, AB25 2ZD, UK, <sup>442</sup>Division of Population Health and Genomics, Ninewells Hospital and Medical School, University of Dundee, Dundee DD1 9SY, United Kingdom, <sup>443</sup>Biomedical and Translational Informatics, Geisinger Health, Danville, PA 17822, USA, <sup>444</sup>Division of Preventive Medicine, Brigham and Women's Hospital, Boston, MA 02215, <sup>445</sup>Harvard Medical School, Boston, MA 02115, USA, <sup>446</sup>Department of Biomedical Informatics, Vanderbilt University Medical Center, Nashville, TN, USA, <sup>447</sup>Departments of Medicine (Medical Genetics) and Genome Sciences, University of Washington Medical Center, Seattle, WA, USA, <sup>448</sup>Center for Autoimmune Genomics and Etiology, Cincinnati

Children's Hospital Medical Center (CCHMC), Cincinnati, OH, USA, <sup>449</sup>Division of Endocrinology, Metabolism, and Molecular Medicine, Department of Medicine, Northwestern University, Feinberg School of Medicine, Chicago, IL 60618, USA, <sup>450</sup>Department of Anthropology, Northwestern University, Evanston, IL 60208, USA, <sup>451</sup>Center for Genetic Medicine, Northwestern University, Feinberg School of Medicine, Chicago, IL 60618, USA, <sup>452</sup>HUNT Research Centre, Department of Public Health and Nursing, NTNU, Norwegian University of Science and Technology, Levanger, 7600 Norway, <sup>453</sup>Department of Medicine, Levanger Hospital, Nord-Trøndelag Hospital Trust, Levanger, 7600 Norway, <sup>454</sup>Department of Endocrinology, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway, <sup>455</sup>RIKEN Center for Integrative Medical Sciences, Yokohama, Japan, <sup>456</sup>Laboratory for Statistical Analysis, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan, <sup>457</sup>Laboratory of Complex Trait Genomics, Department of Computational Biology and Medical Sciences, Graduate School of Frontier Sciences, The University of Tokyo, Tokyo, Japan, <sup>458</sup>Laboratory of Statistical Immunology, WPI Immunology Frontier Research Center, Osaka University, Osaka, Japan, <sup>459</sup>Integrated Frontier Research for Medical Science Division, Institute for Open and Transdisciplinary Research Initiatives, Osaka University, Osaka, Japan, <sup>460</sup>Division of Molecular Pathology, Institute of Medical Science, The University of Tokyo, Tokyo, Japan, <sup>461</sup>Faculty of Medicine, University of Iceland, Sæmundargötu 2, Reykjavik, 102, Iceland, <sup>462</sup>VA Boston Healthcare System, Boston, MA, USA, <sup>463</sup>VA Informatics and Computing Infrastructure, VA Salt Lake City Health Care System, Salt Lake City, UT, USA, <sup>464</sup>University of Massachusetts, Boston, MA, USA, <sup>465</sup>Department of Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA, <sup>466</sup>Department of Genetics, University of Pennsylvania, Philadelphia, PA, 19104, USA, <sup>467</sup>Cardiovascular Institute, Stanford University School of Medicine, Stanford, California, USA, <sup>468</sup>Corporal Michael J. Crescenz VA Medical Center, Philadelphia, PA, USA, <sup>469</sup>Department of Medicine, Brigham Women's Hospital, Boston, MA, USA, <sup>470</sup>Atlanta VA Medical Center, Atlanta, GA, USA, <sup>471</sup>Division of Cardiology, Emory University School of Medicine, Atlanta, GA, USA, <sup>472</sup>Sydney Brenner Institute for Molecular Bioscience, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, <sup>473</sup>School of Electrical and Information Engineering, University of the Witwatersrand, Johannesburg, South Africa, <sup>474</sup>Division of Human Genetics, National Health Laboratory Service and School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, <sup>475</sup>School of Basic and Medical Biosciences, Faculty of Life Sciences and Medicine, King's College London, London, UK, <sup>476</sup>Departments of Pediatrics and Genetics, Harvard Medical School, Boston, MA, USA, <sup>477</sup>Center for Genomic Medicine, Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA, <sup>478</sup>Cardiology Division, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA, <sup>479</sup>Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA, <sup>480</sup>Program in Medical and Population Genetics, Broad Institute of Harvard and MIT, Cambridge, MA, USA, <sup>481</sup>Cardiovascular Research Center and Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, USA, <sup>482</sup>Department of Biostatistics, Boston University School of Public Health, Boston, MA, USA, <sup>483</sup>Centre for Genetics and Genomics Versus Arthritis, Centre for Musculoskeletal Research, Division of Musculoskeletal and Dermatological Sciences, The University of Manchester, Manchester, UK, <sup>484</sup>Princess Al-Jawhara Al-Brahim Centre of Excellence in Research of Hereditary Disorders (PACER-HD), King Abdulaziz University, Jeddah, Saudi Arabia, <sup>485</sup>Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, MI 48109, USA, <sup>486</sup>Department of Human Genetics, University of Michigan, Ann Arbor, MI 48019, USA

## List of Supplementary Tables

Supplementary Table 2: Lambda GC values by minor allele frequency for ancestry-specific meta-analysis with RAREMETAL

Supplementary Table 4: Lambda GC values by minor allele frequency for multi-ancestry meta-analysis (as performed in MR-MEGA)

Supplementary Table 8: Genetic correlation results calculated from bivariate GREML analysis in UK Biobank and the Million Veteran Program

Supplementary Table 13: Number of individuals by ancestry group included in the GWAS used to generate each set of PRS weights

Supplementary Table 21: Correlation of multi-ancestry polygenic score with principal components in 1KGP3 individuals

Supplementary Table 22: Correlation of mean LDL-C value with PCs in European and African American MGI participants

Supplementary Table 23: Prediction of LDL-C in MGI individuals based on varying numbers of PCs included in the model

**Supplementary Table 2: Lambda GC values by minor allele frequency for ancestry-specific meta-analysis with RAREMETAL**

Common: MAF  $\geq$  5%, Low:  $1\% \leq$  MAF < 5%, Rare: MAF < 1%

| Ancestry | Trait    | All  | Common | Low  | Rare |
|----------|----------|------|--------|------|------|
| AdmAFR   | HDL-C    | 1.02 | 1.11   | 1.02 | 0.98 |
| AdmAFR   | LDL-C    | 1.02 | 1.11   | 1.02 | 0.98 |
| AdmAFR   | TG       | 1.01 | 1.13   | 1.01 | 0.96 |
| AdmAFR   | nonHDL-C | 1.02 | 1.04   | 1.03 | 1.00 |
| AdmAFR   | TC       | 1.02 | 1.13   | 1.02 | 0.97 |
| EAS      | HDL-C    | 1.06 | 1.16   | 1.05 | 1.01 |
| EAS      | LDL-C    | 1.05 | 1.11   | 1.06 | 1.01 |
| EAS      | TG       | 1.05 | 1.13   | 1.07 | 1.01 |
| EAS      | nonHDL-C | 1.05 | 1.16   | 1.05 | 1.01 |
| EAS      | TC       | 1.06 | 1.16   | 1.07 | 1.01 |
| EUR      | HDL-C    | 1.14 | 2.08   | 1.36 | 1.03 |
| EUR      | LDL-C    | 1.13 | 1.45   | 1.19 | 1.07 |
| EUR      | TG       | 1.10 | 1.80   | 1.28 | 1.01 |
| EUR      | nonHDL-C | 1.16 | 1.51   | 1.23 | 1.10 |
| EUR      | TC       | 1.12 | 1.61   | 1.25 | 1.06 |
| HIS      | HDL-C    | 1.03 | 1.08   | 1.02 | 1.02 |
| HIS      | LDL-C    | 1.02 | 1.05   | 1.02 | 1.01 |
| HIS      | TG       | 0.99 | 1.09   | 1.02 | 0.95 |
| HIS      | nonHDL-C | 1.02 | 1.00   | 1.01 | 1.03 |
| HIS      | TC       | 1.02 | 1.07   | 1.01 | 1.00 |
| SAS      | HDL-C    | 1.04 | 1.08   | 1.04 | 1.01 |
| SAS      | LDL-C    | 1.03 | 1.06   | 1.04 | 1.01 |
| SAS      | TG       | 1.04 | 1.08   | 1.05 | 1.02 |
| SAS      | nonHDL-C | 1.03 | 1.06   | 1.04 | 1.02 |
| SAS      | TC       | 1.04 | 1.07   | 1.04 | 1.02 |

**Supplementary Table 4: Lambda GC values by minor allele frequency for multi-ancestry meta-analysis (as performed in MR-MEGA)**

Common:  $MAF \geq 5\%$ , Low:  $1\% \leq MAF < 5\%$ , Rare:  $MAF < 1\%$

|          | All  | Common | Low  | Rare |
|----------|------|--------|------|------|
| HDL-C    | 1.14 | 1.32   | 1.13 | 1.06 |
| LDL-C    | 1.10 | 1.19   | 1.09 | 1.05 |
| logTG    | 1.13 | 1.30   | 1.11 | 1.04 |
| nonHDL-C | 1.09 | 1.16   | 1.07 | 1.05 |
| TC       | 1.10 | 1.22   | 1.10 | 1.05 |

**Supplementary Table 8: Genetic correlation results calculated from bivariate GREML analysis in UK Biobank and the Million Veteran Program**

| Trait    | UK Biobank (AdmAFR and EUR) |         | MVP (AFRAMR and EUR) |          |
|----------|-----------------------------|---------|----------------------|----------|
|          | rG                          | p-value | rG                   | p-value  |
| HDL-C    | 0.844                       | 0.259   | 0.671                | 1.17E-04 |
| LDL-C    | 0.520                       | 0.003   | 0.473                | 4.14E-06 |
| TG       | 0.596                       | 0.022   | 0.685                | 4.80E-04 |
| nonHDL-C | 0.590                       | 0.016   | NA                   | NA       |
| TC       | 0.540                       | 0.003   | 0.537                | 2.59E-06 |

**Supplementary Table 13: Number of individuals by ancestry group included in the GWAS used to generate each set of PRS weights**

| Score                               | AdmAFR | EAS    | EUR     | HIS    | SAS    | Total     |
|-------------------------------------|--------|--------|---------|--------|--------|-----------|
| SAS                                 | 0      | 0      | 0       | 0      | 33,658 | 33,658    |
| HIS                                 | 0      | 0      | 0       | 46,040 | 0      | 46,040    |
| EAS                                 | 0      | 82,587 | 0       | 0      | 0      | 82,587    |
| AdmAFR                              | 87,760 | 0      | 0       | 0      | 0      | 87,760    |
| EUR_2010                            | 0      | 0      | 95,454  | 0      | 0      | 95,454    |
| EUR (100K)                          | 0      | 0      | 99,952  | 0      | 0      | 99,952    |
| EUR_2010_AdmaFR                     | 87,760 | 0      | 95,454  | 0      | 0      | 183,214   |
| EUR (200K)                          | 0      | 0      | 200,026 | 0      | 0      | 200,026   |
| EUR_2010_nonEUR                     | 87,760 | 82,587 | 95,454  | 46,040 | 40,473 | 352,314   |
| EUR (400K)                          | 0      | 0      | 400,016 | 0      | 0      | 400,016   |
| EUR                                 | 0      | 0      | 831,666 | 0      | 0      | 831,666   |
| ALL                                 | 87,760 | 82,587 | 831,666 | 46,040 | 40,473 | 1,088,526 |
| AdmaFR (MVP only)                   | 62,033 | 0      | 0       | 0      | 0      | 62,033    |
| ALL<br>(100K, 20% each ancestry)    | 20,779 | 19,813 | 21,802  | 20,323 | 20,441 | 103,158   |
| EUR (50K) +<br>AdmaFR (MVP only)    | 62,033 | 0      | 50,754  | 0      | 0      | 112,787   |
| ALL<br>(100K, original proportions) | 8,052  | 8,291  | 76,575  | 3,899  | 3,668  | 100,485   |

**Supplementary Table 21: Correlation of multi-ancestry polygenic score with principal components in 1KGP3 individuals**

| PC | Pearson_R | Pvalue   |
|----|-----------|----------|
| 1  | -0.676    | 0        |
| 2  | -0.009    | 0.670281 |
| 3  | -0.080    | 6.59E-05 |
| 4  | -0.003    | 0.900171 |
| 5  | -0.049    | 0.014626 |
| 6  | -0.033    | 0.100402 |
| 7  | -0.059    | 0.003025 |
| 8  | -0.003    | 0.893794 |
| 9  | -0.017    | 0.388338 |
| 10 | -0.045    | 0.025012 |
| 11 | -0.008    | 0.694459 |
| 12 | -0.009    | 0.652035 |
| 13 | -0.023    | 0.240671 |
| 14 | 0.038     | 0.056858 |
| 15 | -0.030    | 0.133212 |
| 16 | -0.007    | 0.724553 |
| 17 | 0.005     | 0.810559 |
| 18 | 0.031     | 0.119962 |
| 19 | 0.013     | 0.504673 |
| 20 | 0.000     | 0.990678 |

**Supplementary Table 22: Correlation of mean LDL-C value with PCs in European and African American MGI participants**

| PC | African American |        | European  |        |
|----|------------------|--------|-----------|--------|
|    | Pearson_R        | Pvalue | Pearson_R | Pvalue |
| 1  | -0.012           | 0.662  | 0.004     | 0.631  |
| 2  | -0.013           | 0.628  | -0.011    | 0.143  |
| 3  | 0.003            | 0.912  | -0.004    | 0.589  |
| 4  | -0.013           | 0.641  | -0.012    | 0.103  |
| 5  | -0.015           | 0.593  | 0.012     | 0.114  |
| 6  | -0.010           | 0.708  | -0.010    | 0.184  |
| 7  | -0.005           | 0.859  | -0.008    | 0.300  |
| 8  | -0.005           | 0.862  | -0.009    | 0.261  |
| 9  | -0.014           | 0.601  | 0.009     | 0.214  |
| 10 | -0.006           | 0.819  | 0.006     | 0.466  |
| 11 | 0.011            | 0.696  | 0.009     | 0.257  |
| 12 | 0.012            | 0.656  | 0.005     | 0.491  |
| 13 | 0.001            | 0.963  | 0.009     | 0.219  |
| 14 | 0.002            | 0.934  | 0.005     | 0.471  |
| 15 | -0.006           | 0.837  | -0.002    | 0.762  |
| 16 | 0.008            | 0.779  | -0.001    | 0.895  |
| 17 | -0.001           | 0.965  | -0.009    | 0.251  |
| 18 | -0.058           | 0.034  | -0.005    | 0.519  |
| 19 | -0.021           | 0.445  | 0.000     | 0.997  |
| 20 | -0.013           | 0.645  | 0.004     | 0.580  |

**Supplementary Table 23: Prediction of LDL-C in MGI individuals based on varying numbers of PCs included in the model**

The polygenic score was normalized within each ancestry group separately

| Model                                                               | adj_R2 | Lower_95_CI | Upper_95_CI | Ancestry         |
|---------------------------------------------------------------------|--------|-------------|-------------|------------------|
| gender+birth_year+BATCH                                             | 0.022  | 0.009       | 0.041       | African American |
| gender+BATCH+birth_year+PC1-4                                       | 0.019  | 0.009       | 0.044       | African American |
| gender+BATCH+birth_year+PC1-10                                      | 0.017  | 0.008       | 0.048       | African American |
| gender+BATCH+birth_year+PC1-20                                      | 0.014  | 0.011       | 0.054       | African American |
| gender+BATCH+birth_year+PC1-4+normalized multi-ancestry risk score  | 0.122  | 0.094       | 0.159       | African American |
| gender+BATCH+birth_year+PC1-10+normalized multi-ancestry risk score | 0.119  | 0.097       | 0.164       | African American |
| gender+BATCH+birth_year+PC1-20+normalized multi-ancestry risk score | 0.115  | 0.098       | 0.167       | African American |
| normalized multi-ancestry risk score                                | 0.092  | 0.065       | 0.124       | African American |
| normalized AdmAFR risk score                                        | 0.084  | 0.060       | 0.114       | African American |
| normalized EUR risk score                                           | 0.040  | 0.020       | 0.062       | African American |
| gender+BATCH+birth_year+PC1-4+normalized AdmAFR risk score          | 0.115  | 0.089       | 0.155       | African American |
| gender+BATCH+birth_year+PC1-10+normalized AdmAFR risk score         | 0.112  | 0.088       | 0.157       | African American |
| gender+BATCH+birth_year+PC1-20+normalized AdmAFR risk score         | 0.108  | 0.092       | 0.159       | African American |
| gender+BATCH+birth_year+PC1-4+normalized EUR risk score             | 0.062  | 0.044       | 0.095       | African American |
| gender+BATCH+birth_year+PC1-10+normalized EUR risk score            | 0.059  | 0.044       | 0.099       | African American |
| gender+BATCH+birth_year+PC1-20+normalized EUR risk score            | 0.055  | 0.046       | 0.099       | African American |
| gender+birth_year+BATCH                                             | 0.013  | 0.010       | 0.017       | European         |
| gender+BATCH+birth_year+PC1-4                                       | 0.014  | 0.011       | 0.018       | European         |
| gender+BATCH+birth_year+PC1-10                                      | 0.014  | 0.011       | 0.018       | European         |
| gender+BATCH+birth_year+PC1-20                                      | 0.013  | 0.011       | 0.018       | European         |
| gender+BATCH+birth_year+PC1-4+normalized multi-ancestry risk score  | 0.130  | 0.122       | 0.140       | European         |
| gender+BATCH+birth_year+PC1-10+normalized multi-ancestry risk score | 0.130  | 0.121       | 0.141       | European         |
| gender+BATCH+birth_year+PC1-20+normalized multi-ancestry risk score | 0.130  | 0.121       | 0.140       | European         |
| normalized multi-ancestry risk score                                | 0.117  | 0.109       | 0.127       | European         |
| normalized AdmAFR risk score                                        | 0.060  | 0.053       | 0.067       | European         |
| normalized EUR risk score                                           | 0.116  | 0.107       | 0.126       | European         |

|                                                             |       |       |       |          |
|-------------------------------------------------------------|-------|-------|-------|----------|
| gender+BATCH+birth_year+PC1-4+normalized AdmAFR risk score  | 0.074 | 0.066 | 0.082 | European |
| gender+BATCH+birth_year+PC1-10+normalized AdmAFR risk score | 0.074 | 0.067 | 0.083 | European |
| gender+BATCH+birth_year+PC1-20+normalized AdmAFR risk score | 0.074 | 0.068 | 0.082 | European |
| gender+BATCH+birth_year+PC1-4+normalized EUR risk score     | 0.129 | 0.120 | 0.140 | European |
| gender+BATCH+birth_year+PC1-10+normalized EUR risk score    | 0.129 | 0.120 | 0.140 | European |
| gender+BATCH+birth_year+PC1-20+normalized EUR risk score    | 0.129 | 0.121 | 0.140 | European |

## **List of Supplementary Figures**

Supplementary Figure 1: Ancestral diversity of contributing cohorts

Supplementary Figure 2: QQ Plots from each single-ancestry meta-analysis

Supplementary Figure 3: Effect sizes and allele frequencies of identified index variants from ancestry-specific meta-analysis

Supplementary Figure 4: QQ plots from multi-ancestry meta-analysis

Supplementary Figure 5: Comparison of association results for ancestry-specific and multi-ancestry analysis

Supplementary Figure 6: Effect sizes by ancestry for unique index variants from ancestry-specific meta-analysis

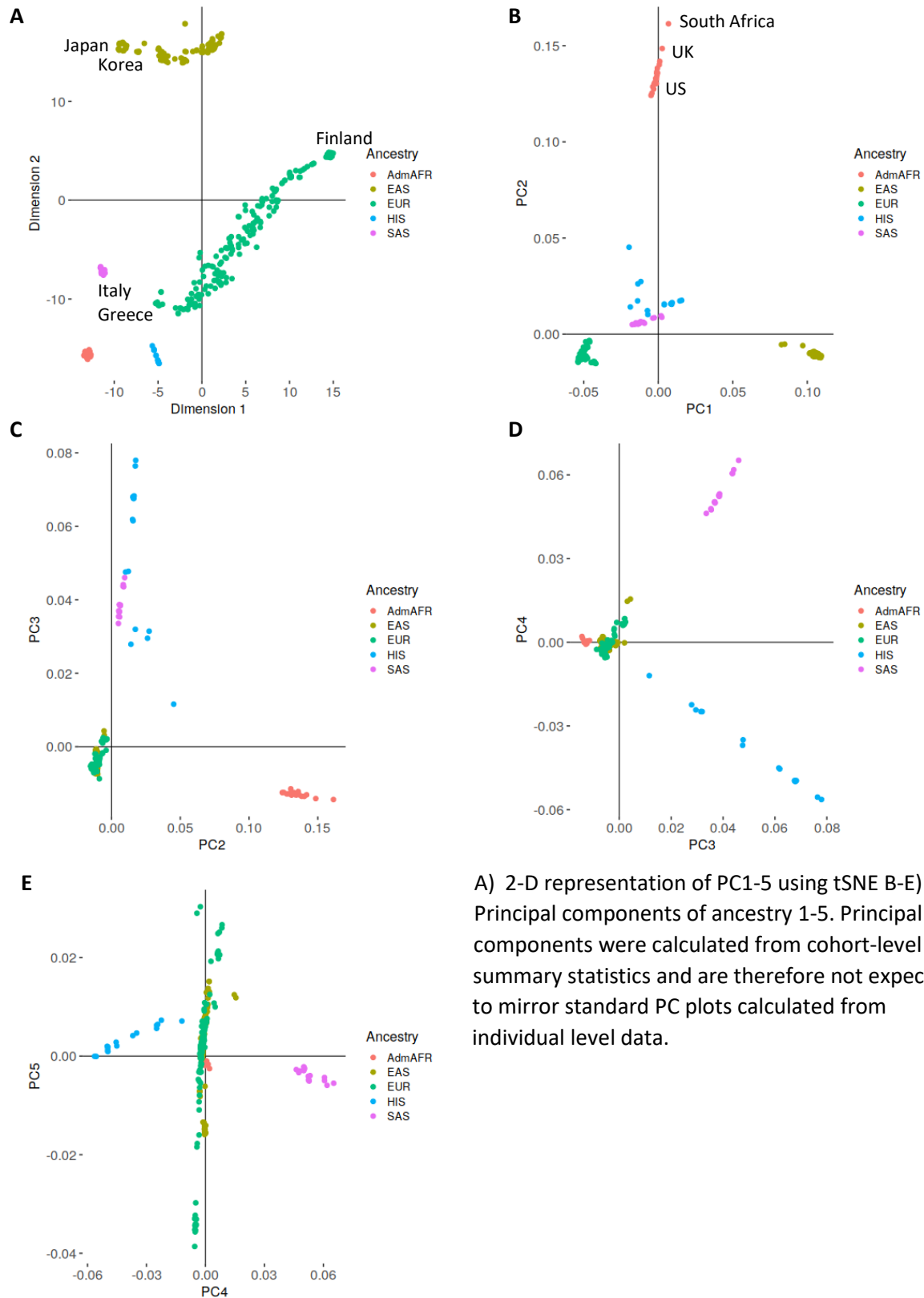
Supplementary Figure 7: Genetic impact correlation estimates between ancestries for each trait analyzed

Supplementary Figure 8: Genetic effect correlation estimates between ancestries for each trait analyzed

Supplementary Figure 9: Comparison of PRS source ancestry and sample size with prediction in European and African American individuals

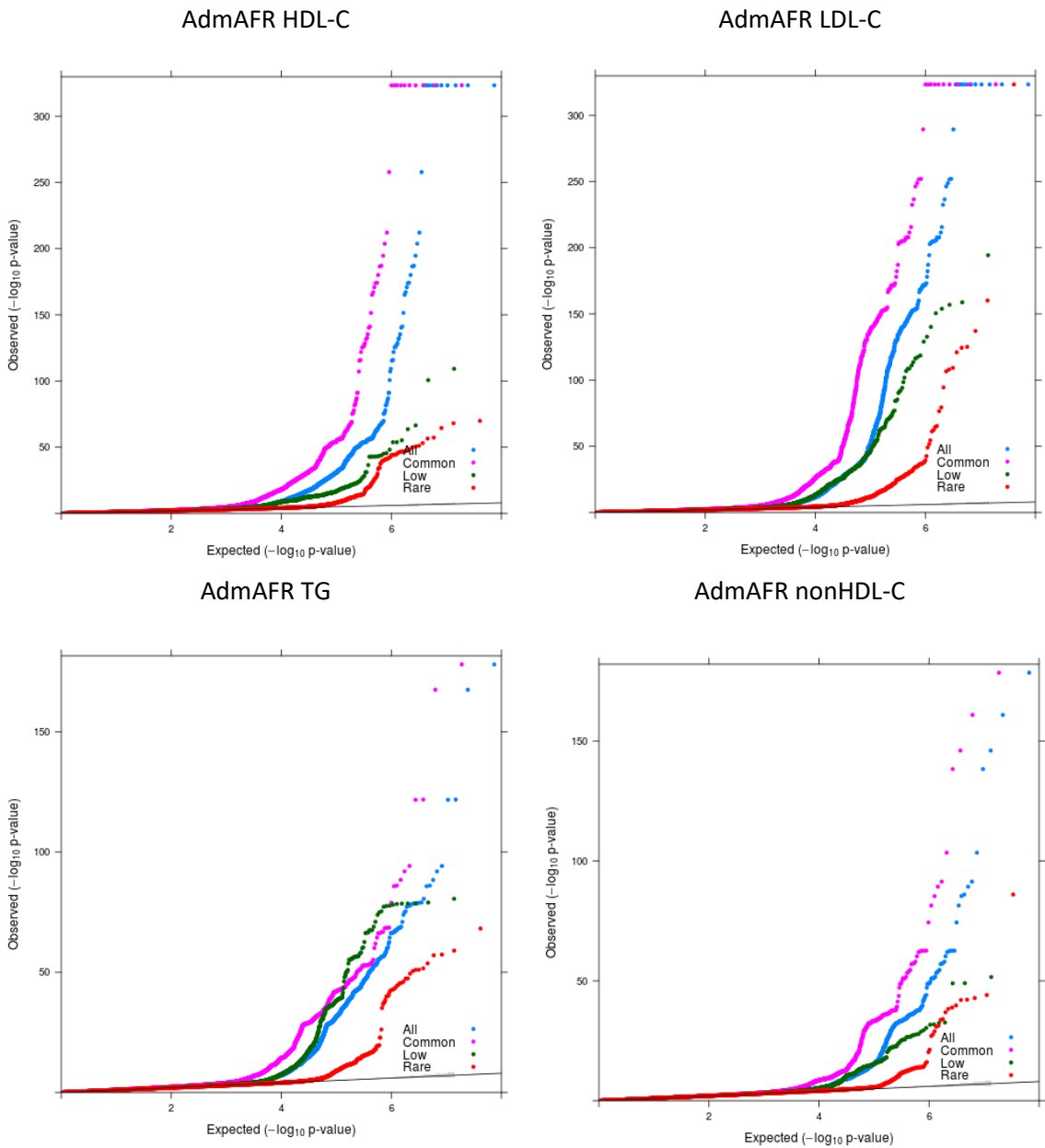
Supplementary Figure 10: Comparison of original and conditional effect sizes

**Supplementary Figure 1: Ancestral diversity of contributing cohorts**

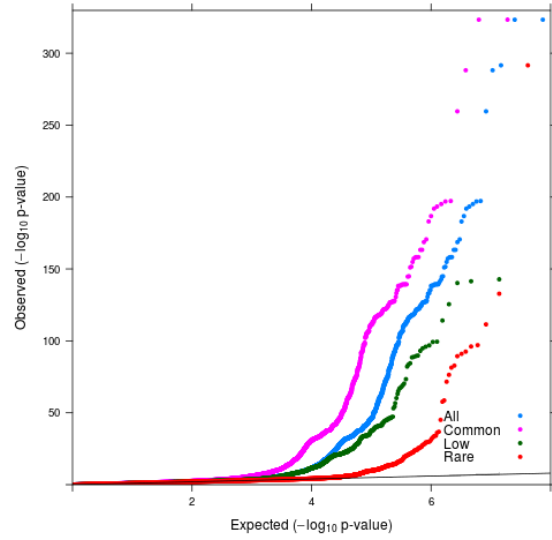


A) 2-D representation of PC1-5 using tSNE B-E) Principal components of ancestry 1-5. Principal components were calculated from cohort-level summary statistics and are therefore not expected to mirror standard PC plots calculated from individual level data.

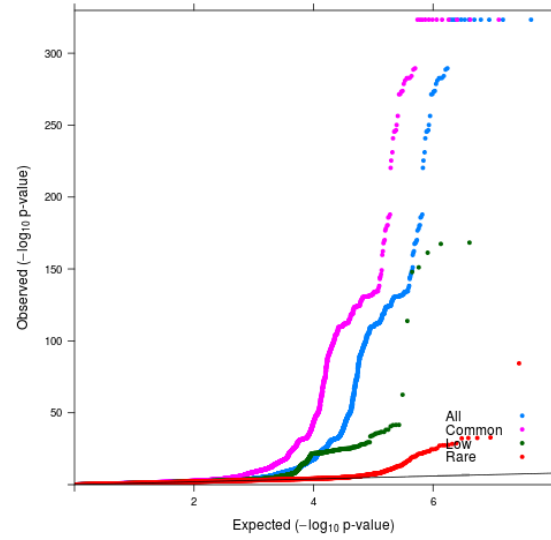
Supplementary Figure 2: QQ Plots from each single-ancestry meta-analysis



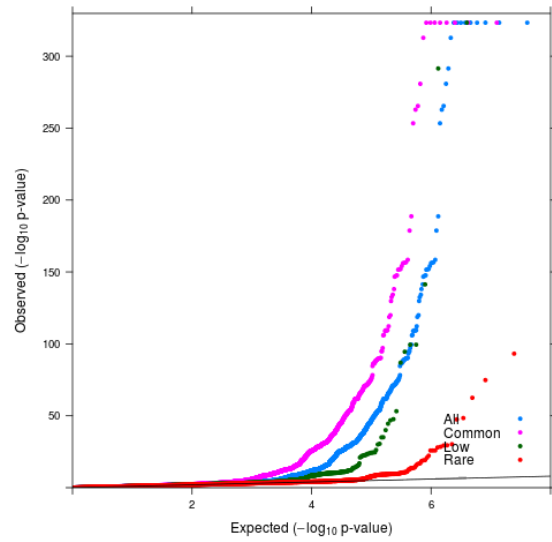
AdmAFR TC



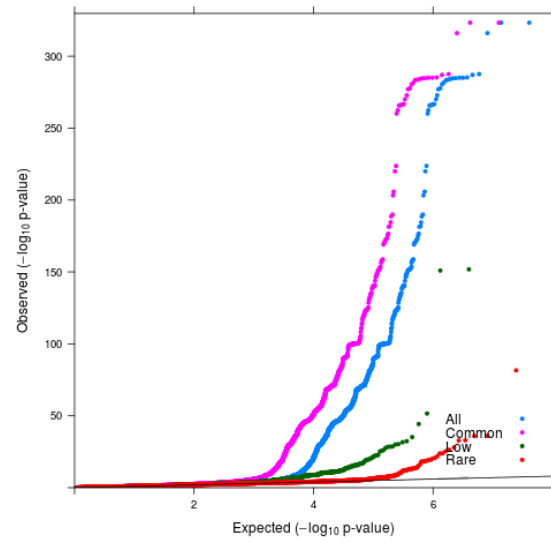
EAS HDL-C



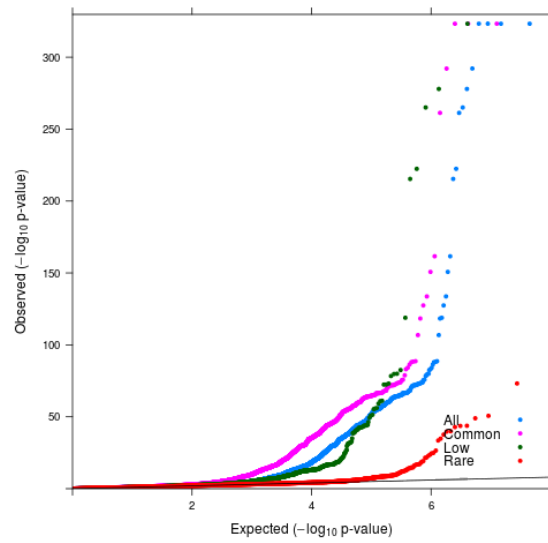
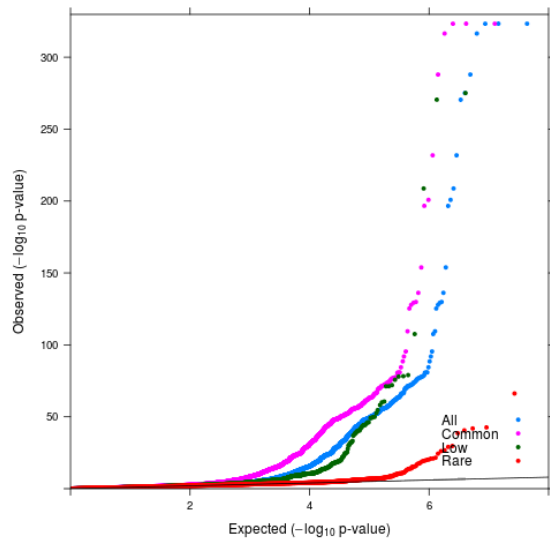
EAS LDL-C



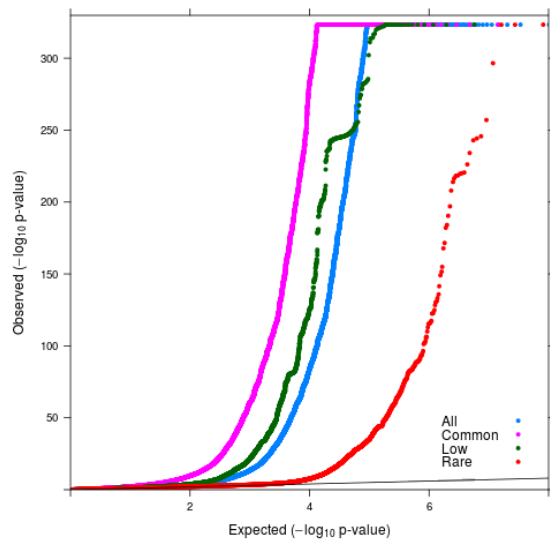
EAS TG



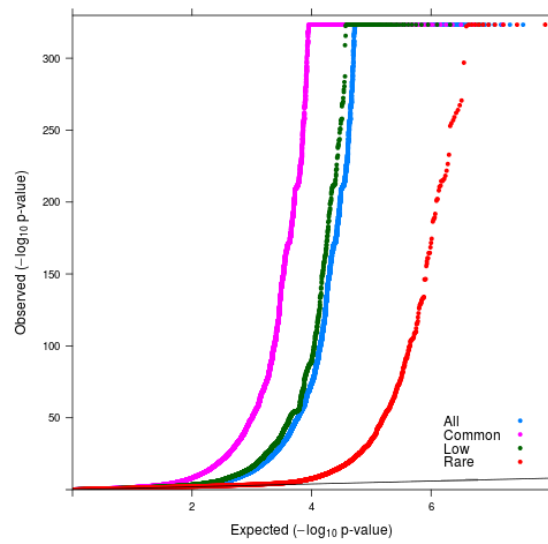
EAS nonHDL-C

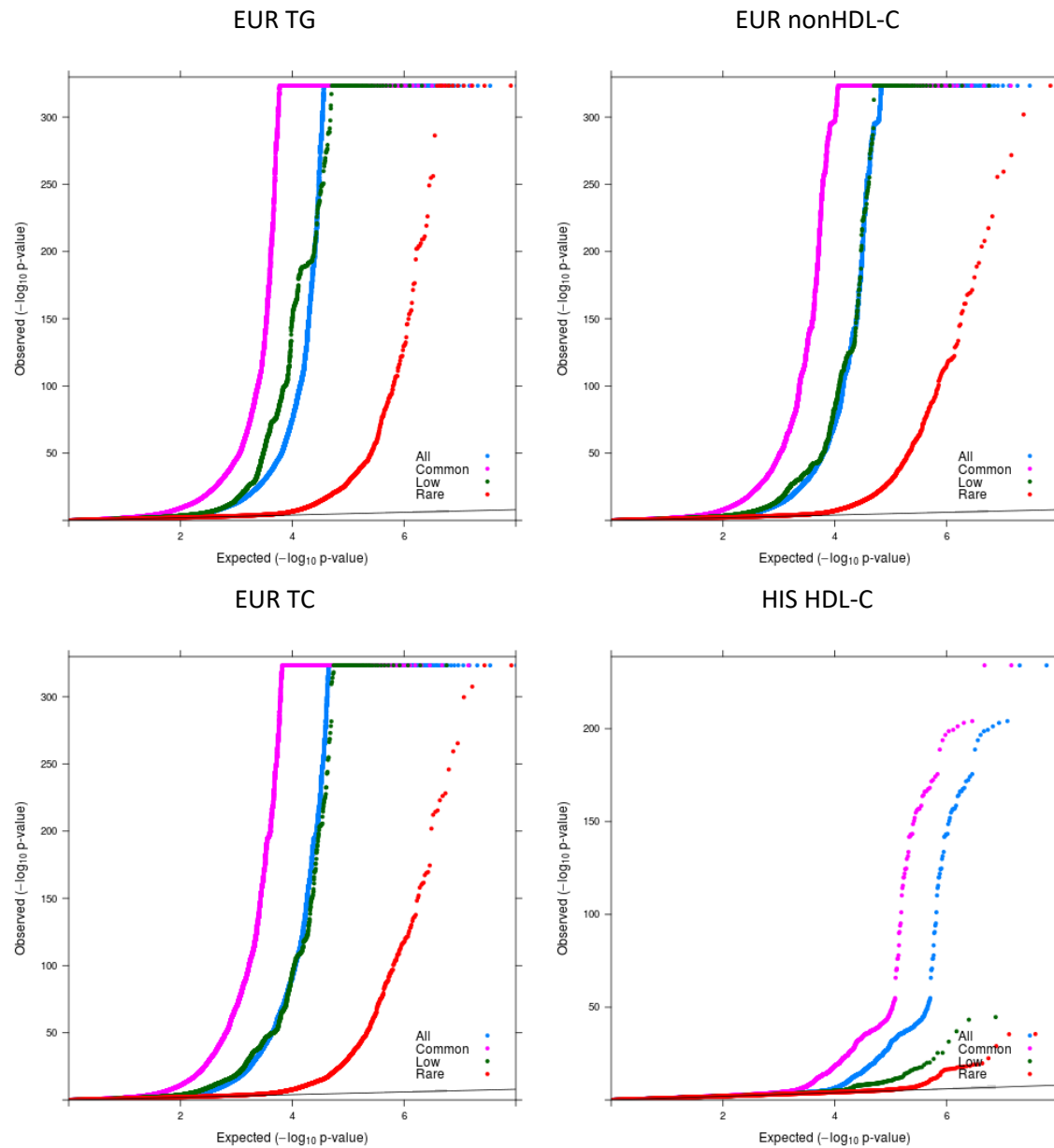


EUR HDL-C

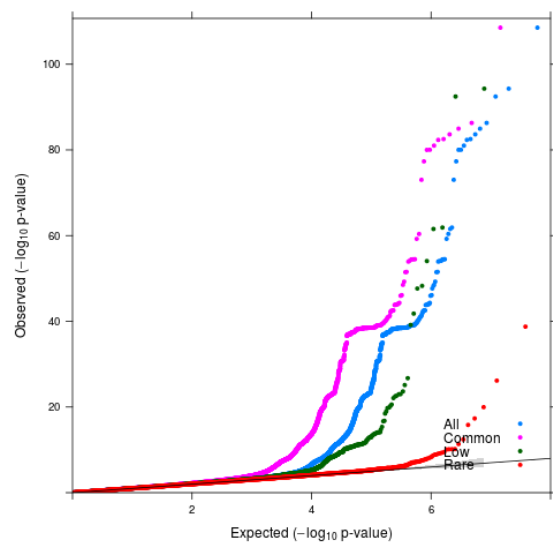


EUR LDL-C

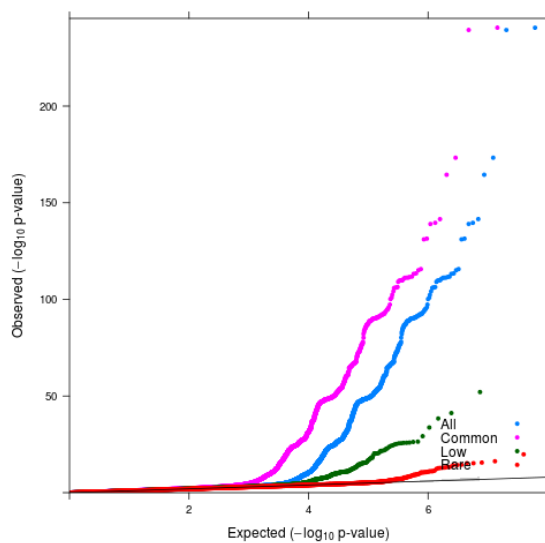




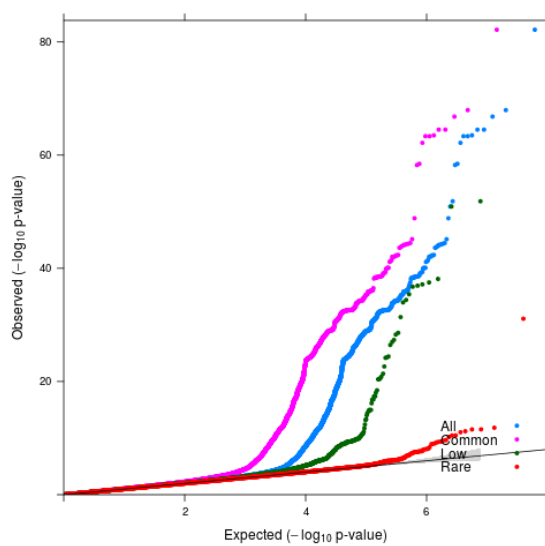
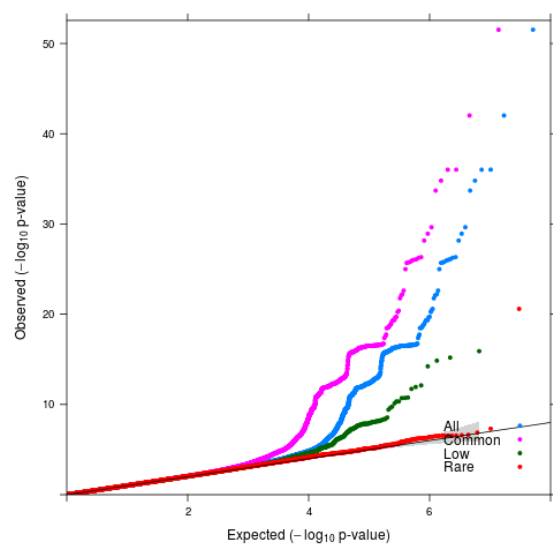
HIS LDL-C



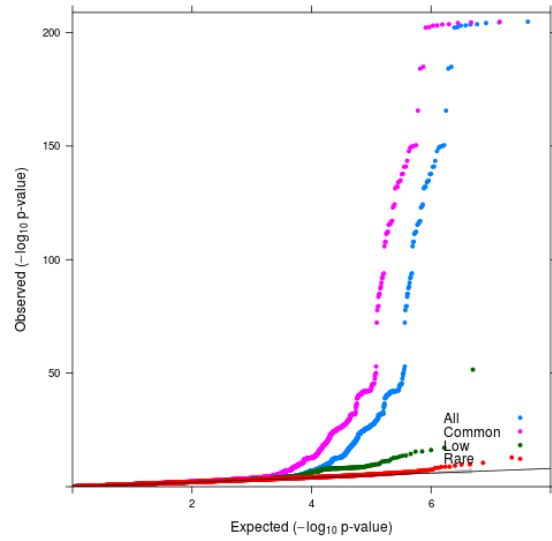
HIS TG



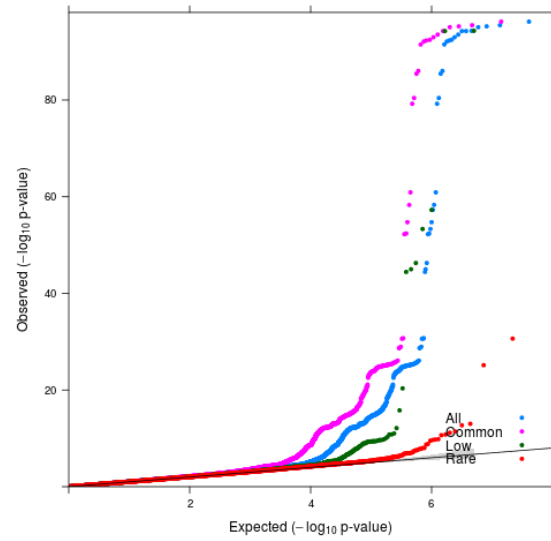
HIS nonHDL-C



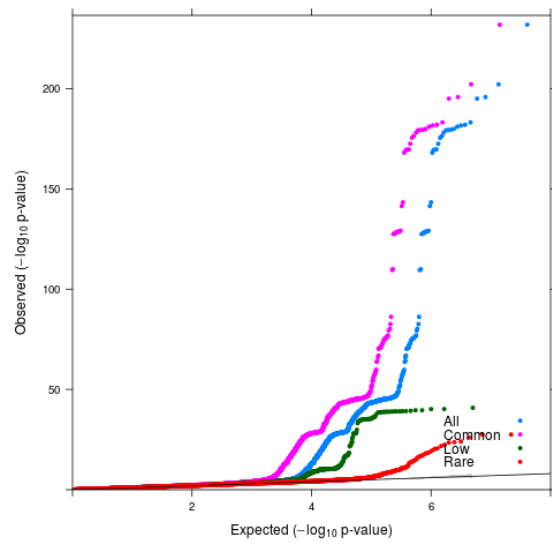
SAS HDL-C



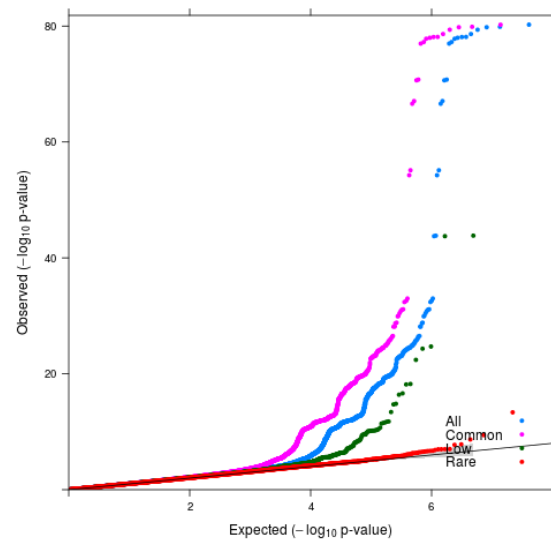
SAS LDL-C



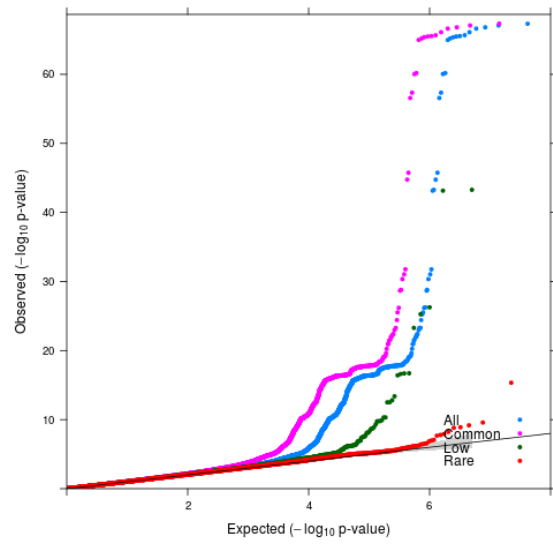
SAS TG



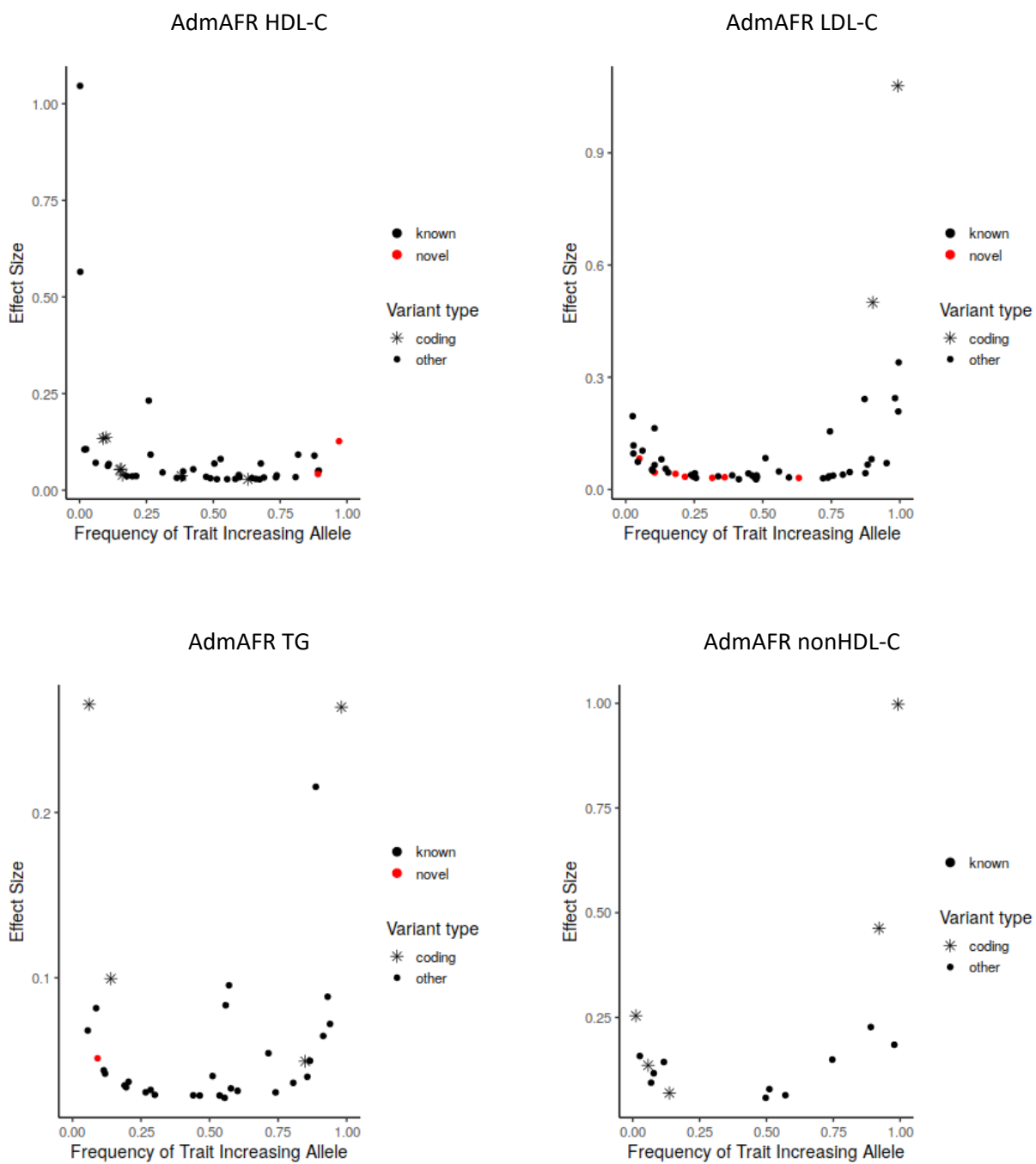
SAS nonHDL-C

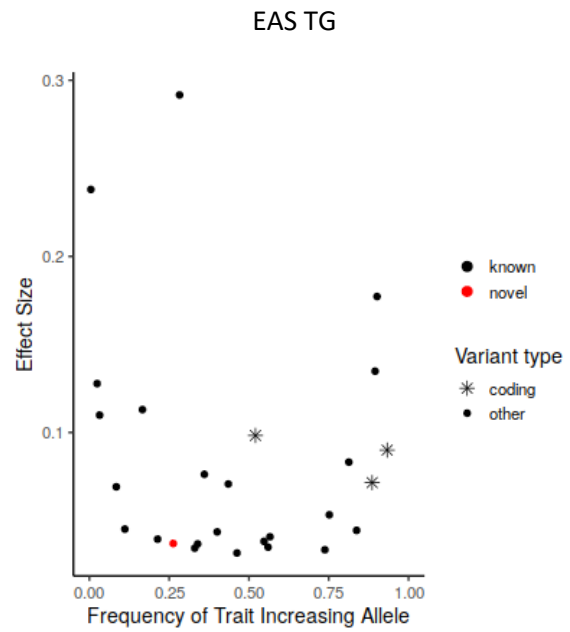
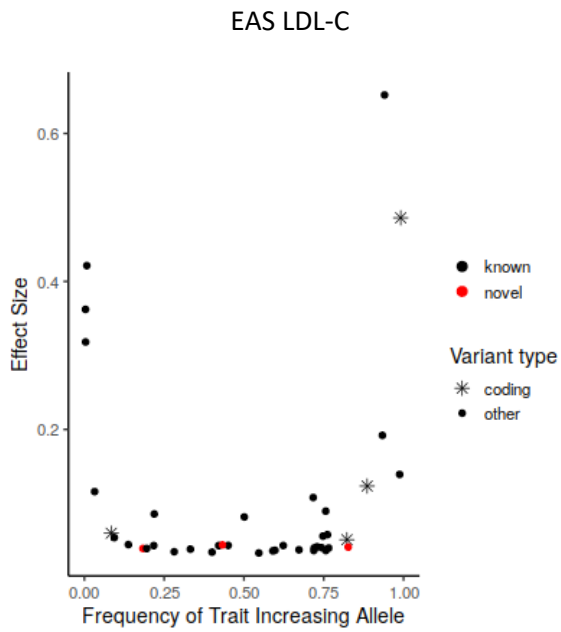
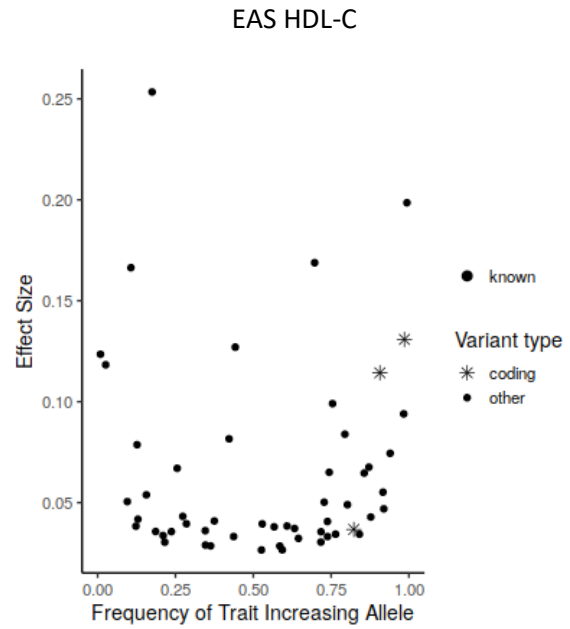
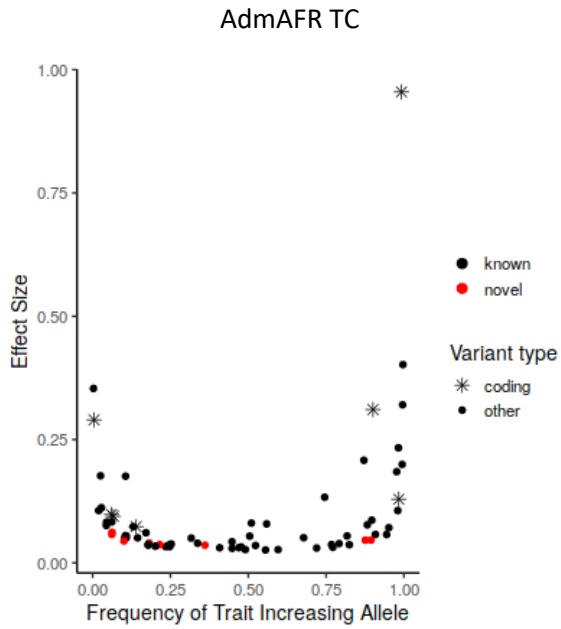


## SAS TC

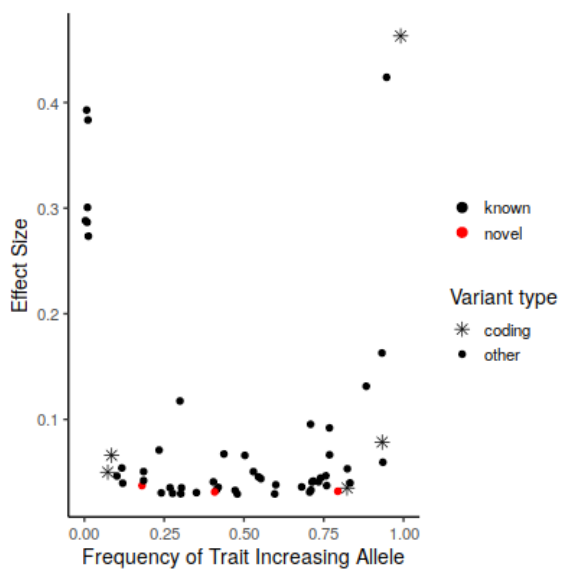


**Supplementary Figure 3: Effect sizes and allele frequencies of identified index variants from ancestry-specific meta-analysis**

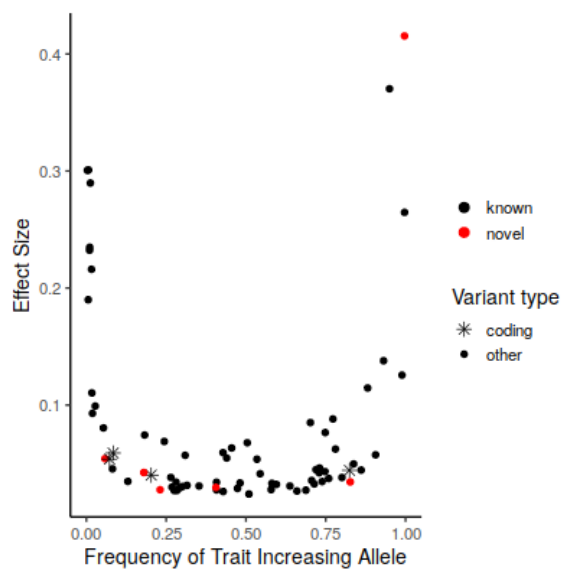




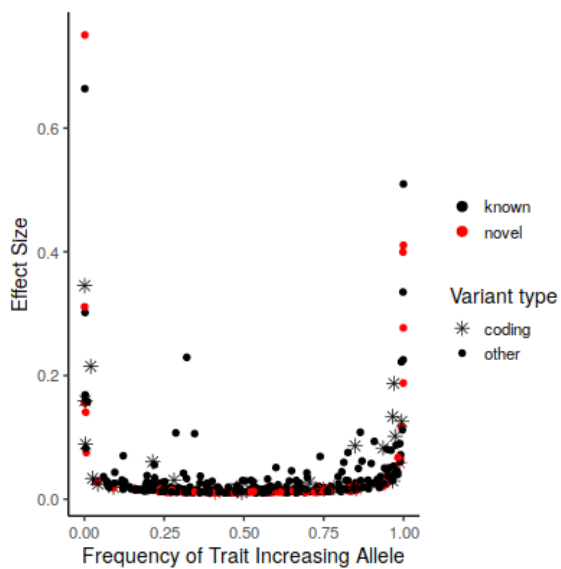
EAS nonHDL-C



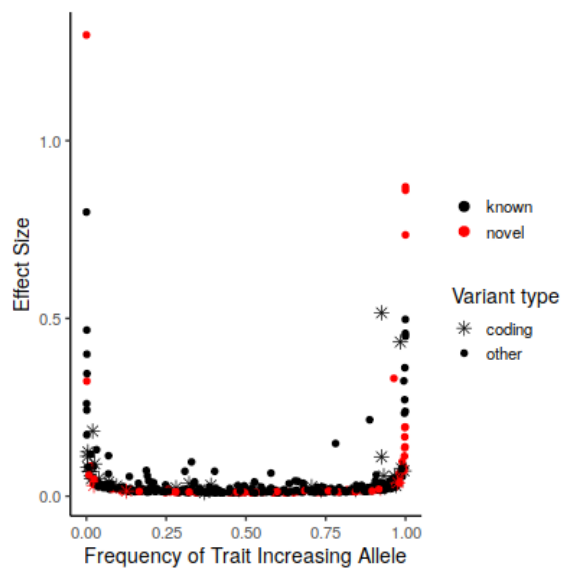
EAS TC

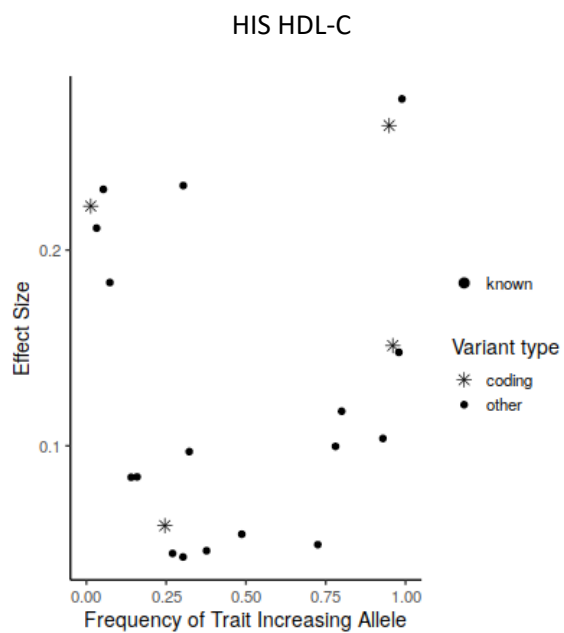
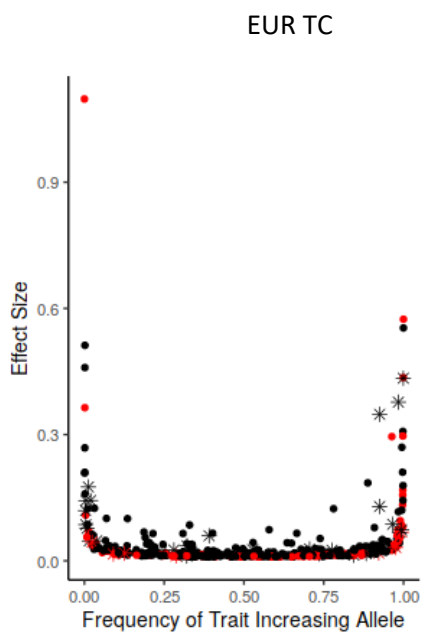
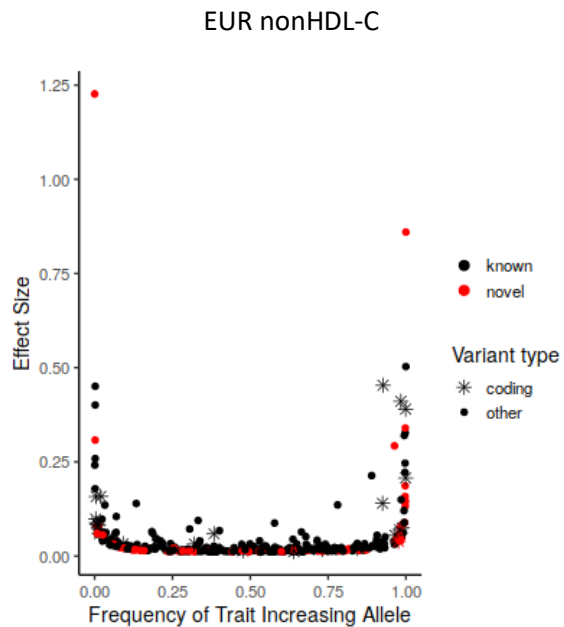
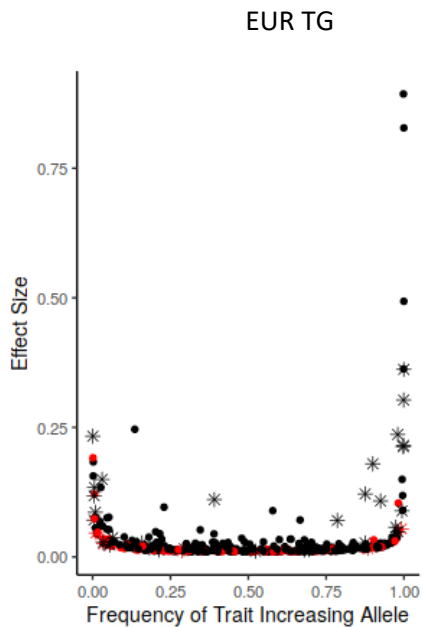


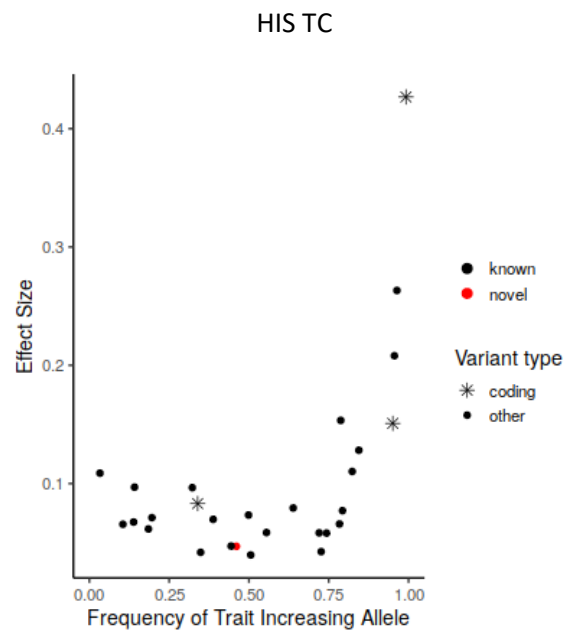
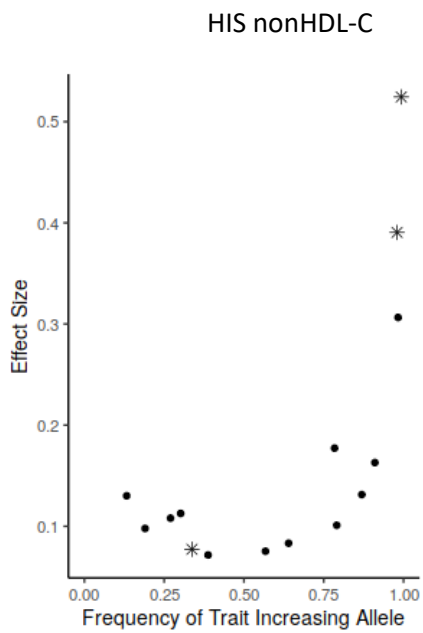
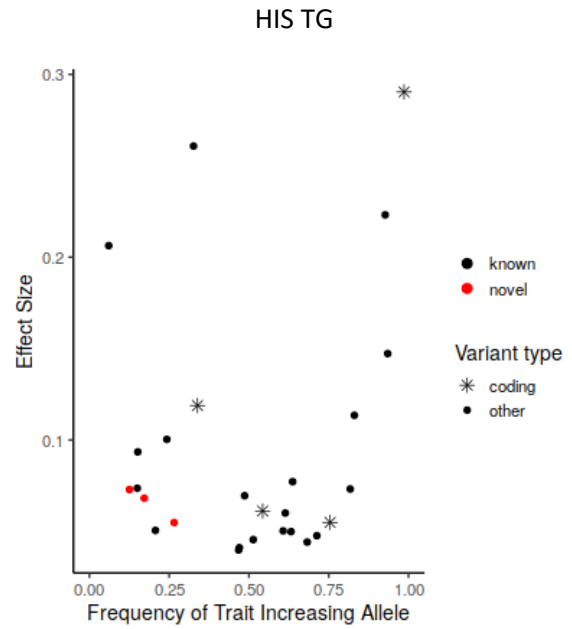
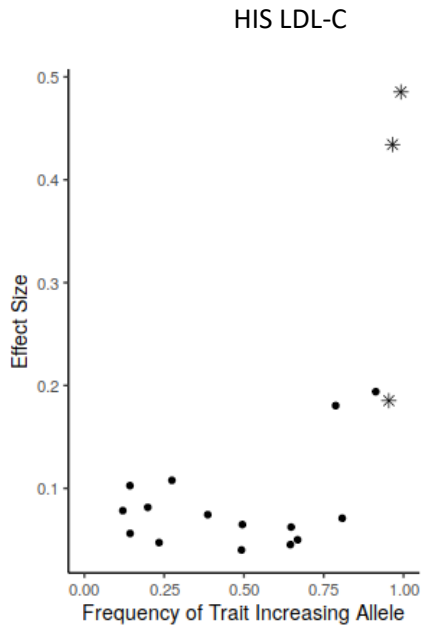
EUR HDL-C

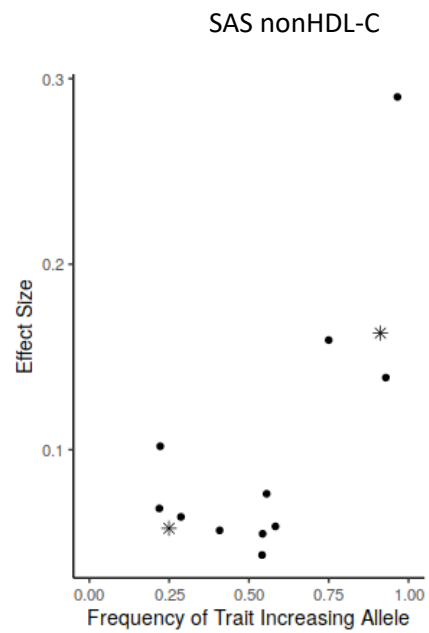
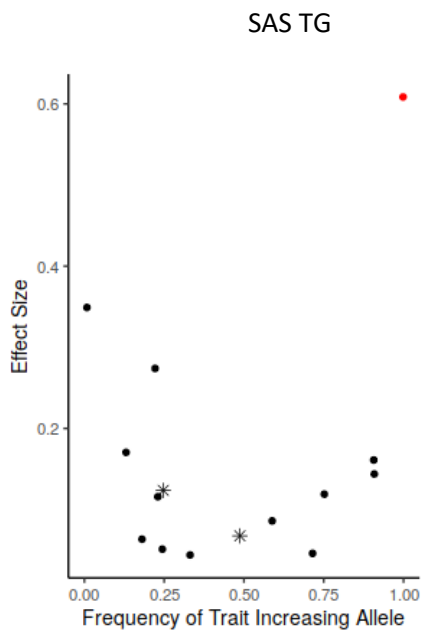
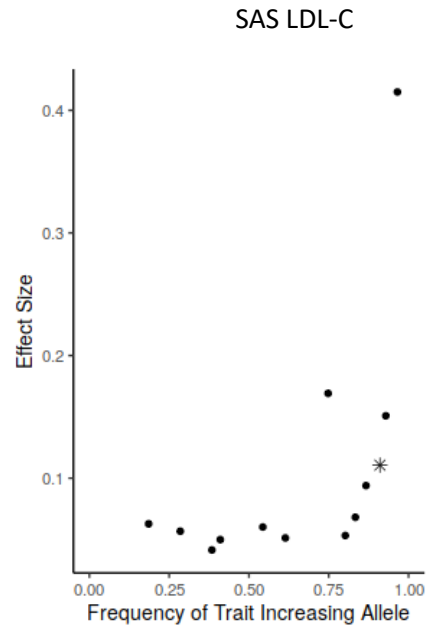
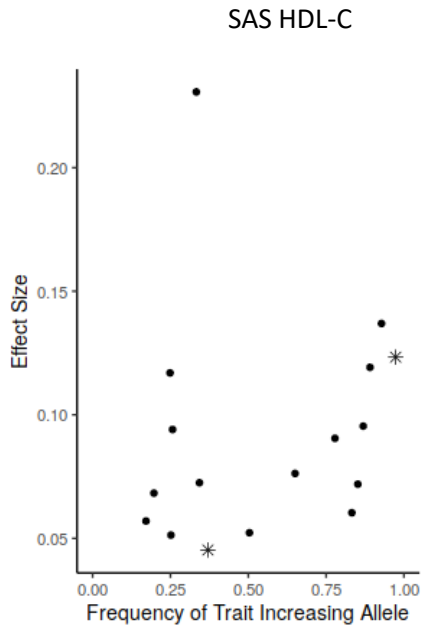


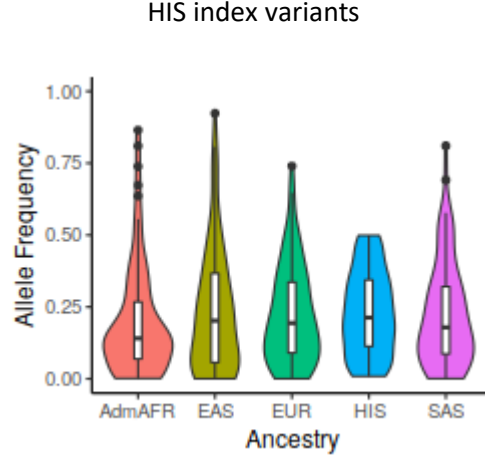
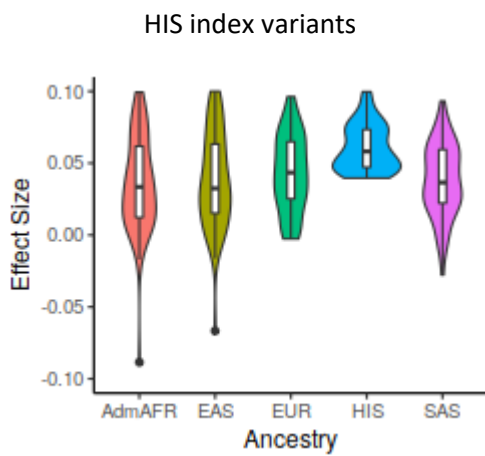
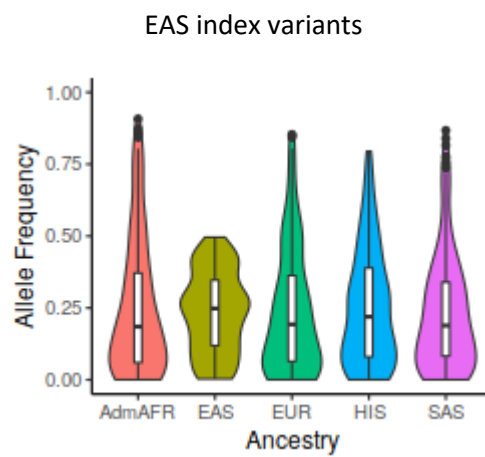
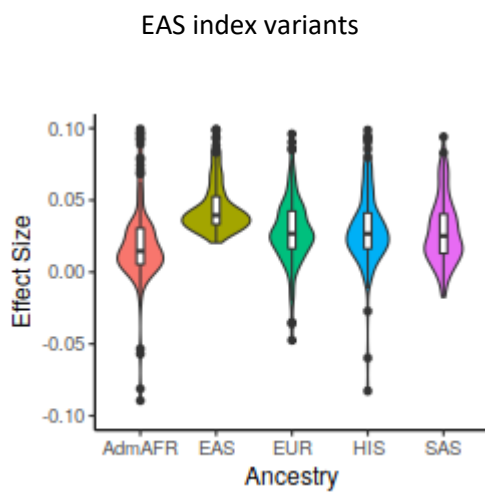
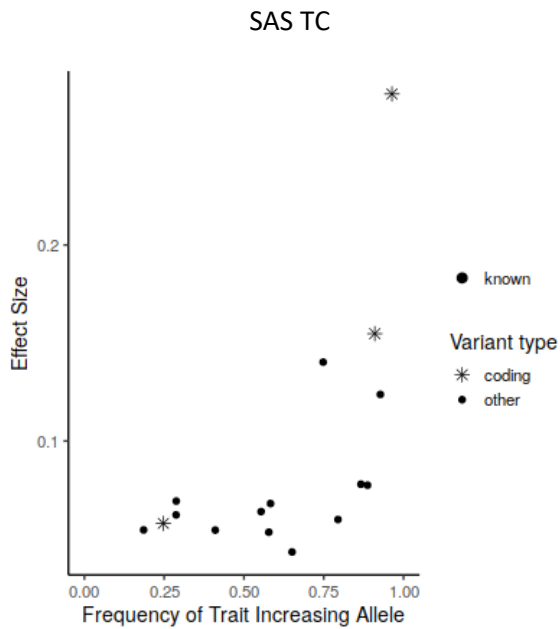
EUR LDL-C



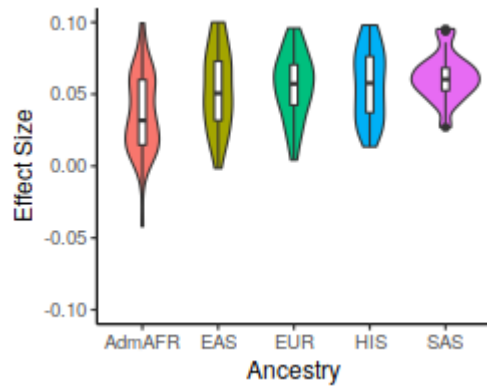




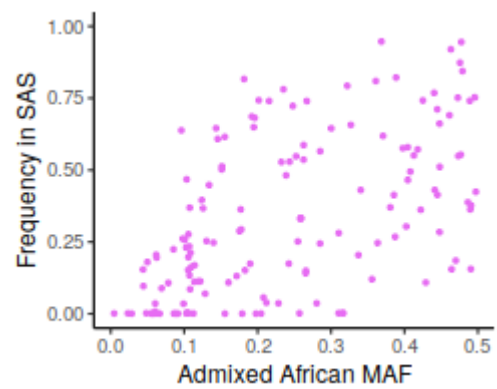
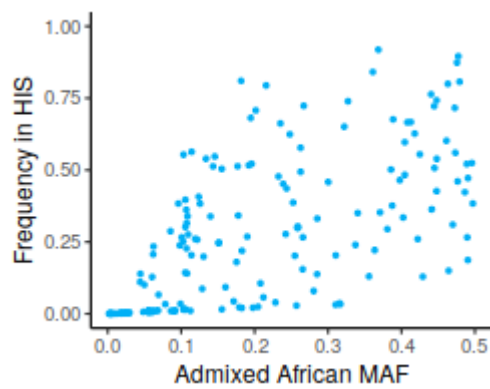
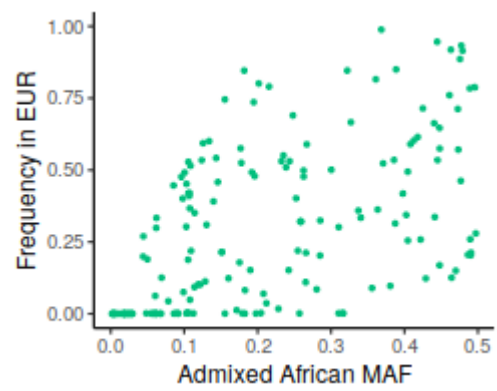
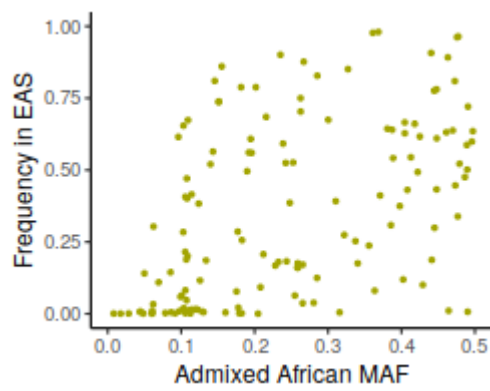
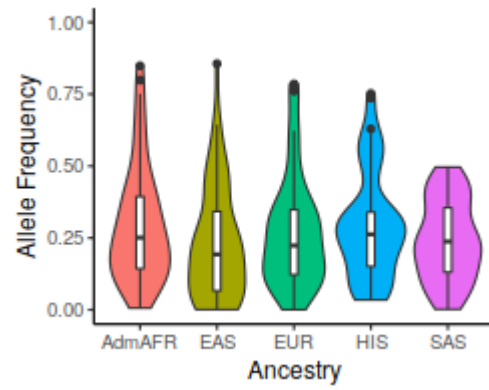




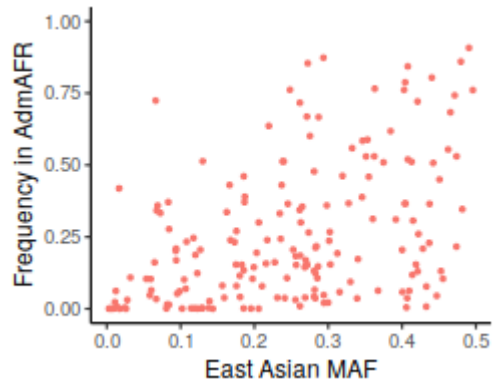
SAS index variants



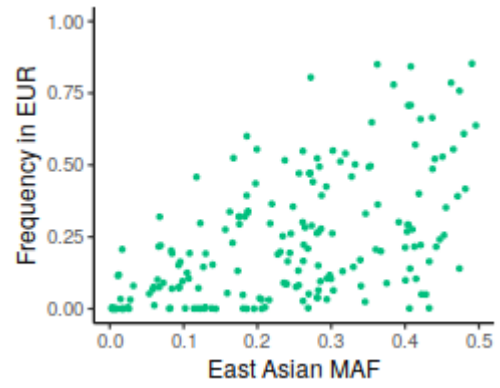
SAS index variants



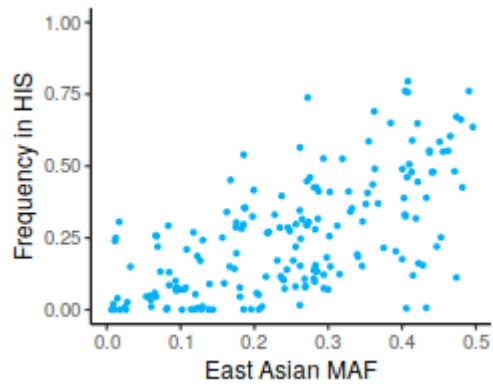
EAS index variants



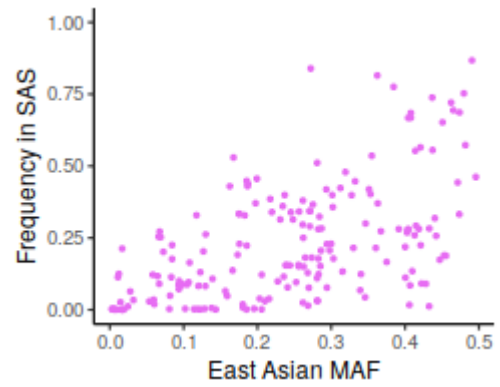
EAS index variants



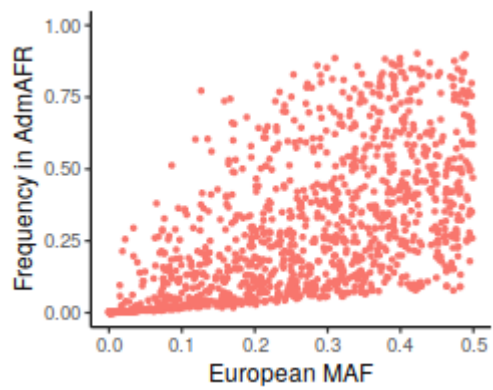
EAS index variants



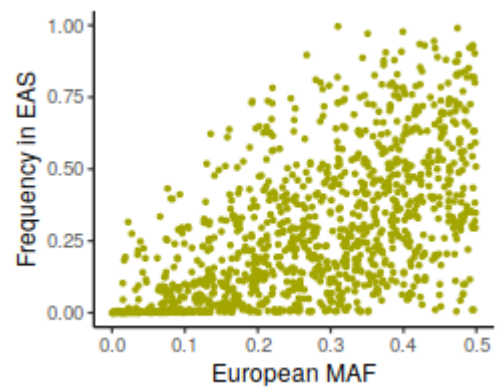
EAS index variants



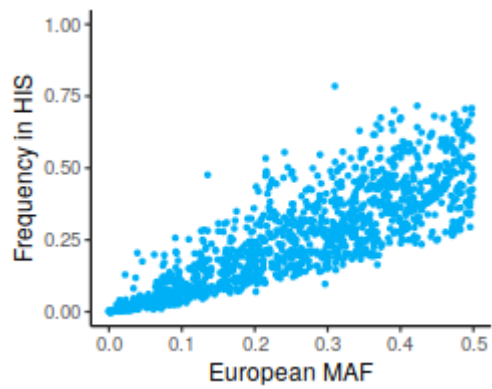
EUR index variants



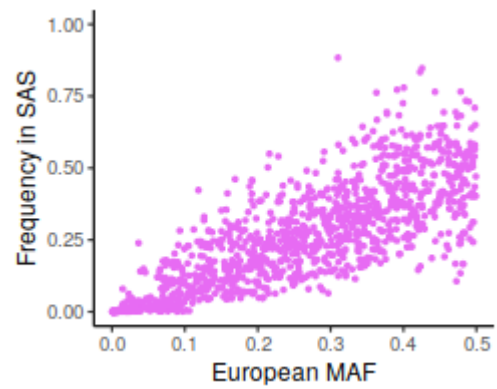
EUR index variants



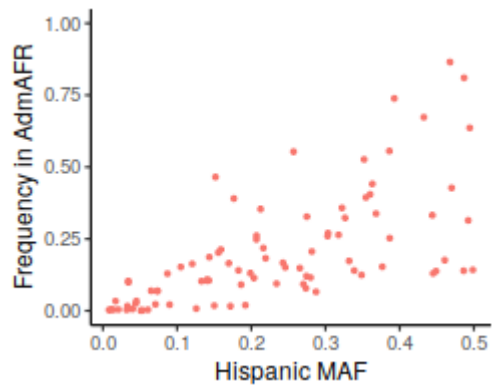
EUR index variants



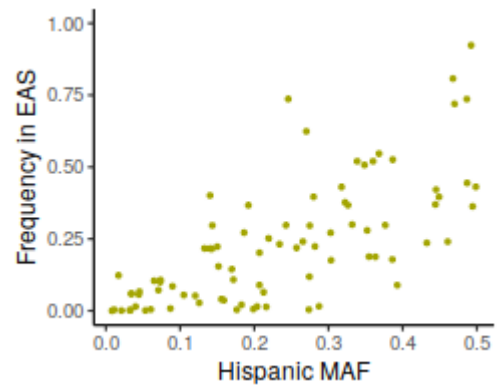
EUR index variants



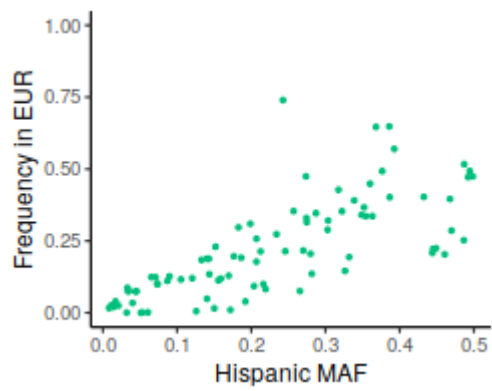
HIS index variants



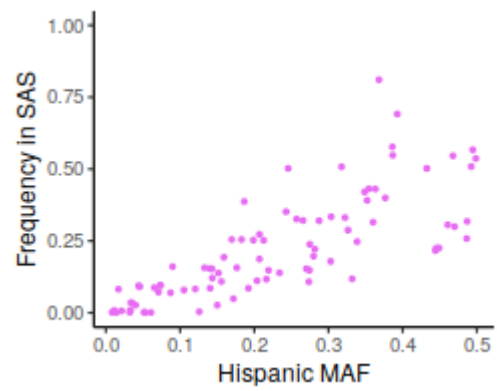
HIS index variants



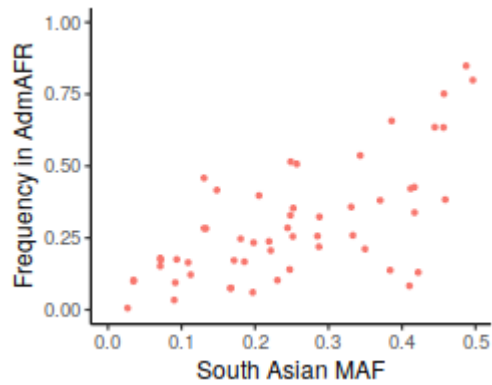
HIS index variants



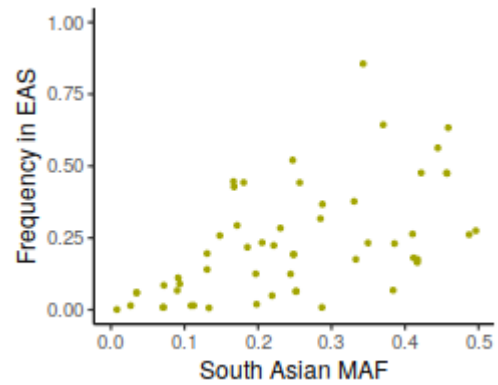
HIS index variants



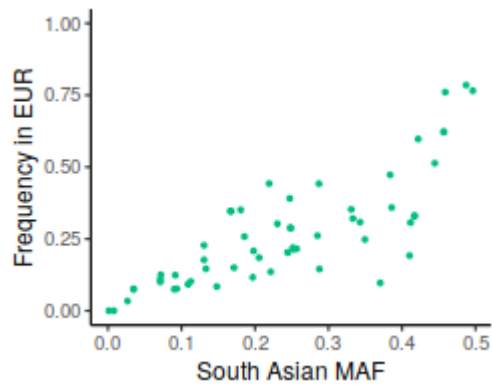
SAS index variants



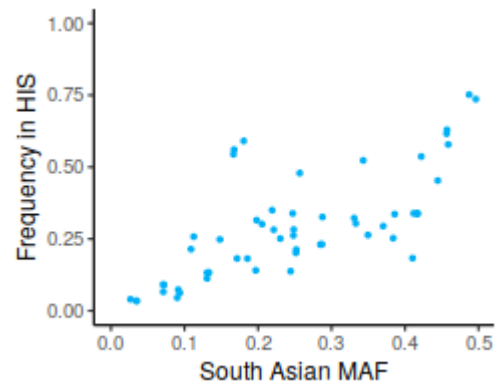
SAS index variants



SAS index variants

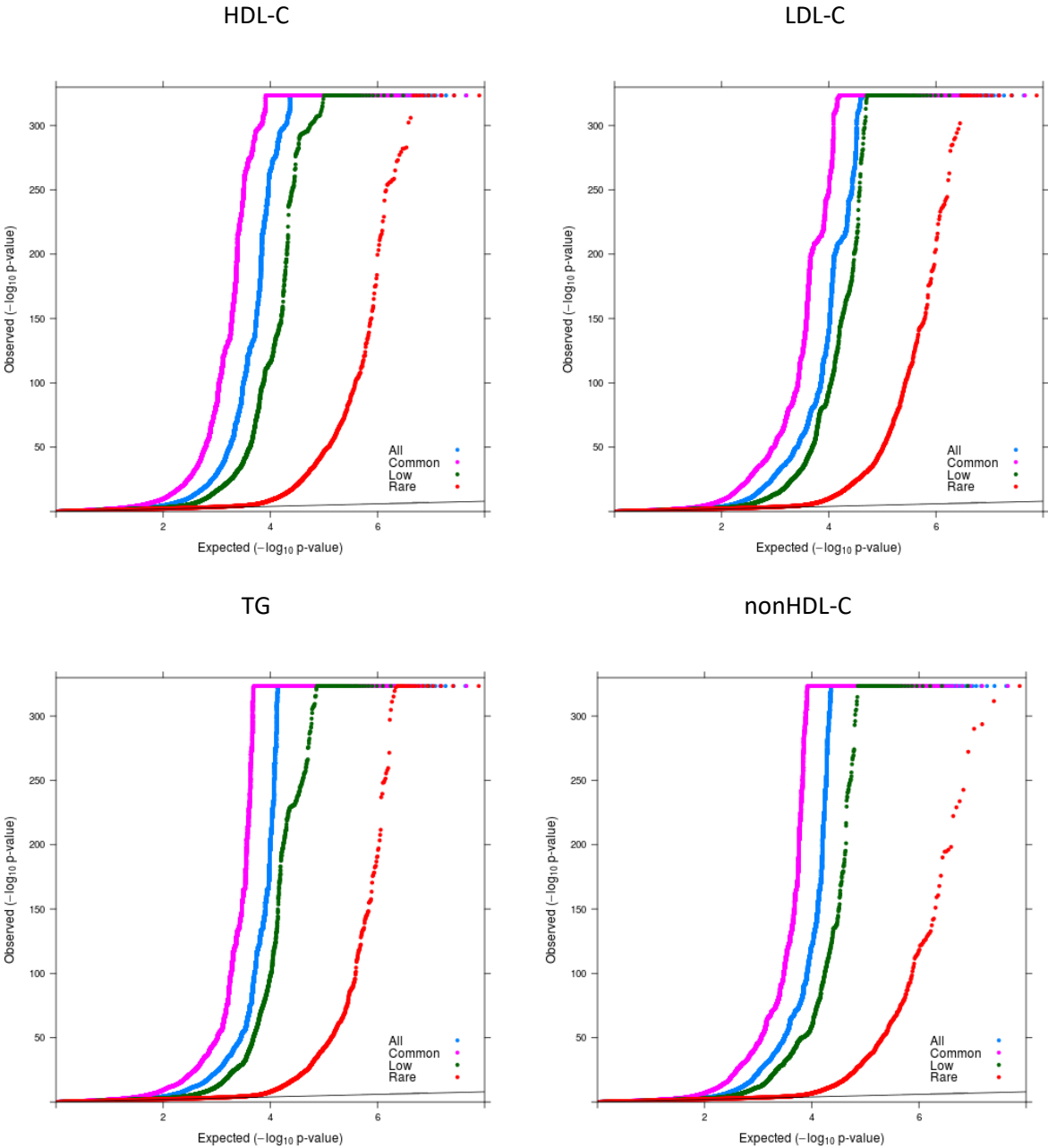


SAS index variants

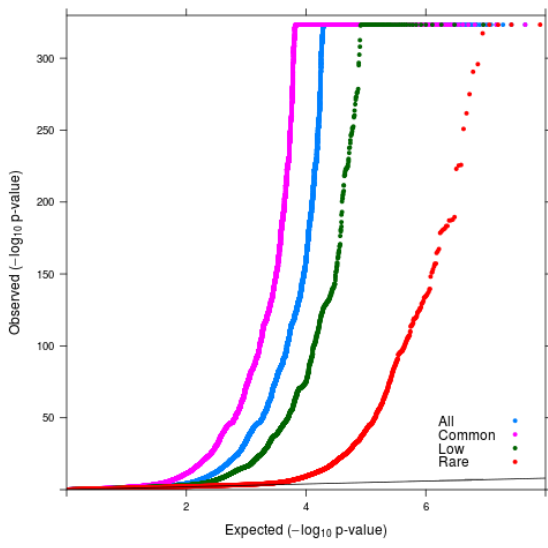


Sample sizes for each index variant are given in Supplementary Table 3 and for each ancestry overall in Table 1. Boxplots depict the median value as the center, first and third quartiles as box boundaries and whiskers extending 1.5 times the inter-quartile range, with points beyond this region shown individually.

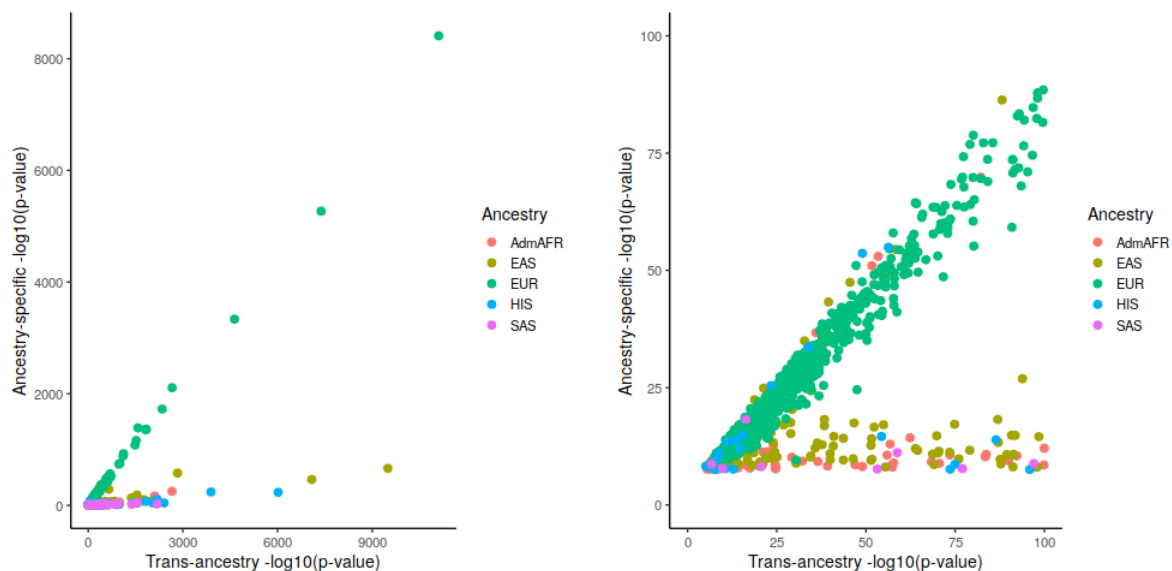
Supplementary Figure 4: QQ plots from multi-ancestry meta-analysis



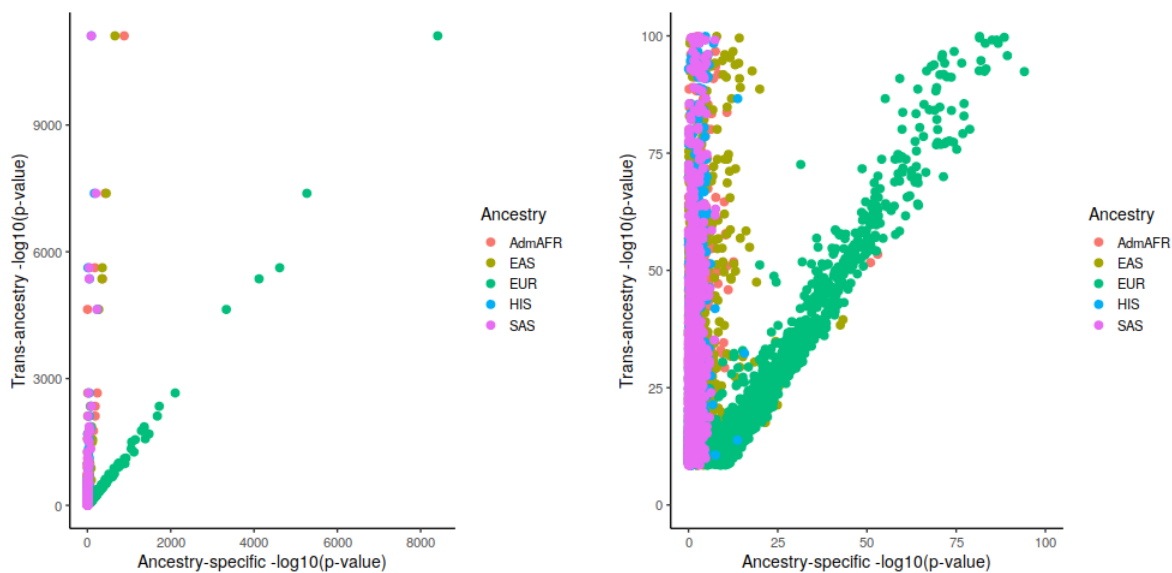
TC



**Supplementary Figure 5: Comparison of association results for ancestry-specific and multi-ancestry analysis**

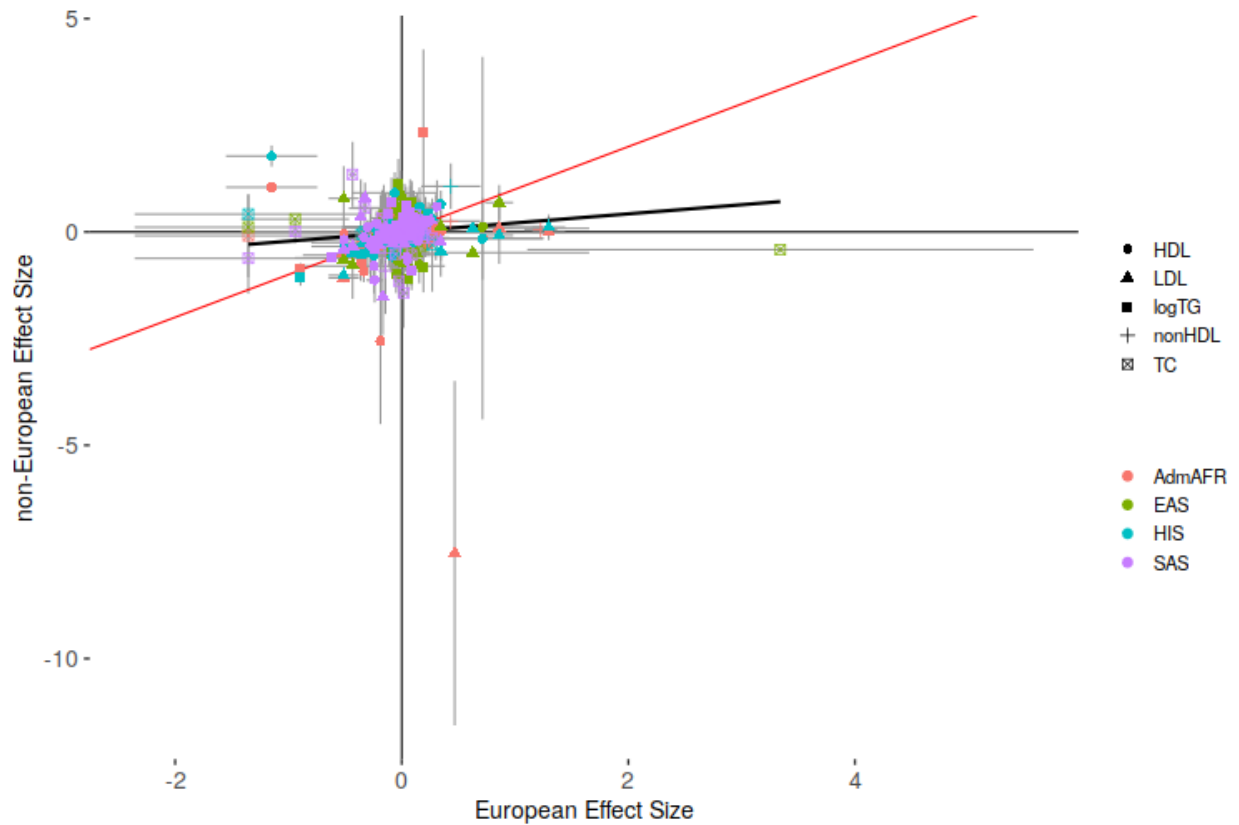


A) Multi-ancestry association results for variants identified in ancestry-specific analysis

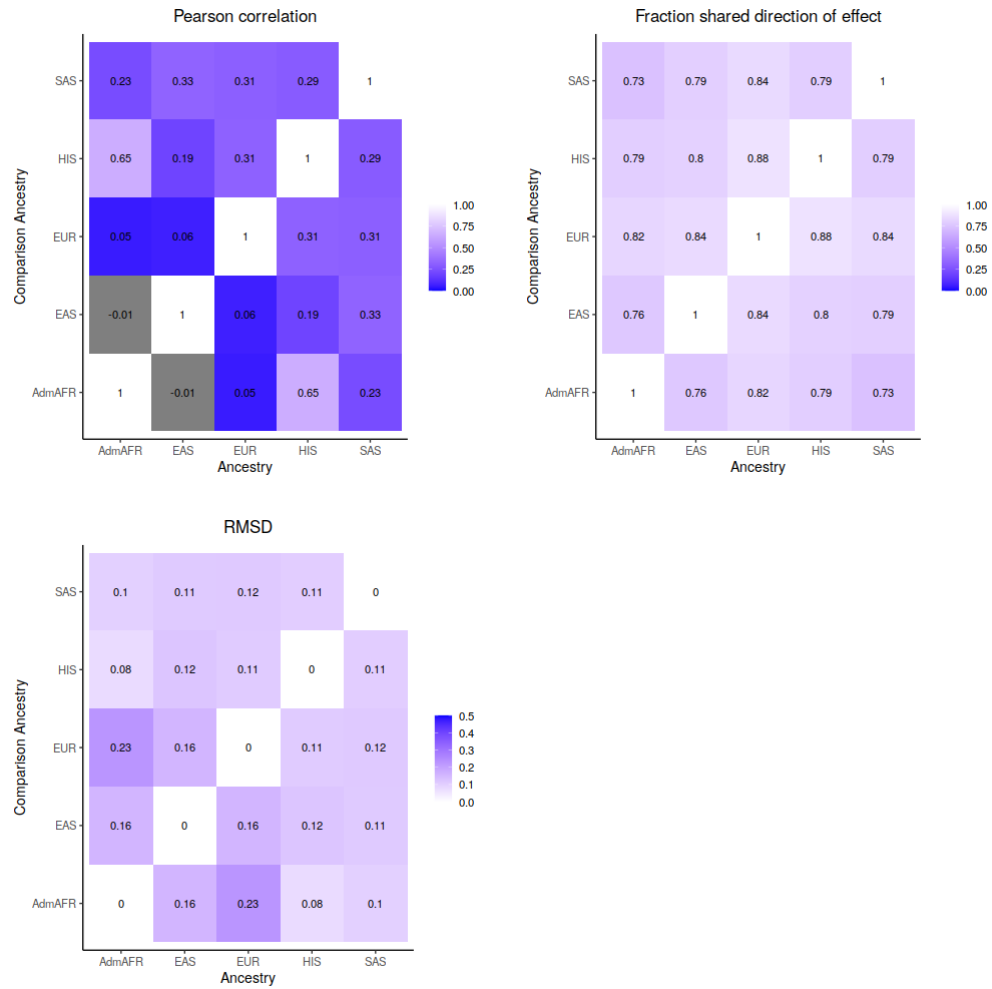


B) Ancestry-specific association results for variants identified in multi-ancestry analysis

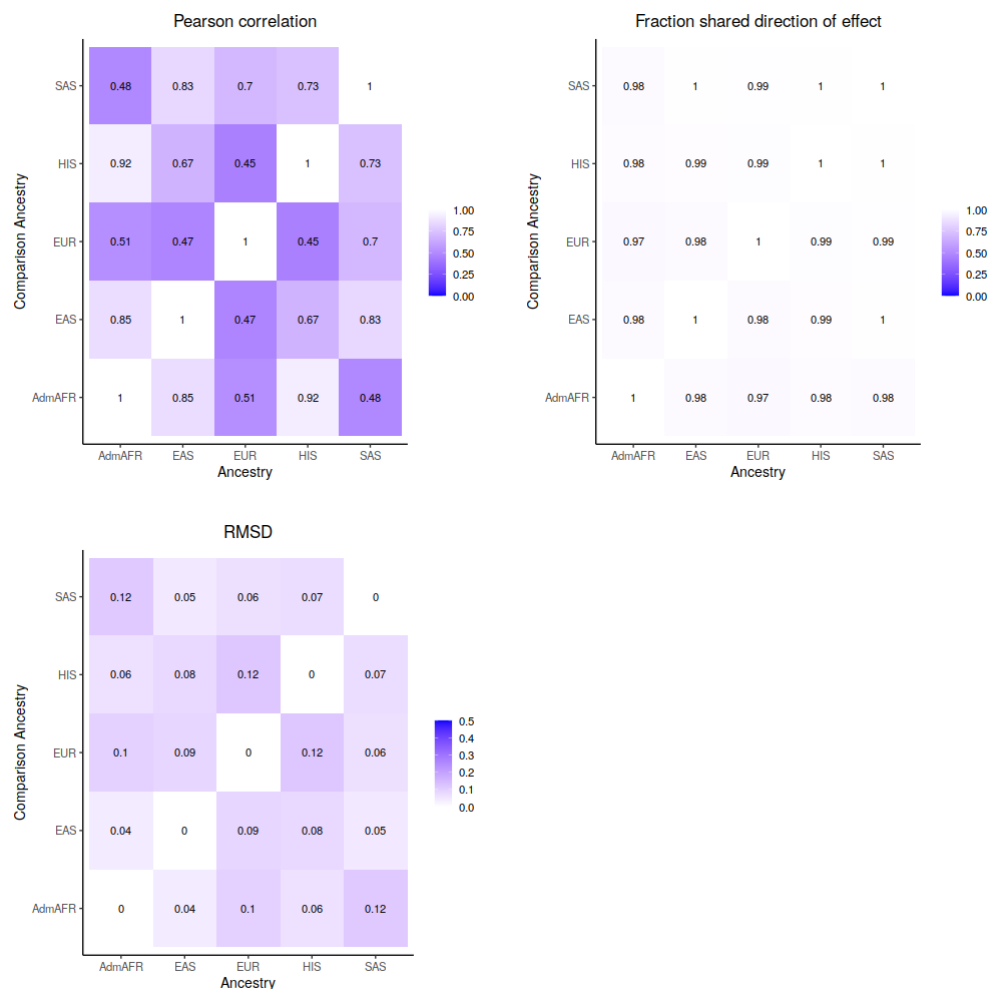
**Supplementary Figure 6: Effect sizes by ancestry for unique index variants from ancestry-specific meta-analysis**



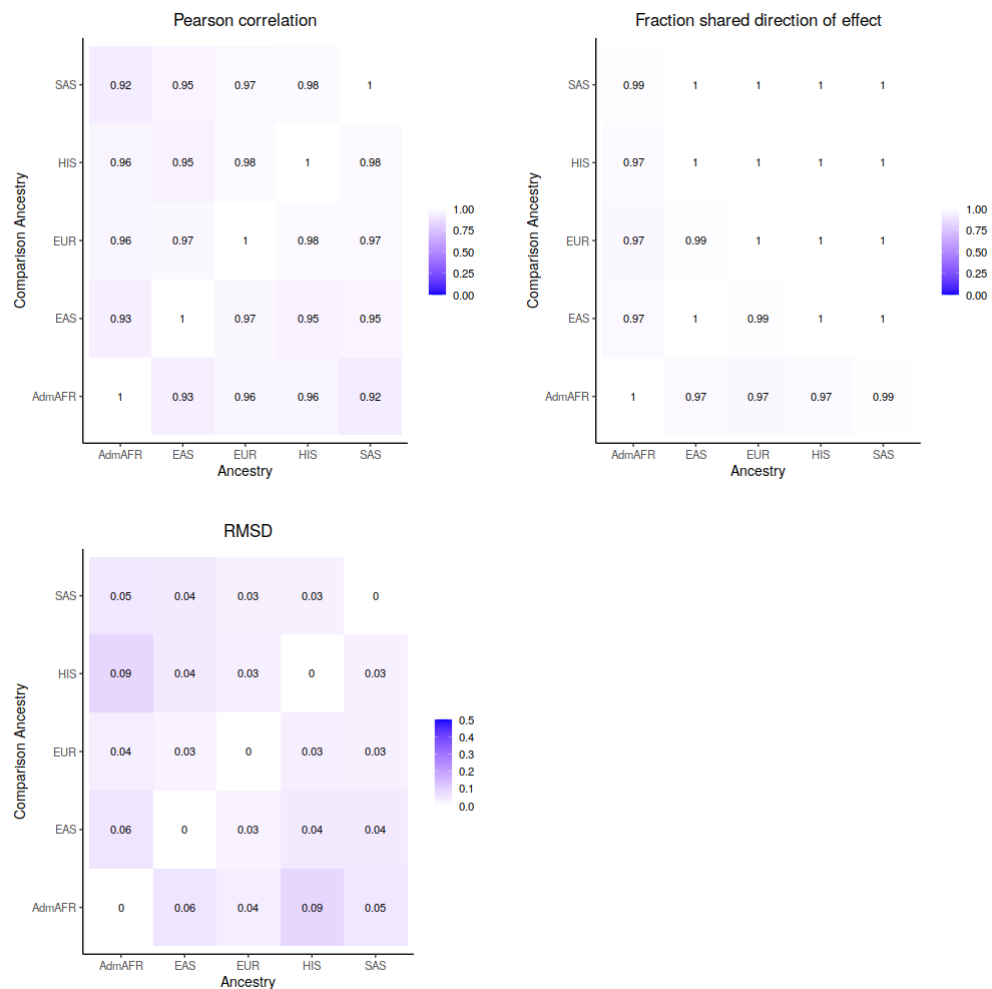
- A) Comparison of effect sizes (with standard errors) for all variants,  $R^2=0.02$ . This plot includes all unique index variants ( $p\text{-value} < 5 \times 10^{-8}$  in at least one ancestry as given by RAREMETAL) compared against the effect sizes in the other ancestries, without filtering of variants based on their significance in the compared ancestry group. Association results for all index variants are given in Supplementary Table 3. The corresponding effect size values are given in Supplementary Table 6. The European effect size = non-European effect size line is given in red while a linear regression line is given in black.



B) Pairwise correlation of effect sizes, fraction of shared direction of effect, and comparison of the magnitude of effect size differences (given as RMSD) between ancestries for all variants

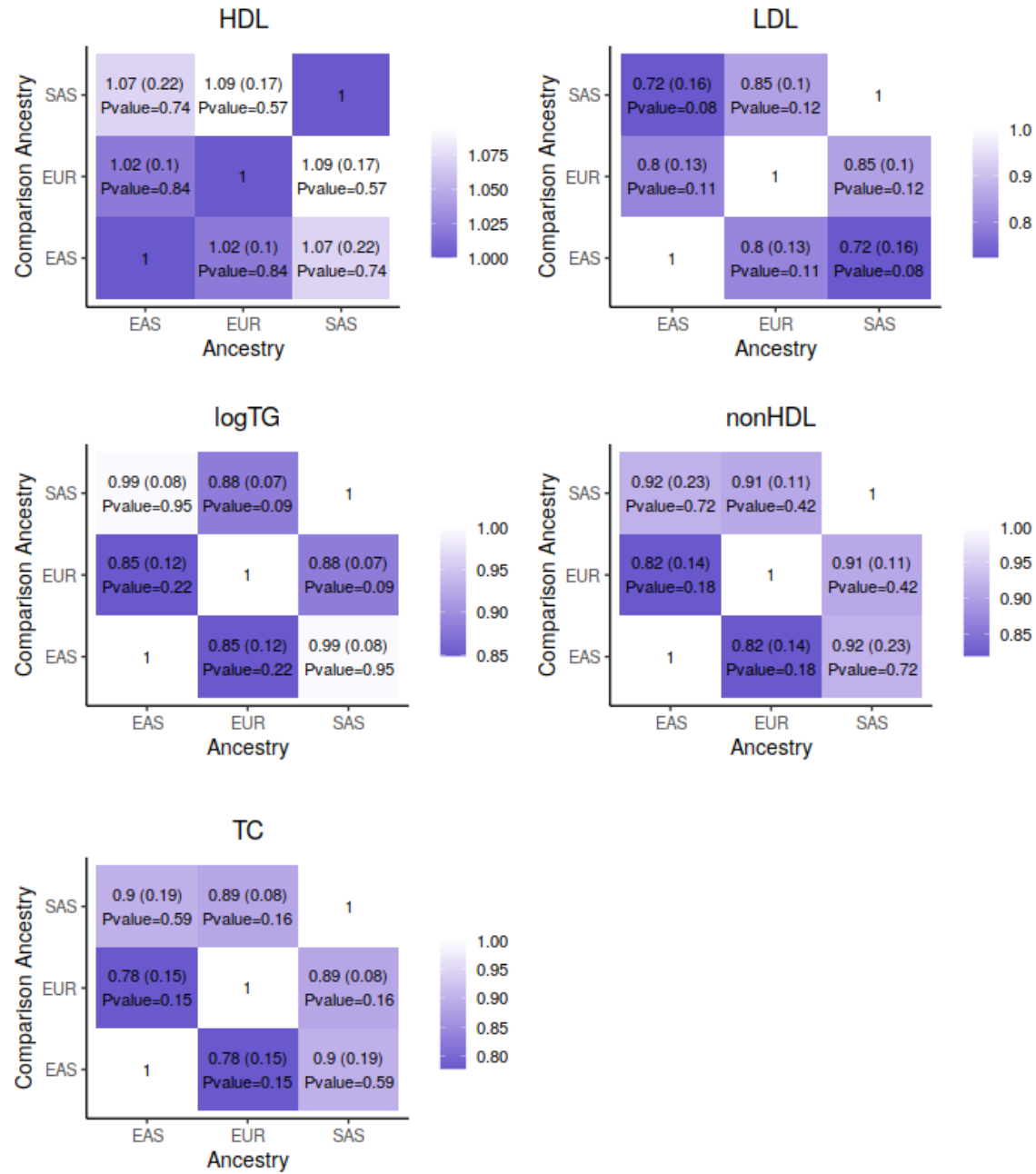


- C) Pairwise correlation of effect sizes, fraction of shared direction of effect, and comparison of the magnitude of effect size differences between ancestries for variants reaching nominal significance ( $p$ -value  $< 0.05$  as given by RAREMETAL) in both compared ancestries. Association results for all index variants are given in Supplementary Table 3.



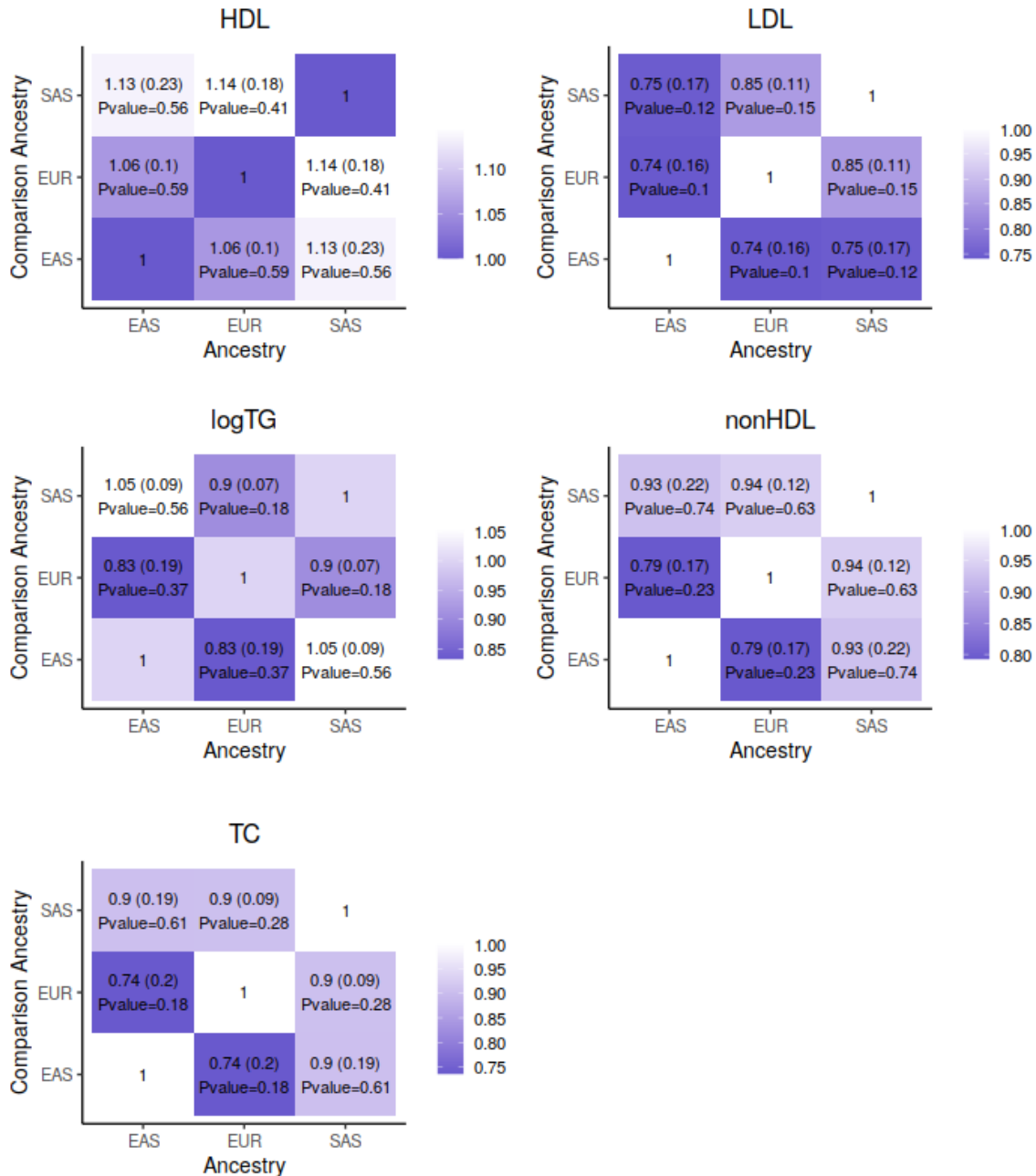
D) Pairwise correlation of effect sizes, fraction of shared direction of effect, and comparison of the magnitude of effect size differences between ancestries for variants reaching genome-wide significance ( $p\text{-value} < 5 \times 10^{-8}$  as given by RAREMETAL) in both compared ancestries. Association results for all index variants are given in Supplementary Table 3.

**Supplementary Figure 7: Genetic impact correlation estimates between ancestries for each trait analyzed**



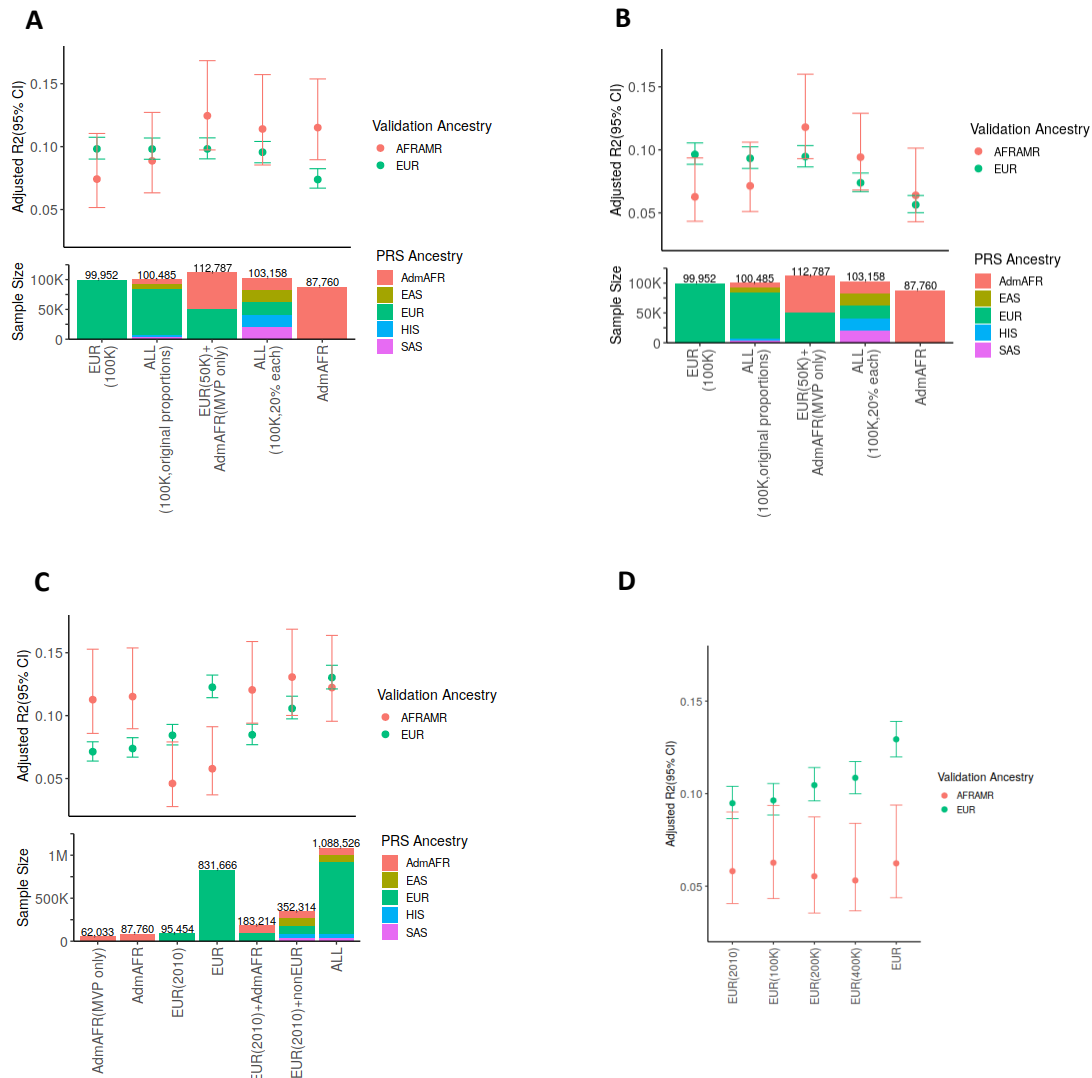
Correlation estimates were calculated with Popcorn and are given followed by the standard error in parentheses. Correlations were not significantly less than 1 (p-value > 0.05).

**Supplementary Figure 8: Genetic effect correlation estimates between ancestries for each trait analyzed**



Correlation estimates were calculated with Popcorn and are given followed by the standard error in parentheses. Correlations were not significantly less than 1 (p-value > 0.05).

## Supplementary Figure 9: Comparison of PRS source ancestry and sample size with prediction in European and African American individuals



Error bars represent 95% confidence intervals. The Michigan Genomics Initiative includes 17,190 European-ancestry individuals and 1,341 African American individuals. The Million Veteran Program includes 68,381 European-ancestry individuals and 18,251 African American individuals.

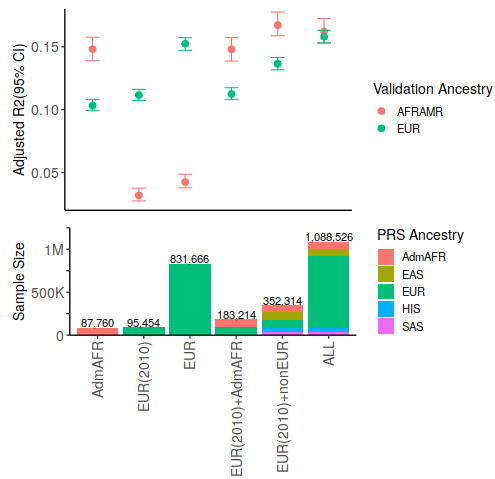
A) At constant sample size (~100,000) and using only pruning and thresholding to create risk scores used for prediction in the Michigan Genomics Initiative (MGI)

B) At constant sample size (~100,000) and using only PRS-CS to create risk scores used for prediction in the Michigan Genomics Initiative (MGI)

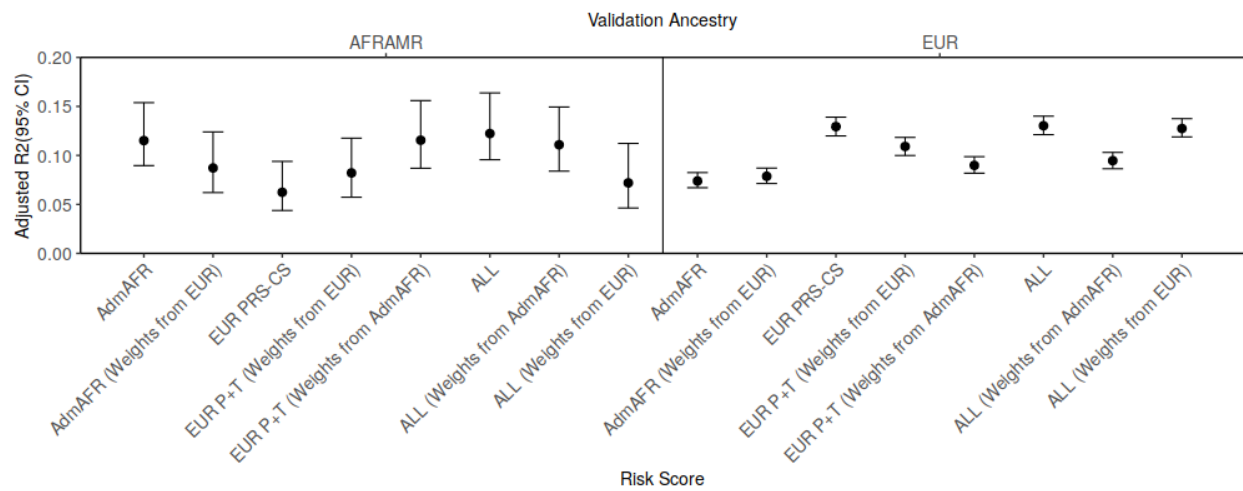
C) Using only pruning and thresholding to create risk scores with variable numbers of individuals from each ancestry group tested in the Michigan Genomics Initiative (MGI)

D) Using only PRS-CS with variable numbers of European individuals tested in the Michigan Genomics Initiative (MGI)

E



F

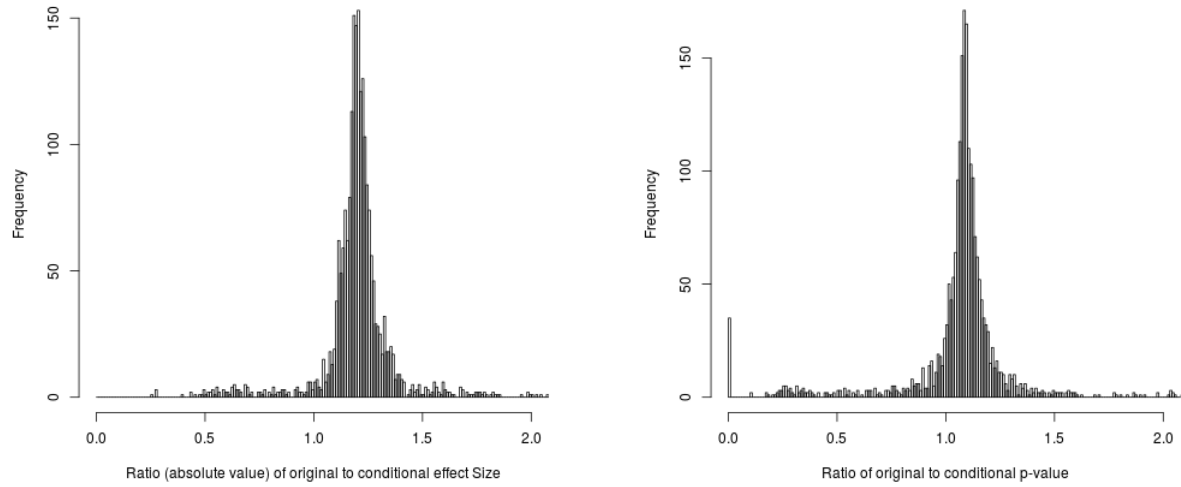


E) Using only pruning and thresholding to create risk scores with variable numbers of individuals from each ancestry group tested in the Million Veteran's Program (MVP)

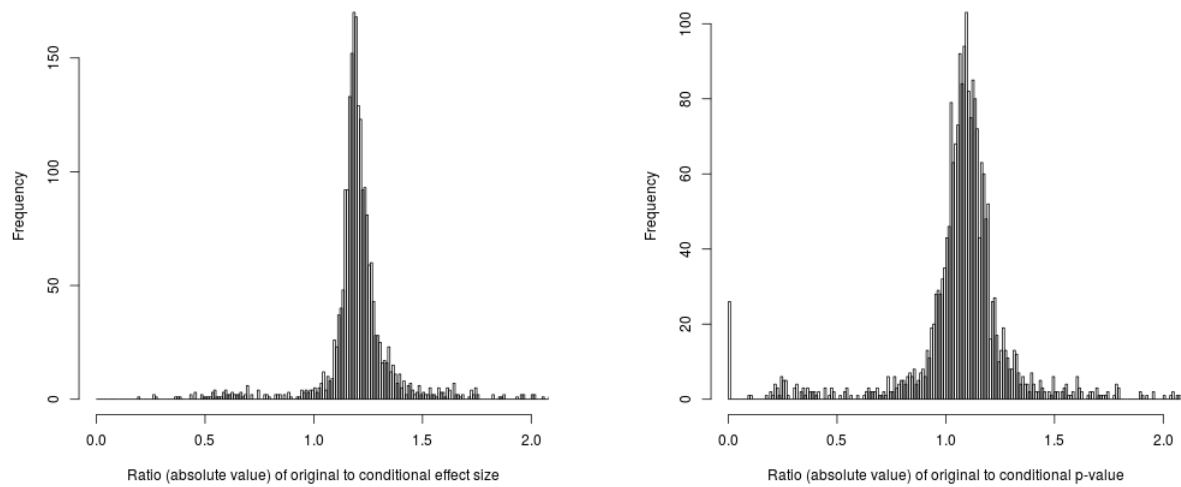
F) Comparison of effect size source ancestry with prediction in MGI

## Supplementary Figure 10: Comparison of original and conditional effect sizes

**A**



**B**



A) From ancestry-specific meta-analysis

B) From multi-ancestry meta-analysis

The x-axis of each plot is truncated at a ratio of 2 to aid in visualization.

## Supplementary Notes

### Comparison of associated variants by ancestry group

We assessed whether the ancestry-specific variants were enriched by trait or ancestry. The six Hispanic-specific index variants were all associated with triglycerides and concentrated within a region in length of several megabases on chromosome 11 that has been previously identified to be associated with high TG levels among individuals with Indigenous American ancestry<sup>29,30</sup>. Other ancestry-specific associated variants were relatively evenly distributed among the different lipid traits (**Supplementary Table 3, Supplementary Figure 3**).

Approximately 0.5% of tested genome-wide variants reached significance ( $P < 5 \times 10^{-8}$ ) for at least one trait. The associated regions encompass 13% of the genome across all traits based on the minimum and maximum positions of variants that reach genome-wide significance at each locus. By trait, 7%, 5%, 6%, 5%, and 6% of the genome was associated with HDL-C, LDL-C, TG, nonHDL-C, and TC, respectively. Overall, the novel multi-ancestry index variants reaching genome wide significance explained ~0.8% of the variance in each trait, with all variants explaining 12%, 13%, 9%, 13%, and 12% of the variance across all ancestries, for HDL-C, LDL-C, TG, nonHDL-C, and TC, respectively. Using population-specific effect size estimates and allele frequencies, we find that the proportion of variance explained by the multi-ancestry index variants within each ancestry on average is 28%, 11%, and 17% lower in Admixed Africans, East Asians, and South Asians and 1% and 6% higher in Europeans and Hispanics, respectively, relative to the multi-ancestry estimate (**Supplementary Table 19**). For variants successfully imputed into all ancestry groups, this corresponds to 8%, 9%, 11%, 11%, and 9% of the variance for Admixed African, East Asian, European, Hispanic, and South Asian individuals, respectively. However, it is important to note that genes involved in lipid levels can be effective therapeutic targets in all ancestry groups even if naturally occurring variation, for example in the non-coding region, has a small effect on the trait (e.g. HMGCR<sup>29</sup> and statins) or if genetic variants have a differential impact by ancestry.

### Improvement in credible sets by ancestry group

In order to quantify the improvement in fine-mapping through multi-ancestry meta-analysis, we grouped the 2,286 index variants into 1,486 independent association signals based on an LD  $r^2$  threshold of 0.7 between index variants. This was done to avoid double-counting overlapping association signals. Considering all independent association signals under the assumption of a single, shared causal variant, we found a median 40% reduction in credible set size for regions with improved fine-mapping in the multi-ancestry meta-analysis. We next aimed to determine whether differences in linkage disequilibrium patterns or allele frequency differences were driving this improvement. Starting with the independent association signals, we selected for further analysis the 151 signals that reached a significance threshold of  $p\text{-value} < 5 \times 10^{-8}$  in both the Admixed African and European meta-analyses alone. For each of these regions, we manually inspected LocusZoom plots from the Admixed African and European ancestry-specific meta-analyses and from multi-ancestry meta-analysis to exclude any loci with apparent secondary signals within the region. Of the 69 association signals selected for further analysis (**Supplementary Table 20**), 36 (52%) had the smallest 99% credible set from the multi-ancestry meta-analysis, 6 (9%) from the Admixed African ancestry meta-analysis, 3 (4%) from the European ancestry

meta-analysis, and 24 (35%) had equivalent fine-mapping in two or more analyses. Among the 36 signals with improved fine-mapping, we observed a median 50% reduction in credible set size.

We next focused our comparisons on the 36 association signals with improved fine-mapping in the multi-ancestry meta-analysis. The multi-ancestry index variants at these signals were more common in Admixed Africans than Europeans 56% of the time (20/36), with a median 1.3-fold difference. We then identified all variants in 1000 Genomes that were in strong linkage disequilibrium ( $r^2 > 0.8$ ) with the multi-ancestry index variant in Africans or Europeans. Nearly all loci (33/36, 92%) with improved fine-mapping had fewer variants in high LD among Africans compared to Europeans. For example, in 1000 Genomes Africans there was a median of 6 variants having  $r^2 > 0.8$  with the multi-ancestry index variant compared to a median of 40 variants having  $r^2 > 0.8$  in Europeans. Therefore, the improved fine-mapping observed in the multi-ancestry meta-analysis appears to be primarily due to the smaller number of variants in high LD with the lead index variant in Africans relative to Europeans rather than differences in allele frequency between populations.

### **Polygenic scores by ancestry group**

Previous studies have suggested that population stratification may influence the predictive ability of polygenic scores across diverse populations<sup>26</sup>. We tested for correlation between the multi-ancestry polygenic score and principal components of ancestry (PCs) in 1000 Genomes individuals. Significant correlation was observed between the multi-ancestry polygenic score and PCs 1 and 3 only (p-value < 0.0025; 0.05/20 tested PCs; **Supplementary Table 21**). Within the MGI cohort, we found that median LDL-C values were not significantly correlated with any of the first twenty principal components (p-value > 0.0025) and prediction of LDL-C as measured by adjusted  $R^2$  was similar when either PCs 1-4, 1-10, or 1-20 were included as covariates in the model with the ancestry-specific or multi-ancestry polygenic scores (**Supplementary Tables 22 and 23**). We note that normalization of LDL polygenic scores should be performed within each ancestry.

We next aimed to determine the underlying basis for the success of the LDL-C multi-ancestry score. Several factors may influence the predictive ability of a polygenic score, including the GWAS-related factors of sample size and ancestry makeup and factors related to PRS method such as variant selection and estimation of polygenic score weights. Polygenic scores developed from the GWAS with the largest sample sizes (European or multi-ancestry) were less sensitive to the optimizing approach (i.e. weights derived from PRS-CS or a variety of p-value thresholds performed similarly), whereas the other ancestry-specific scores showed much more variable performance of the PRS depending on the optimizing parameters (**Extended Data Figure 6b**). In order to identify which factors were most important, we created five different GWAS at fixed sample sizes of ~100k: EUR and AdmAFR single-ancestry GWAS, a half EUR, half AdmAFR bi-ancestry GWAS, and two multi-ancestry GWAS, one with equal numbers of the five ancestries and one where each ancestry matched the proportion in the full 1.65m meta-analysis. Using a pruning and thresholding approach, we created optimized polygenic score weights for each of these five different GWAS meta-analyses. As expected, LDL-C prediction in admixed African individuals was relatively poor from an entirely European ancestry GWAS, irrespective of the sample size (adjusted  $R^2$  MVP = 0.03-0.04, **Supplementary Figure 10, Supplementary Table 17**). The ancestry matched single-ancestry scores were similar or slightly worse predictors of LDL-C compared to the multi-ancestry scores (**Supplementary Figure 10**). The multi-ancestry score with equal proportions

of each ancestry group predicted LDL-C better among African Americans, and both multi-ancestry scores predicted LDL-C similarly well among Europeans. Lastly, the ancestry-mismatched scores predicted LDL-C less well in African Americans (65% of multi-ancestry polygenic score) than the ancestry-mismatched score predicted LDL-C in European Americans (77% of multi-ancestry polygenic score).

We next examined the improvement in prediction of LDL-C with increasing sample size. We generated polygenic scores from MVP AdmAFR only, the full AdmAFR meta-analysis, the 2010 Global Lipids Genetics Consortium LDL-C meta-analysis<sup>4</sup> (EUR N=95,454, imputed with HapMap) and subsets of the European and multi-ancestry meta-analyses. Increasing the sample size of the discovery GWAS with ancestry-matched samples led to an increased prediction accuracy for both admixed African and European ancestry individuals. For example, we observed a 36% increase in the predictive accuracy of LDL-C polygenic scores (adjusted  $R^2$  MVP = 0.11 and 0.15, respectively) with the nine-fold increase in sample size between the 2010 and present European-specific polygenic score.

Finally, we aimed to investigate the role of variant selection and weights in polygenic score performance. Poor performance of ancestry mismatched scores could be caused by either missing ancestry-specific variants in the score or by differing LD with the underlying causal variant between ancestry groups leading to imperfect variant weights. Starting with ancestry mismatched pruning and thresholding scores, we attempted to ‘correct’ the ancestry mismatch by first applying ancestry-matched weights. This helps with future study design questions – e.g. would a single pre-defined set of variants on an array be useful for all ancestries if we applied updated ancestry-specific weights? We used the predictive ability of the pruning and thresholding multi-ancestry score as the ‘gold standard’ because it achieved the highest  $R^2$  for any polygenic score. In admixed African individuals, we recovered 87% of the gold standard polygenic score when we used the European variant list with admixed African weights compared to just 47% when using the European variant list with weights from Europeans (**Extended Data Figure 7, Supplementary Figures 10, Supplementary Table 17**).

We then examined the role of optimizing variants selected for polygenic scores. We found that European ancestry GWAS-derived score had improved prediction in individuals with admixed African ancestry when the variant selection parameters (such as p-value thresholds for pruning and threshold) were selected based on optimizing the score in admixed African ancestry rather than in Europeans. Using parameters optimized from only European individuals led to prediction in admixed African individuals that was just 47% of the gold standard while using parameters optimized in admixed African individuals (a more stringent p-value threshold of  $5 \times 10^{-10}$ ) resulted in prediction that was 67% of the gold standard (**Supplementary Table 17**), even with European weights. Finally, using the AFR ancestry-matched weights and ancestry-matched variant list from a single-ancestry AFR GWAS resulted in 94% of the gold standard (multi-ancestry) polygenic score performance. Taken together, our findings suggest that polygenic scores derived from ancestry-mismatched GWAS may be improved by substituting ancestry-specific weights for the selected variants when ancestry-matched GWAS of sufficient sample sizes are not available, and/or by optimizing the variant selection in ancestry-matched individuals.

We noted that the LDL-C polygenic score showed greater variability in prediction of LDL-C for cohorts within Africa than it did among African American cohorts. Mean lipid levels within each cohort also exhibited greater variation between the continental African cohorts compared to all other ancestry

groups. Additional studies are needed to better understand both the genetic and environmental factors influencing LDL-C levels.

## Supplementary Methods: Derivation of approximate Bayes factors

Consider two models,  $M_0$  and  $M_1$ . Let  $\hat{\theta}_k$  denote the maximum likelihood estimates of model parameters under model  $M_k$  and let  $d_k$  denote the dimension of model  $M_k$ . The Schwarz Criterion is given by

$$S = \log f(y|\hat{\theta}_1, M_1) - \log f(y|\hat{\theta}_0, M_0) - \frac{(d_1 - d_0)}{2} \log(n)$$

where  $y$  are observed data and  $n$  is the sample size. The Bayes' factor in favour of model  $M_1$  over  $M_0$  is then approximated by  $\exp(S)$ .

In the context of our study, the null model  $M_0$  corresponds to allelic effect sizes fixed at 0, whilst under the alternative model  $M_1$  allelic effect sizes are unconstrained. The difference in log-likelihoods between the two models is given by  $X^2/2$ , where  $X^2$  is the deviance between the two models, which is approximated by the observed chi-square statistic,

$$X^2 = \frac{\beta^2}{SE^2}$$

It then follows that

$$BF \approx \exp \left[ \frac{X^2 - \log(n)}{2} \right]$$

### References:

- Kass RE, Raftery AE (1995). Bayes factors. *Journal of the American Statistical Association*, 90: 773-795.
- Schwarz G (1978). Estimating the dimension of a model. *Annals of Statistics*, 6: 461-464.