Supplementary Material

Meta-analysis of 49,549 individuals imputed with the 1000 Genomes Project reveals an exonic damaging variant in *ANGPTL4* determining fasting TG levels.

Appendix 1: The Lifelines Cohort Study

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Appendix 2: CHARGE Lipids Working Group

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Supplementary Methods

Study descriptions

All studies were performed with the approval of the local medical ethics committees, and written informed consent was obtained from all participants.

Athero-Express Biobank Study (AEGS). The Athero-Express Biobank Study (http://www.atheroexpress.nl) is an ongoing multicenter longitudinal biobank study that started in 2002, and has been described elsewhere[1]. In short, patients undergoing carotid (CEA) and femoral endarterectomy at two Dutch tertiary referral centers for vascular surgery are included, and during endarterectomy blood and plaque material is obtained and stored at -80ºC. For this study, we only considered CEA patients.

Airwave. The Airwave Health Monitoring Study1 was established to evaluate possible health risks associated with the use of TETRA, a digital communication system used by police forces and other emergency services in Great Britain since 2001. The study has been broadened to investigate more generally the health of the work force. For this study we considered participants with available genetic data. The study has ethical approval from the National Health Service Multi-site Research Ethics Committee and participants have consented to the use of their data and samples for research purposes.

Age, Gene/Environment Susceptibility (AGES) Study. The Age, Gene/Environment Susceptibility (AGES Reykjavik) Study was initiated to examine genetic susceptibility and gene/environment interaction as these contribute to phenotypes common in old age, and represents a continuation of the Reykjavik Study cohort begun in 1967. The study is approved by the Icelandic National Bioethics Committee, (VSN: 00-063) and the Data Protection Authority. The researchers are indebted to the participants for their willingness to participate in the study.

Atherosclerosis Risk in Communities (ARIC) Study. The ARIC study has been described in detail previously[2]. Men and women aged 45-64 years at baseline were recruited from four communities: Forsyth County, North Carolina; Jackson, Mississippi; Minneapolis, Minnesota; and Washington County, Maryland. A total of 15,792 individuals, predominantly White and African American, participated in the baseline examination in 1987-1989, with three triennial follow-up examinations and a fifth exam in 2011-2013. All ARIC individuals provided written, informed consent to participate in research protocols that were approved by the University of North Carolina at Chapel Hill, Chapel Hill, NC institutional review board.

Cardiovascular Health Study (CHS). The CHS is a population-based cohort study of risk factors for CHD and stroke in adults greater than or equal to 65 years years conducted across four field centers[3]. The original predominantly Caucasian cohort of 5,201 persons was recruited in 1989-1990 from random samples of the Medicare eligibility lists; subsequently, an additional predominantly African-American cohort of 687 persons were enrolled for a total sample of 5,888. DNA was extracted from blood samples drawn on all participants at their baseline examination. Genotyping was later performed at the General Clinical Research Center's Phenotyping/Genotyping Laboratory at Cedars-Sinai on participants who consented to genetic testing and had DNA available. European ancestry participants who were free of clinical cardiovascular disease at baseline were genotyped using the Illumina 370CNV BeadChip system and African-Americans were genotyped using the Illumina HumanOmni1-Quad_v1 BeadChip system. For European ancestry participants, additional genotypes from the ITMAT-Broad-CARe (IBC) Illumina iSELECT chip were also used for imputation. CHS participants with available lipid measures for whom genotyping was successful constitute the CHS sample for this study. For this study the European ancestry (EA) samples were included in the discovery phase and the African American (AA) samples were included in the replication phase. CHS was approved by institutional review committees at each site, the subjects gave informed consent, and those included in the present analysis consented to the use of their genetic information for the study of cardiovascular disease.

CROATIA-Korcula, CROATIA-Split and CROATIA-Vis (CR-Korcula, CR-Split, CR-Vis). The CROATIA-Vis study includes unselected adult participants who were recruited in a population-based study during 2003 and 2004 in the villages of Vis and Komiza on the Dalmatian island of Vis. All subjects visited the clinical research centre in the region where they were examined in person and where fasting blood was drawn. Biochemical and physiological measurements were performed, detailed genealogies reconstructed, questionnaire of lifestyle and environmental exposures collected, and blood samples stored for further analyses. CROATIA-Korcula participants were recruited in the same manner from the Dalmatian island of Korcula in 2007 and

CROATIA-Split from the mainland Croatian city of Split in 2009-2010. All studies received appropriate ethical approval, and all participants gave informed consent.

Erasmus Rucphen Family (ERF) Study. The ERF study has been described in detail previously[4]. A total of approximately 3,000 participants descend from 22 couples who lived in the Rucphen region in The Netherlands in the 19th century. The 2,755 individuals with genotype data and lipid measurements were included in the current analysis.

Framingham Heart Study (FHS). The FHS funded by the National Heart Lung and Blood Institute, is an observational population-based cohort study composed of three generations of Framingham (MA) residents predominately of European descent. The Original cohort (N = 5,209) was enrolled in 1948[5]. The children and spouses of the Original cohort comprise the Offspring cohort (N = 5,124), which was enrolled in 1971-1975[6]. The Third Generation (N = 4,095) consists mostly of the children of the Offspring cohort, and was enrolled in 2002 to 2005[7]. All participants were examined every 4-8 years. DNA for surviving participants was collected in the late 1990s and early 2000s (1995-2005). Cholesterol and genetic data from 3,863 Offspring subjects and 3,508 Third Generation subjects contribute to this paper. All lipids were measured on fasting individuals according to LRC guidelines.

Family Heart Study (FamHS). The collection of phenotypes and covariates as well as clinical examination have been previously described for the Family Heart Study[8]. In brief, the FamHS began in 1992 with the ascertainment of 1,200 families, half randomly sampled and half selected because of an excess of CHD or risk factor abnormalities as compared with age- and sex-specific population rates. The families, with approximately 6,000 subjects, were sampled from four population-based parent studies: the Framingham Heart Study, the Utah Family Tree Study, and two centers for the ARIC study. The participants attended a clinic visit between the years 1994-1996 and a broad range of phenotypes was assessed in the general domains of CHD, atherosclerosis, cardiac and vascular function, inflammation and hemostasis, lipids and lipoproteins, blood pressure, diabetes and insulin resistance, pulmonary function, diet, habitual physical activity, anthropometry, medical history and medication use. Approximately 8 years later, 2,756 EA subjects belonging to the 510 of the largest and most informative pedigrees were invited for a second clinical exam (2002-2004). The most important CHD risk factors were measured again. Also, a computed tomography (CT) examination provided measures of coronary and aortic calcification, and abdominal and liver fat burden. Medical history and medication use were updated. In addition, 633 African American (AA) subjects were recruited at an additional ARIC field center at the University of Alabama in Birmingham. Several CHD risk factors were measured, including lipids, parameters of glucose metabolism, blood pressure, anthropometry, and

CT coronary and aortic calcification scores. Informed consent was obtained from all participants, and this project was approved by the Institutional Review Boards of all participating institutions. A total of 3,794 EA subjects, from the first clinic visit, and 612 AA subjects participated in the current study.

Finnish Cardiovascular Study (FINCAVAS). The purpose of the Finnish Cardiovascular Study (FINCAVAS) is to construct a risk profile - using genetic, haemodynamic and electrocardiographic (ECG) markers - of individuals at high risk of cardiovascular diseases, events and deaths. All patients scheduled for an exercise stress test at Tampere University Hospital and willing to participate have been recruited between October 2001 and December 2007. The final number of participants is 4,567. In addition to repeated measurement of heart rate and blood pressure, digital high-resolution ECG at 500 Hz was recorded continuously during the entire exercise test, including the resting and recovery phases. About 20% of the patients were examined with coronary angiography. Genetic variations known or suspected to alter cardiovascular function or pathophysiology were analysed to elucidate the effects and interactions of these candidate genes, exercise and commonly used cardiovascular medications.

FINRISK. For each Finrisk (1992, 1997, 2002, 2007) cohort2, a representative random sample is selected from the 25 – 74 year old inhabitants in five regions of Finland. The survey includes a mailed questionnaire and a clinical examination where a blood sample is drawn. A total of 23,036 individuals participated in the cohorts, and gave written informed consent.

Generation Scotland: Scottish Family Health Study (GS:SFHS) . The GS:SFHS is a collaboration between the Scottish Universities and the NHS, funded by the Chief Scientist Office of the Scottish Government. GS:SFHS is a family-based genetic epidemiology cohort with DNA, other biological samples (serum, urine and cryopreserved whole blood) and socio-demographic and clinical data from ~24,000 volunteers, aged 18-98 years, in ~7,000 family groups. Participants were recruited across Scotland, with some family members from further afield, from 2006-2011. Most (87%) participants were born in Scotland and 96% in the United Kingdom or Ireland. The cohort profile has been published[9]. GS:SFHS operates under appropriate ethical approvals, and all participants gave written informed consent.

Jackson Heart Study (JHS). JHS is a large, population-based observational study evaluating the etiology of cardiovascular diseases and related disorders among African Americans residing in the three counties (Hinds, Madison, and Rankin) that make up the Jackson, Mississippi metropolitan area. Data and biologic materials have been collected from 5,301 participants, including a nested family cohort of 1,498 members of 264 families. The age at enrollment for the unrelated cohort was 35-84 years; the family cohort included related individuals >21 years old. During a baseline examination (2000-

2004) and two follow-up examinations (2005-2008 and 2009-2012), participants provided extensive medical and social history, had an array of physical and biochemical measurements and diagnostic procedures, and provided blood for genomic DNA.. The study population is characterized by a high prevalence of diabetes, hypertension, obesity, and related disorders. Annual follow-up interviews and cohort surveillance are ongoing.

Lifelines. LifeLines[10] is a multi-disciplinary prospective population-based cohort study examining in a unique three-generation design the health and health-related behaviours of 165,000 persons living in the North East region of The Netherlands. It employs a broad range of investigative procedures in assessing the biomedical, socio-demographic, behavioural, physical and psychological factors which contribute to the health and disease of the general population, with a special focus on multimorbidity and complex genetics. This study only includes the individuals of which both genotype and lipid measurements were available.

Leiden Longevity Study (LLS). The LLS has been designed to investigate biomarkers of healthy ageing and longevity[11] and has been described in detail previously[12]. It is a family-based study consisting of 1,671 offspring of 421 nonagenarian sibling pairs of Dutch descent, and their 744 partners.

The London Life Sciences Prospective Population Study (LOLIPOP). LOLIPOP is an ongoing prospective cohort study of approximately 28K individuals aged 35-75 years, recruited from the lists of 58 General Practitioners in West London, United Kingdom between 2003 and 2008. The study includes both European and Indian Asian subjects. Indian Asian participants reported having all four grandparents born on the Indian subcontinent (India, Pakistan, Sri Lanka, or Bangladesh), whilst European participants were of self-classified whites born in Europe.

Loyola-GxE. The Kingston GxE cohort was obtained from a survey conducted in Kingston, Jamaica as part of a larger project to examine gene by environment interactions in the determination of blood pressure among adults 25-74 years. The International Collaborative Study of Hypertension in Blacks (ICSHIB)3,4 provided the sampling frame. The principal criterion for eligibility was a body mass index in either the top or bottom third of BMI for the Jamaican population. Participants were identified principally from the records of the Heart Foundation of Jamaica, a non-governmental organization based in Kingston, which provides low-cost screening services (height and weight, blood pressure, glucose, cholesterol) to the general public. Other participants were identified from among participants in family studies of blood pressure at the Tropical Metabolism Research Unit (TMRU) and from among staff members at the University of the West Indies, Mona.

Loyola-SPT. Participants were recruited from Spanish Town, a stable, residential urban area neighboring the capital city of Kingston, Jamaica as part of the International Collaborative Study of Hypertension in Blacks (ICSHIB)3,4. A stratified random sampling scheme was used to recruit adult males and females aged 25–74 years from the general population. Spanish Town was chosen because its demographic make-up was broadly representative of Jamaica as a whole.

Multi-Ethnic Study of Atherosclerosis (MESA). MESA is a study of the characteristics of subclinical cardiovascular disease (disease detected non-invasively before it has produced clinical signs and symptoms) and the risk factors that predict progression to clinically overt cardiovascular disease or progression of the subclinical disease[13]. MESA researchers study a diverse, population-based sample of 6,814 asymptomatic at baseline men and women aged 45-84. Thirty-eight percent of the recruited participants are white (MESA-CAU), 28% African-American (MESA-AFA), 22% Hispanic (MESA-HIS), and 12% Asian, predominantly of Chinese descent (MESA-CHN). Participants were recruited from six field centers across the United States: Wake Forest University, Columbia University, Johns Hopkins University, University of Minnesota, Northwestern University and University of California - Los Angeles.

The Netherlands Epidemiology of Obesity (NEO) study[14]**.** The NEO was designed for extensive phenotyping to investigate pathways that lead to obesity-related diseases. The NEO study is a population-based, prospective cohort study that includes 6,671 individuals aged 45–65 years living in the greater area of Leiden, the Netherlands, with an oversampling of individuals with overweight or obesity. At baseline, information on demography, lifestyle, and medical history have been collected by questionnaires. In addition, samples of 24-h urine, fasting and postprandial blood plasma and serum, and DNA were collected. Participants underwent an extensive physical examination, including anthropometry, electrocardiography, spirometry, and measurement of the carotid artery intima-media thickness by ultrasonography. In random subsamples of participants, magnetic resonance imaging of abdominal fat, pulse wave velocity of the aorta, heart, and brain, magnetic resonance spectroscopy of the liver, indirect calorimetry, dual energy X-ray absorptiometry, or accelerometry measurements were performed. The collection of data started in September 2008 and completed at the end of September 2012. Participants are followed for the incidence of obesity-related diseases and mortality.

Netherlands Twin Register and Netherlands Study of Depression and Anxiety (NTR-NESDA). The sample used in the analyses in this study consisted of 5,764 participants of the Netherlands Twin Register (NTR). NTR participants are ascertained because of the presence of twins or triplets in the family and consist of multiples, their parents, siblings and spouses. Twins are born in all strata of society and NTR represents a general sample from the Dutch population. Age ranged between 12 and 89 (median 39), and 62.4% was female[15,16]. The other 1,816 samples originated from the

NESDA cohort with available phenotype data. NESDA is a longitudinal study focusing on the course and consequences of depression and anxiety disorders. Subjects for NESDA were recruited from three sources, namely the general population, mental health organizations and general practices. The vast majority of NESDA subjects is selected for depression and anxiety, but the sample also includes healthy controls without lifetime psychiatric disorders. Age ranged between 18 and 65 in NESDA (median 43), and the proportion of females was 66.1%[17]. For all analysis, we excluded one monozygotic twin per pair. Additional corrections for family resemblance are analysis specific, and described where appropriate. Lipids were measured from fasting blood samples following standard protocols as described in van Reedt Dortland *et al.*[18] and Willemsen *et al*.[16].

Orkney Complex Disease studies (ORCADES). The Orkney Complex Disease Study (ORCADES) is a family-based, cross-sectional study in the isolated Scottish archipelago of Orkney. Genetic diversity in this population is decreased compared to Mainland Scotland, consistent with the high levels of endogamy historically. Fasting blood samples were collected and over 300 health-related phenotypes and environmental exposures were measured in each individual. All participants gave informed consent and the study was approved by Research Ethics Committees in Orkney and Aberdeen[19].

Prevention of Renal and Vascular End stage Disease study (PREVEND). This is an ongoing prospective study investigating the natural course of increased levels of urinary albumin excretion and its relation to renal and cardiovascular disease. Details of the protocol have been described elsewhere[20] (www.prevend.org). Blood samples were obtained in the morning hours. Red blood cell measurements were performed at the 2nd visit (about 4.2 years from baseline).

Prospective Study of Pravastatin in the Elderly at Risk (PROSPER). A detailed description of the study has been published elsewhere[21-23]. PROSPER was a prospective multicenter randomized placebo-controlled trial to assess whether treatment with pravastatin diminishes the risk of major vascular events in elderly. Between December 1997 and May 1999, we screened and enrolled subjects in Scotland (Glasgow), Ireland (Cork), and the Netherlands (Leiden). Men and women aged 70-82 years were recruited if they had pre-existing vascular disease or increased risk of such disease because of smoking, hypertension, or diabetes. A total number of 5,804 subjects were randomly assigned to pravastatin or placebo. A large number of prospective tests were performed including Biobank tests and cognitive function measurements. A whole genome wide screening has been performed in the sequential PHASE project with the use of the Illumina 660K beadchip. Of 5,763 subjects DNA was available for genotyping.

Rotterdam Study cohort I (RS-I). The Rotterdam Study is an ongoing prospective population-based cohort study, focused on chronic disabling conditions of the elderly. The study comprises an outbred ethnically homogenous population of Dutch

Caucasian origin. The rationale of the study has been described in detail elsewhere[24]. In summary, 7,983 men and women aged 55 years or older, living in Ommoord, a suburb of Rotterdam, the Netherlands, were invited to participate in the first phase. Fasting blood samples were taken during the participant's third visit to the research center.

Rotterdam Study cohort II (RS-II). The Rotterdam Study cohort II prospective population-based cohort study comprises 3,011 residents aged 55 years and older from the same district of Rotterdam. The rationale and study designs of this cohort is similar to that of the RS-I[24]. The baseline measurements, including the fasting HDL measurements, took place during the first visit.

Rotterdam Study cohort III (RS-III). The Rotterdam Study cohort III prospective population-based cohort study comprised 3,932 residents aged 45 years and older from the same district of Rotterdam. The rationale and study designs of this cohort is similar to that of the RS-I[24]. The baseline measurements, including the fasting HDL measurements, took place during the first visit.

TRacking Adolescents' Individual Lives Survey (TRAILS). TRAILS is a prospective cohort study of Dutch adolescents with bi- or triennial measurements from age 11 to up until adulthood, which consists of a general population and a clinical cohort (for a cohort profile see Oldehinkel *et al*.[25]]. In the population cohort, five assessment waves have been completed to date, which ran from March 2001 to July 2002 (T1), September 2003 to December 2004 (T2), September 2005 to August 2007 (T3), October 2008 to September 2010 (T4), and January 2012 to December 2013 (T5). Data for the present study were collected during the third assessment wave. At T1, 2230 (pre)adolescents were enrolled in the study (response rate 76.0%, mean age 11.09, SD 0.55, 50.8% girls[26], of whom 81.4% (N = 1816, mean age 16.27, SD 0.73, 52.3% girls) participated at T3. We obtained a blood sample after >8 h of fasting for the measurement of triglycerides, total cholesterol, HDL cholesterol and LDL cholesterol (Roche Diagnostics).

Young Finns Study (YFS). The YFS is a population-based follow up-study started in 1980. The main aim of the YFS is to determine the contribution made by childhood lifestyle, biological and psychological measures to the risk of cardiovascular diseases in adulthood. In 1980, over 3,500 children and adolescents all around Finland participated in the baseline study. The follow-up studies have been conducted mainly with 3-year intervals. The latest 30-year follow-up study was conducted in 2010-11 (ages 33-49 years) with 2,063 participants. The study was approved by the local ethics committees (University Hospitals of Helsinki, Turku, Tampere, Kuopio and Oulu) and was conducted following the guidelines of the Declaration of Helsinki. All participants gave their written informed consent.

Study samples and phenotypes

In most studies, HDL-C, TC and TG were measured at fasting in subjects and the LDL-C was calculated using the Friedewald formula. Cohorts with fasting lipid values contributed to all four analyses, cohorts with non-fasting values, only contributed to the HDL-C and TC analysis. All cohorts used measurements in mg/dl. We did not adjust for lipid lowering medication in studies with information only on lipid lowering medication before 1994. For studies with information only on lipid lowering medication after 1994, we replaced the TC measurements by TC/0.8 for those individuals using lipid lowering medication. For studies with information specifically on statin use, regardless of the year, we replaced the TC by TC/0.8 for subjects on statin medication. When the TC is adjusted, we also used this adjusted TC measurement for the Friedewald equation. When only measured LDL-C was available in a cohort, we used LDL-C/0.7 for those on medication when data was collected after 1994. We natural log transformed the TG measurements.

The total number of individuals in the discovery phase was 59,409, 48,780, 60,024 and 49,549 for HDL-C, LDL-C, TC and TG respectively. The total number of individuals in the replication phase was 84,598, 72,486, 83,739 and 73,519 for HDL-C, LDL-C, TC and TG respectively. The percentage of European samples was 74.21%, 69.45%, 74.46% and 69.45% in the discovery analysis of HDL-C, LDL-C, TC and TG respectively and 85.02%, 82.88%, 84.83% and 82.74% in the replication analysis of HDL-C, LDL-C, TC and TG respectively.

A summary of the details of all cohorts participating in this study can be found in Supplemental Table 1.

Genotyping and imputations

All cohorts were genotyped using commercially available Affymetrix or Illumina genotyping arrays, or custom Perlegen arrays (Supplemental Table 2). Quality control was performed independently for each study. To facilitate meta-analysis and replication, each discovery and replication cohort performed genotype imputation using IMPUTE2[27] or Minimac[28] with reference to the 1000 Genomes Project reference panel (version Phase 1 integrated release v3, April 2012, all populations).

Association analysis in discovery cohorts

Within each discovery cohort (AGES, ARIC (EA, AA), CHS (EA), CR-Korcula, CR-Split, CR-Vis, ERF, FHS, FamHS (EA), GS:SFHS, JHS, MESA (AFA, CAU, CHN, HIS), ORCADES, RS-I, RS-II and RS-III), each genotyped or imputed variant was tested for association with each of the lipid traits, assuming an additive genetic model. The lipid measurements were adjusted for sex, age and age2 in all cohorts and if necessary also for

cohort-specific covariates (Supplemental Table 1). Linear regression was employed for studies with unrelated individuals, and linear mixed effects models were used to account for family structure in the family-based studies.

Meta-analysis of discovery cohorts

The association results of all discovery cohorts for all variants were combined using inverse variance weighting as applied by METAL[29]. This tool also applies genomic control by automatically correcting the test statistics to account for small amounts of population stratification or unaccounted relatedness and the tool also allows for heterogeneity. We used the following filters for the variants: $0.3 < R^2$ (measurement for the imputation quality) < 1.0 and expected minor allele count (expMAC = $2 \cdot MAF \cdot R^2 \cdot$ sample size) > 10 prior to meta-analysis. After meta-analysis of all available variants, we excluded the variants that were not present in at least 4 cohorts, to prevent false positive findings.

Selection of independent variants

In order to select only variants that were independently associated with each of the lipid traits, we used the GCTA tool[30], version 1.13. This tool performs a stepwise selection procedure to select independent SNP associations by a conditional and joint analysis approach. It utilizes summary-level statistics from the meta-analysis and linkage disequilibrium (LD) corrections between SNPs are estimated from the 1000 Genomes Project (1000G Phase I Integrated Release Version 22 Haplotypes (2010-11 data freeze, 2012-02-14 haplotypes)). To identify novel loci associated with circulating lipid levels, we selected from the list of variants identified by GCTA, those variants located more than 0.5Mb away from previously identified loci[31,32].

Test previous published results

The meta-analysis of HDL-C, LDL-C, TC and TG as published by Teslovich *et al.*[31] and GLGC[32] identified respectively 95 and 62 loci. Within the meta-analysis of all discovery cohorts, we tested these loci. The experiment-wide significance threshold required to keep type I error rate at 5% is $3.18 \cdot 10^{-4}$ for the comparison with the results of the study of Teslovich *et al.*[31] (Bonferroni correction based on 157 variants) and $6.02 \cdot 10^{-4}$ for the comparison with the results of the study of GLGC[32] (Bonferroni correction based on 83 variants).

Replication in an independent sample

The significant, independent variants which were genome-wide significant in the initial discovery phase (p-value < $5 \cdot 10^{-8}$), were selected for replication in a sample of 23 independent cohorts: Airwave, AEGS, CHS (AA), FamHS (AA), FINCAVAS, FINRISK, Lifelines, LLS, LOLIPOP (EW610, EWA, EWP, IA317, IA610, IAP, OmniEE), Loyola (GXE, SPT), NEO, NTR-NESDA, PREVEND, PROSPER, TRAILS and YFS. The lipid measurements were adjusted for sex, age and age^2 in all cohorts and if necessary also for cohort-specific covariates (Supplemental Table 1). The association results of all replication cohorts were combined and the standard error based weights were calculated by METAL[29]. The experiment-wide significance threshold required to keep type I error rate at 5% is $2.63 \cdot 10^{-3}$ (Bonferroni correction based on 19 variants).

Meta-analysis of all discovery and replication cohorts together and per ethnicity

The significant, independent variants which were genome-wide significant in the initial discovery phase (p-value < $5 \cdot 10^{-8}$), which were selected for replication, were also meta-analysis in the individuals of the discovery and replication stage together. We also meta-analysis the European individuals of the discovery and replication stage together, as well as the African individuals and the Asian (Indian Asians and Chinese Asians) individuals.

Bioinformatic analysis

The biological relevance of the replicated findings was validated by bioinformatic analysis with genenetwork (http://genenetwork.nl/), dbSNP, GeneCards and STRING interaction network. Specifically, to facilitate the manual process of assigning genes to a locus, we used an automated workflow developed in-house to generate reports containing the associated protein, enzyme, metabolic reaction, pathway, and disease phenotypes about each gene within a distance of +/- 200 kbp of the locus. In addition, SNVs published in the GWAS catalog[33] and eQTLs from the GTEx-eQTL database (http://www.ncbi.nlm.nih.gov/gtex/GTEX2) were given. In detail, the reports created by our workflow were based on the dbSNP[34], NCBI-Gene (http://www.ncbi.nlm.nih.gov/gene), GTEx-eQTL, GWAS catalog, ConsensusPathDB[35], UniProtKB[36], OMIM[37], Gene Ontology[38], TCDB[39], ExPASy[40] and KEGG database[41]. The databases had been downloaded earlier from the respective ftp servers and have been integrated offline. For the KEGG database the last freely available version was used (30-6-2011). Locuszoom version 1.1 was used to plot the regional association results. Further, for comparison and to predict the functionality of the variants, annotations were also performed using the dbNSFP (database of human non-synonymous SNPs and their functional predictions, http://varianttools.sourceforge.net/Annotation/DbNSFP) and Seattle (http://snp.gs.washington.edu/SeattleSeqAnnotation131/) databases. These databases

gave functional prediction results from four different programs (polyPhen2[42], SIFT, MutationTaster[43] and LRT[44], apart from gene and variant annotations.

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Supplementary Tables

Supplemental table 1A. Baseline characteristics for all participating cohorts: ancestry, fasting status and cohort specific covariates.

Cohort	Discovery or replication	Fasted	LDL-C	Ancestry	Cohort specific covariates (sex, age and age2 were used for all cohorts)
AEGS	Replication	yes	measured	European	year-of-surgery, chip-type and PC1-10
Airwave	Replication	yes	no available data	European	PC1-4
AGES	Discovery	yes	Friedwald	European	PC1-2
ARIC (AA)	Discovery	not all	Friedwald	European	center
ARIC (EA)	Discovery	not all	Friedwald	African American	center
CHS (AA)	Replication	yes	Friedwald	African American	study site
CHS (EA)	Discovery	yes	Friedwald	European	study site
CR-Korcula	Discovery	yes	Friedewald	European	none
CR-Split	Discovery	yes	Friedewald	European	none
CR-Vis	Discovery	yes	Friedewald	European	none
ERF	Discovery	yes	measured	European	family relationships (grammar-gamma from GenABEL version 1.7.6)
FHS	Discovery	yes	Friedewald	European	PC1-10, and cohort-generation indicator
FamHS (AA)	Replication	yes	measured	African American	10 PCs
FamHS (EA)	Discovery	yes	measured	European	field centers, Illumina chips (550k, 610K, and 1M), 5 PCs
FINCAVAS	Replication	yes	Friedewald	European	study center, trait associated PCs
FINRISK	Replication	partly	Friedewald	European	original genotyping set
GS:SFHS	Discovery	majority	Friedewald	European	none
JHS	Discovery	yes	Friedewald	African American	first 10 PCs of ancestry
LifeLines	Replication	yes	Friedewald	European	PC1-10
LLS	Replication	no	NA	European	family relationships (QT-assoc)
LOLIPOP (EW610)	Replication	yes	Friedwald	European	PC1-5
LOLIPOP (EWA)	Replication	yes	Friedwald	European	PC1-5
LOLIPOP (EWP)	Replication	yes	Friedwald	European	PC1-5
LOLIPOP (IA610)	Replication	yes	Friedwald	Indian Asians	CHD, cohort, PC1-5
LOLIPOP (IA317)	Replication	yes	Friedwald	Indian Asians	PC1-5
LOLIPOP (IAOmniEE)	Replication	yes	Friedwald	Indian Asians	batch, PC1-5
LOLIPOP (IAP)	Replication	yes	Friedwald	Indian Asians	PC1-5

Loyola-GxE	Replication	yes	measured	African descent (Jamaican)	PC1-10
Loyola-SPT	Replication	yes	measured	African descent (Jamaican)	PC1-10
MESA (AFA)	Discovery	yes	Friedwald	African American	study site, first PC of ancestry
MESA (CAU)	Discovery	yes	Friedwald	European	study site, first two PCs of ancestry
MESA (CHN)	Discovery	yes	Friedwald	Chinese	study site, first PC of ancestry
MESA (HIS)	Discovery	yes	Friedwald	Hispanic	study site, first three PCs of ancestry
NEO	Replication	yes	Friedwald	European	PC1-3
NTR-NESDA	Replication	yes	Friedwald	European	first three PC's of ancestry and specific PC's
ORCADES	Discovery	yes	Friedewald	European	array, PC1-3, and family relationships (polygenic from GenABEL in combination with palinear from ProbABEL)
PREVEND	Replication	yes	Friedwald	European	PC1-5
PROSPER	Replication	yes	measured	European	PC1-4
RS-I	Discovery	yes	Friedewald	European	none
RS-II	Discovery	yes	Friedewald	European	none
RS-III	Discovery	yes	Friedewald	European	none
TRAILS	Replication	yes	Friedewald	European	PC1-10
YFS	Replication	yes	measured	European	study center, trait associated PCs

Supplemental table 1B. Baseline characteristics for all participating cohorts: HDL-C and TG.

Cohort	HDL-C			TG		
	N (% male)	Mean age (SD), in years	Mean HDL-C (SD), in mg/dL	N (% male)	Mean age (SD), in years	Mean TG log (SD), in mg/dL
AEGS	924 (68.29)	68.28 (9.22)	45.66 (17.48)	932 (68.13)	68.92 (9.41)	4.85 (0.51)
Airwave	7112 (62.21)	40.09 (9.06)	57.44 (14.79)	NA	NA	NA
AGES	3219 (42.00)	76.41 (5.46)	61.18 (17.32)	3219 (42.00)	76.41 (5.46)	4.56 (0.45)
ARIC (AA)	2733 (37.58)	53.40 (5.77)	55.00 (17.35)	2537 (37.33)	53.36 (5.77)	4.58 (0.47)
ARIC (EA)	9471 (46.95)	54.32 (5.69)	50.55 (16.69)	9265 (46.70)	54.33 (5.69)	4.78 (0.51)
CHS (AA)	785 (37)	72.82 (5.63)	58.04 (15.5)	810 (38)	72.86 (5.65)	4.66 (0.43)
CHS (EA)	3188 (39)	72.34 (5.39)	55.3 (15.92)	3261 (39)	72.34 (5.38)	4.84 (0.43)
CR-Korcula	891 (36.0)	56.26 (13.98)	56.48 (13.31)	894 (36.1)	56.45 (13.97)	4.73 (0.50)
CR-Split	490 (42.0)	49.04 (14.57)	53.45 (12.94)	490 (42.0)	49.04 (14.57)	4.74 (0.57)
CR-Vis	945 (42.1)	56.16 (15.54)	42.80 (6.07)	948 (42.2)	56.17 (15.52)	4.90 (0.47)
ERF	2739 (44.61)	48.96 (14.38)	49.18 (14.08)	2739 (44.65)	48.96 (14.38)	4.65 (0.51)
FHS	3481 (47.2)	37.86 (9.70)	52.79 (15.48)	3480 (47.2)	37.86 (9.70)	4.43(0.62)
FamHS (AA)	612 (33.71)	53.31 (10.80)	53.55 (15.39)	612 (33.71)	53.31 (10.80)	4.72 (0.52)
FamHS (EA)	3794 (47.44)	52.09 (13.65)	49.74 (14.83)	3794 (47.44)	52.09 (13.65)	4.85 (0.57)
FINCAVAS	1846 (62.68)	60.32 (11.38)	53.07 (16.97)	1846 (62.68)	60.32 (11.38)	4.73 (0.53)
FINRISK	19834 (47.08)	47.85 (13.26)	55.86 (14.73)	18157 (46.46)	48.00 (13.25)	4.70 (0.52)
GS:SFHS	9538 (41.6)	52.31 (13.56)	57.18 (16.34)	NA	NA	NA
JHS	1985 (39.24)	49.69 (12.03)	50.21 (14.14)	1984 (39.21)	49.68 (12.03)	4.50 (0.54)
LifeLines	12573 (41.66)	49.14 (11.49)	55.83 (14.93)	12574 (41.67)	49.14 (11.49)	4.56 (0.51)

LLS	2282 (45.53)	59.19 (6.82)	55.69 (17.51)	NA	NA	NA
LOLIPOP (EW610)	927 (73.14)	55.96 (9.80)	54.87 (14.72)	927 (73.14)	55.96 (9.80)	4.75 (0.55)
LOLIPOP (EWA)	582 (86.94)	54.38 (10.38)	50.30 (12.03)	582 (86.94)	54.38 (10.38)	4.85 (0.56)
LOLIPOP (EWP)	644 (100)	55.70 (9.08)	48.57 (12.50)	644 (100)	55.70 (9.08)	4.88 (0.61)
LOLIPOP (IA610)	6541 (84.28)	55.39 (10.56)	46.61 (11.68)	6530 (84.27)	55.41 (10.55)	4.93 (0.53)
LOLIPOP (IA317)	2059 (100)	48.25 (10.46)	47.50 (11.91)	2059 (100)	48.25 (10.46)	4.89 (0.49)
LOLIPOP (IAOmniEE)	891 (53.54)	49.60 (9.93)	49.94 (11.61)	892 (53.59)	49.63 (9.96)	4.85 (0.50)
LOLIPOP (IAP)	501 (100)	51.08 (8.35)	47.87 (12.61)	501 (100)	51.08 (8.35)	4.98 (0.56)
Loyola-GxE	599 (22.87)	40.27 (8.47)	51.98 (11.93)	599 (22.87)	40.27 (8.47)	4.31 (0.49)
Loyola-SPT	689 (38.90)	46.49 (13.83)	48.60 (13.13)	689 (38.90)	46.49 (13.83)	4.38 (0.49)
MESA (AFA)	1758 (46.13)	61.69 (10.04)	52.08 (14.42)	1766 (45.86)	61.73 (10.04)	4.51 (0.47)
MESA (CAU)	2492 (48.27)	62.82 (10.17)	52.14 (15.11)	2503 (48.10)	62.84 (10.16)	4.73 (0.52)
MESA (CHN)	703 (49.64)	62.54 (10.33)	48.94 (11.83)	705 (49.50)	62.53 (10.34)	4.82 (0.52)
MESA (HIS)	1407 (48.90)	61.22 (10.13)	47.03 (12.00)	1415 (48.55)	61.25 (10.15)	4.92 (0.49)
NEO	5723 (48.05)	55.97 (5.95)	55.32 (15.95)	5723 (48.05)	55.97 (5.95)	4.71 (0.54)
NTR-NESDA	7564 (36.50)	42.41 (14.51)	56.7 (15.65)	7530 (36.20)	42.37 (14.52)	4.16 (0.4)
ORCADES	1991 (39.68)	53.67 (15.37)	57.22 (15.54)	1991 (39.68)	53.67 (15.37)	4.61 (4.04)
PREVEND	3574 (51.6)	49.65 (12.49)	50.62 (15.37)	3574 (51.6)	49.65 (12.49)	4.69 (0.53)
PROSPER	5244 (48.10)	75.34 (3.35)	49.58 (13.53)	5244 (48.10)	75.34 (3.35)	4.83 (0.42)
RS-I	3410 (57.07)	65.94 (7.04)	53.62 (15.30)	3406 (57.69)	66.18 (7.25)	4.81 (0.43)
RS-II	2137 (45.53)	64.77 (7.98)	52.98 (14.27)	2120 (45.61)	64.77 (7.98)	4.84 (0.44)
RS-III	3037 (43.66)	57.10 (6.85)	52.98 (14.27)	3032 (43.60)	57.11 (6.85)	4.77 (0.48)

TRAILS	990 (47.58)	16.22 (0.66)	56.13 (11.52)	990 (47.58)	16.22 (0.66)	4.12 (042)
YFS	2102 (45.00)	31.73 (4.99)	49.83 (12.23)	2104 (45.06)	31.73 (4.99)	4.64 (0.49)

Supplemental table 1C. Baseline characteristics for all participating cohorts: LDL-C and TC. LLM = lipid lowering medication. Values are after correction for statins, if adjustment for statins was applied. * LDL-C and TC values were not adjusted as data is collected before 1994.

	LDL-C				TC			
Cohort	**N (% male)**	**Mean age (SD), in years**	**Mean LDL-C (SD), in mg/dL**	**# individuals using LLM**	**N (% male)**	**Mean age (SD), in years**	**Mean TC (SD), in mg/dL**	**# individuals using LLM**
AEGS	873 (68.50)	68.32 (9.27)	140.86 (50.23)	653		68.36 (9.23)	215.36 (54.72)	725
Airwave	NA	NA	NA		7112 (62.21)	40.09 (9.06)	203.58 (39.41)	
AGES	3219 (42.00)	76.41 (5.46)	145.44 (36.00)	729	3219 (42.00)	76.41 (5.46)	227.99 (41.19)	729
ARIC (AA)	2521 (37.25)	53.37 (5.77)	138.43 (42.88)	*	2733 (37.61)	53.40 (5.77)	215.76 (44.96)	*
ARIC (EA)	9117 (46.42)	54.32 (5.69)	137.60 (37.59)	*	9469 (46.95)	54.32 (5.69)	214.94 (40.73)	*
CHS (AA)	779 (37)	72.83 (5.64)	132.13 (40.01)	33	807 (38)	72.86 (5.66)	212.49 (42.41)	33
CHS (EA)	3188 (39)	72.36 (5.4)	131.18 (36.37)	44	3259 (39)	72.33 (5.38)	213.75 (39.71)	46
CR-Korcula	888 (35.9)	56.27 (13.98)	149.50 (40.51)	32	894 (36.1)	56.24 (13.97)	231.80 (47.82)	32
CR-Split	478 (40.6)	49.11 (14.67)	147.89 (41.56)	1	490 (42.0)	49.04 (14.57)	227.52 (48.92)	1
CR-Vis	944 (42.2)	56.19 (15.51)	126.18 (37.08)	25	947 (42.2)	56.20 (15.49)	198.40 (38.58)	25
ERF	2724 (44.46)	48.92 (14.39)	150.13 (39.21)	348	2739 (44.61)	48.92 (14.39)	220.90 (43.06)	351
FHS	3406 (46.8)	37.81 (9.69)	119.76 (34.69)	305	3480 (47.2)	37.86 (9.70)	192.97 (38.04)	305
FamHS (AA)	612 (33.71)	53.31 (10.80)	123.16 (42.58)	62	612 (33.71)	53.31 (10.80)	193.94 (40.83)	62
FamHS (EA)	3794 (47.44)	52.09 (13.65)	130.28 (40.38)	356	3794 (47.44)	52.09 (13.65)	208.00 (42.39)	356
FINCAVAS	1817 (62.25)	60.43 (11.38)	122.36 (41.24)	774	1846 (62.68)	60.32 (11.38)	201.58 (47.91)	789
FINRISK	17881 (45.96)	47.98 (13.27)	130.11 (38.96)	1111	19834 (47.08)	47.85 (13.26)	210.64 (43.43)	1267
GS:SFHS	NA	NA	NA	NA	9556 (41.6)	52.31 (13.56)	207.26 (41.35)	1384

JHS	1962 (38.94)	49.66 (12.01)	129.79 (39.34)	165	1984 (39.21)	49.68 (12.03)	200.49 (41.66)	167
LifeLines	12454 (41.26)	49.16 (11.50)	123.23 (35.37)	NA	12574 (41.67)	49.14 (11.49)	201.08 (39.70)	NA
LLS	NA	NA	NA	NA	2262 (45.58)	59.18 (6.81)	219.71 (43.46)	169
LOLIPOP (EW610)	906 (72.96)	50.07 (9.85)	133.70 (34.60)	NA	927 (73.14)	55.96 (9.80)	215.29 (41.09)	NA
LOLIPOP (EWA)	566 (86.57)	54.43 (10.41)	122.08 (36.73)	NA	582 (86.94)	54.38 (10.38)	201.41 (42.07)	NA
LOLIPOP (EWP)	610 (100)	55.87 (9.09)	118.77 (36.58)	NA	644 (100)	55.70 (9.08)	198.50 (43.64)	NA
LOLIPOP (IA610)	6322 (83.83)	55.59 (10.57)	117.74 (37.76)	NA	6548 (84.30)	55.38 (10.57)	195.64 (45.11)	NA
LOLIPOP (IA317)	2059 (100)	48.25 (10.46)	129.17 (35.04)	NA	2059 (100)	48.25 (10.46)	206.54 (41.32)	NA
LOLIPOP (IAOmniEE)	872 (52.64)	49.70 (9.95)	126.10 (36.05)	NA	892 (53.59)	49.63 (9.96)	204.84 (42.05)	NA
LOLIPOP (IAP)	476 (100)	51.30 (8.36)	132.71 (35.86)	NA	501 (100)	51.08 (8.35)	212.37 (42.53)	NA
Loyola-GxE	599 (22.87)	40.27 (8.47)	135.40 (38.82)	0	599 (22.87)	40.27 (8.47)	204.28 (43.11)	0
Loyola-SPT	689 (38.90)	46.49 (13.83)	123.43 (39.32)	0	689 (38.90)	46.49 (13.83)	190.21 (42.94)	0
MESA (AFA)	1754 (46.01)	61.71 (10.04)	123.38 (35.37)	293	1763 (46.06)	61.71 (10.04)	196.31 (38.15)	295
MESA (CAU)	2471 (48.04)	62.87 (10.18)	125.07 (31.80)	461	2499 (48.10)	62.84 (10.17)	203.44 (35.53)	469
MESA (CHN)	689 (49.78)	62.60 (10.37)	120.95 (29.84)	91	702 (49.72)	62.59 (10.33)	198.28 (33.65)	94
MESA (HIS)	1381 (48.44)	61.29 (10.15)	126.29 (34.63)	191	1412 (48.51)	61.24 (10.15)	204.70 (39.69)	198
NEO	5646 (47.61)	55.99 (5.94)	145.38 (36.10)	885	5723 (48.05)	55.97 (5.95)	226.24 (40.22)	885
NTR-NESDA	7501 (36.20)	42.36 (14.53)	131.09 (39.05)	0	7564 (36.50)	42.4 (14.51)	197.99 (41.37)	0
ORCADES	1991 (39.68)	53.67 (15.37)	146.28 (39.1)	145	1991 (39.68)	53.67 (15.37)	211.37 (42.35)	145
PREVEND	3497 (51.2)	49.66 (12.53)	156.15 (52.17	346	3626 (51.58)	49.63 (12.49)	218.41 (42.02)	346
PROSPER	5244 (48.10)	75.34 (3.35)	146.46 (30.73)	0	5244 (48.10)	75.34 (3.35)	219.87 (34.93)	0
RS-I	3233 (56.85)	65.92 (7.04)	53.62 (15.30)	396	3996 (56.68)	65.96 (7.05)	228.591 (37.40)	491

RS-II	2062 (45.68)	64.79 (8.00)	147.47 (33.27)	273	2101 (45.88)	64.79 (7.99)	227.88 (36.80)	275
RS-III	2958 (43.61)	57.1 (6.89)	143.22 (38.69)	648	2996 (44.13)	57.08 (6.86)	224.57 (42.53)	662
TRAILS	990 (47.58)	16.22 (0.66)	78.20 (24.36)	0	990 (47.58)	16.22 (0.66)	147.84 (27.69)	0
YFS	2093 (44.82)	31.70 (4.99)	125.93 (32.51)	7	2104 (45.06)	31.73 (4.99)	199.16 (37.81)	7

Supplemental table 2. SNP genotyping and imputation details of the participating cohorts.

MAF = minor allele frequency; HWE = Hardy-Weinberg equilibrium

Cohort	chip	QC	Reference panel for imputations	Tool used for imputations
AEGS	Affymetrix SNP 5.0 (AEGS1) and Affymetrix AxiomCEU (AEGS2)	Individual call rate > 0.97, SNP call rate > 0.97, MAF >0.03, HWE > 1E-06	1000 Genomes Project reference panel (version Phase 1 integrated release v3)	SHAPEIT2 and IMPUTE2
Airwave	Illumina HumanCoreExome-12v1-1	Individual call rate > 0.98, SNP call rate > 0.98, MAF >0.01, HWE > 1E-06	1000 Genomes Project reference panel (version Phase 1 integrated release v3)	SHAPEIT2 and Minimac
AGES	Illlumina Hu370CNV	MAF >0.01, >97% complete, HWE >1e-06	1000 Genomes Project reference panel (version Phase 1 integrated release v3)	MaCH and Minimac
ARIC (AA and EA)	Affy 6.0	MAF >0.01, >95% complete, HWE >0.00001	1000 Genomes Project reference panel (version Phase 1 integrated release v3).	Shapelt (v1.r532) and IMPUTE2
CHS (AA)	Illumina Omni1M	Genotypes were called using the Illumina BeadStudio software. Samples were excluded from analysis for sex mismatch, discordance with prior genotyping, or call rate < 95%. The following exclusions were applied to identify a final set SNPs for imputation: call rate < 97%, HWE P < 10-5, > 2 duplicate errors or Mendelian inconsistencies (for reference trios), heterozygote frequency = 0.	1000G phase 1 version 3 (all ancestries)	IMPUTE V2
CHS (EA)	Illumina 370CNV and CARe IBC	Genotypes were called using the Illumina BeadStudio software. Samples were excluded from analysis for sex mismatch, discordance with prior genotyping, or call rate	1000G phase 1 version 3 (all ancestries)	MaCH and Minimac

		< 95%. The following exclusions were applied to identify a final set SNPs for imputation: call rate < 97%, HWE P < 10-5, > 2 duplicate errors or Mendelian inconsistencies (for reference trios), heterozygote frequency = 0.		
CR-Korcula, CR-Split	Illumina HumanHap370CNV	Individual call rate > 0.97, SNP call rate > 0.98, MAF >0.01, HWE > 1E-06	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	SHAPEIT2 and IMPUTE2
CR-Vis	Illumina Infinium HumanHap300v1	Individual call rate > 0.97, SNP call rate > 0.98, MAF >0.01, HWE > 1E-06	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	SHAPEIT2 and IMPUTE2
ERF	various Illumina and Affymetrix chips	callrate > 0.98, per individual callrate > 0.96, HWE p-value > 5 · 10-8 and MAF > 0.005. IBS, sex chromosome and ethnicity checks were also performed.	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	MaCH (1.0.18c) and Minimac (minimac-beta-2012-03-14).
FHS	Affymetrix 500K and MIPS 50K combined	BRLMM calling; Sample callrate > 0.97; SNP callrate > 0.97; HWE p value >10-6; for imputation MAF > 0.01 and Mendelian errors <1000	1000 Genomes Project reference panel (version Phase 1 integrated release v3, April 2012, all populations)	Minimac versions released 2012-05-29 and 2012-08-15
FamHS (AA)	ILLUMINA 1M chip	callrate > 0.98, per individual callrate > 0.98, HWE p-value > 1E-06 and MAF > 0.01. Mendelian errors, familial relationships based on IBS, sex and ethnicity checks were also performed	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	MaCH (1.0.18c) and Minimac (minimac-beta-2012-03-14).
FamHS (EA)	ILLUMINA 550K, ILLUMINA 610K, and ILLUMINA 1M chips	callrate > 0.98, per individual callrate > 0.98, HWE p-value > 1E-06 and MAF > 0.01. Mendelian errors, familial relationships based on IBS, sex and ethnicity checks were also performed	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	MaCH (1.0.18c) and Minimac (minimac-beta-2012-03-14).

FINCAVAS	Metabochip	callrate > 0.98, per individual callrate > 0.95, HWE p-value > 10-6 and MAF > 0.01. IBS, sex chromosome and heterozygosity checks were also performed.	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	SHAPEIT (v2.r644) and IMPUTE (v2.3.0)
FINRISK	Illumina 610K, Illumina CoreExome	SNP callrate: 95% (99% for MAF < 5%), MAF: 1%, HWE: 1e-6, Individual callrate 95%, non-Europeans excluded based on MDS, relatedness threshold 0.1	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	SHAPEIT2 and IMPUTE2
GS:SFHS	Illumina OMNI Express + Exome	OMNI chip - Individual call rate > 0.97, SNP call rate > 0.98, MAF >0.01, HWE > 1E-06 Exome chip - Individual call rate > 0.99, SNP call rate > 0.98, MAF >0.0001, HWE > 1E-06	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	SHAPEIT2 and IMPUTE2
JHS	Affy 6.0	SNP level callrate > 90%, sample level callrate >95%, MAF >0.01, HWE > 1E-06	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	MACH and Minimac
LifeLines	Illumina Cyto SNP12 v2	SNP QC: callrate > 0.95, HWE p-value > 10-4, MAF > 0.001. Sample QC: callrate > 0.95, heterozygosity (<4SD from mean), IBS<0.35, sex match with phenotype, caucasian.	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	Minimac v2012.10.3
LLS	Illumina Human660W / Illumina OmniExpress	callrate > 0.95, per individual callrate > 0.95, HWE p-value > 1 · 10-4 and MAF > 0.01. IBS and sex chromosome checks were also performed.	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	IMPUTE (v2.2)
LOLIPOP (EW610)	Illumina Human610	maf > 0.01, call rate > 95%, pHWE>10E-6, sample call rate > 95%, removed samples of duplicates, gender discrepancy and relatedness	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	IMPUTE (v2.3)

LOLIPOP (EWA)	Affymetrix 500K	maf > 0.01, call rate > 95%, pHWE>10E-6, sample call rate > 95%, removed samples of duplicates, gender discrepancy and relatedness	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	IMPUTE (v2.3)
LOLIPOP (EWP)	Perlegen custom	maf > 0.01, call rate > 95%, pHWE>10E-6, sample call rate > 95%, removed samples of duplicates, samples ascertained on Adult Treatment Panel (ATP) III criteria for metabolic syndrome	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	IMPUTE (v2.3)
LOLIPOP (IA610)	Illumina Human610	maf > 0.01, call rate > 95%, pHWE>10E-6, sample call rate > 95%, removed samples of duplicates, gender discrepancy, ethnic outliers, and relatedness. Enriched with CHD cases (a case-control study)	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	IMPUTE (v2.3)
LOLIPOP (IA317)	Illumina HumanHap300K	maf > 0.01, call rate > 95%, pHWE>10E-6, sample call rate > 95%, removed samples of duplicates, gender discrepancy, ethnic outliers, and relatedness. Samples enriched for insulin resistance and component phenotypes.	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	IMPUTE (v2.3)
LOLIPOP (IAOmniEE)	OmniExpressExome BeadChip	maf > 0.01, call rate > 99%, pHWE>10E-6, sample call rate > 98%, removed samples of duplicates, gender discrepancy, ethnic outliers, relatedness and extreme heterozygosity	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	IMPUTE (v2.3)
LOLIPOP (IAP)	Perlegen custom	maf > 0.01, call rate > 95%, pHWE>10E-6, sample call rate > 95%, removed samples of duplicates, samples ascertained on Adult Treatment Panel (ATP) III criteria for metabolic syndrome	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	IMPUTE (v2.3)
Loyola-GxE	Illumina Metabochip	SNP QC: Callrate > 95%, HWE p-value > 10-6, MAF > 0.001; Sample QC: missing phenotype data, heterozygosity, PCA outliers, IBD cryptic relatedness	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	MaCH-Admix

Loyola-SPT	Illumina Metabochip	SNP QC: Callrate > 95%, HWE p-value > 10-6, MAF > 0.001; Sample QC: missing phenotype data, heterozygosity, PCA outliers, IBD cryptic relatedness	1001 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	MaCH-Admix
MESA (AFA, CAU, CHN and HIS)	Affy 6.0	SNP level callrate > 95%, sample level callrate > 95%, HWEMAF > 0 (remove monomorphic SNPs).	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	IMPUTE v2.2.2
NEO	Illumina HumanCoreExome-24v1-0_A	SNP QC: callrate > 0.98, HWE p-value > 10-6, MAF > 0. Sample QC: callrate > 0.98, heterozygosity, IBS<0.25	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	IMPUTE (v2.2)
NTR-NESDA	various Illumina and Affymetrix chips	MAF < 0.01, HWE p-value < 1 · 10-5 and call rate < 0.95, Samples were excluded in case of sex mismatch, genotype missing rate > 0.1 or Plink F inbreeding value was either > 0.10 or < -0.10 (heterozygosity). Imputation quality cutoff R2 < 0.30	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	MaCH (version 1.0.18) and Minimac (version 2012.10.9 beta)
ORCADES	Illumina Hap300, Omni1, OmniX	Callrate >97%, per individual callrate>98%, HWE p-value >10-6 , monomorphic SNPs, MAF >0.001, ethnic outliers, duplicates, gender mismatch, excess IBS or Mendelian inconsistency incompatible with pedigree	1000 Genomes Phase 1 integrated release version 3 haplotypes	IMPUTE v2.2.2
PREVEND	Illumina CytoSNP12 v2	Individuals were excluded based on callrate <95%, etnicity (PC outliers), IBS, sex inconsitencies, exclusion of SNPs with Callrate <95% and pHWE<10E-6)	1000 Genomes Project reference panel (version Phase 1 integrated release v3, April 2012, all populations).	Shapeit and Impute2
PROSPER	Illumina 660K Beadchip	Callrate >97,5%, HWE p-value 1.0x10-6. IBS, sex and ethnicity checks were also performed.	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	Impute

RS-I and RS-II	Illumina 550K	MAF < 0.05, SNP callrate < 0.95 and/or HWE p-value < 1 · 10-7	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	MaCH and Minimac
RS-III	Illumina 610K and 660K	MAF < 0.05, SNP callrate < 0.95 and/or HWE p-value < 1 · 10-7	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	MaCH and Minimac
TRAILS	Illumina Cyto SNP12 v2	SNP QC: callrate > 0.95, HWE p-value > 10-4, MAF > 0.01. Sample QC: callrate > 0.95, heterozygosity (<4SD from mean), IBS<0.35, sex match with phenotype, caucasian.	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	IMPUTE v2.2.2
YFS	Illumuna 670k custom	callrate > 0.95, per individual callrate > 0.95, HWE p-value > 10-6 and MAF > 0.01. IBS, sex chromosome, cryptic relatedness and heterozygosity checks were also performed.	1000 Genomes Project reference panel (version Phase 1 integrated release v3, March 2012, all populations).	SHAPEIT (v1) and IMPUTE (v2.2.2)

Supplemental table 3. Replication of the variants of Teslovich *et al.*[31]

Trait	Chr:Position	A1/A2	Teslovich *et al.*				This study				
			MAF	β_{A1}	SE_{β}	*p*-value	MAF	β_{A1}	SE_{β}	*p*-value	replicated
LDL	1:25,775,733	A/T	0.47	1.1	0.18	1.24E-10	0.488	1.020	0.239	1.96E-05	y
TC	1:25,775,733	A/T	0.47	1.22	0.19	4.12E-11	0.479	0.992	0.234	2.25E-05	y
HDL	1:40,028,180	G/A	0.23	0.48	0.09	3.99E-10	0.227	0.547	0.106	2.22E-07	y
LDL	1:55,504,650	G/A	0.3	-2.01	0.22	1.93E-28	0.336	-1.883	0.274	5.92E-12	y
TC	1:55,504,650	G/A	0.3	-1.96	0.24	3.84E-24	0.338	-1.710	0.262	6.69E-11	y
TG	1:63,025,942	G/T	0.32	4.94	0.4	8.84E-43	0.379	0.029	0.003	1.24E-19	y
LDL	1:63,050,598	G/T	0.32	1.59	0.19	2.63E-18	0.338	1.678	0.237	1.42E-12	y
TC	1:63,050,598	G/T	0.32	2.6	0.2	4.90E-41	0.342	2.959	0.235	2.29E-36	y
TC	1:93,009,438	C/A	0.21	1.18	0.24	2.78E-08	0.199	0.997	0.307	1.15E-03	n
LDL	1:109,818,306	G/T	0.22	5.65	0.21	9.70E-171	0.241	5.745	0.288	1.70E-88	y
TC	1:109,818,306	G/T	0.22	5.41	0.24	5.77E-131	0.241	5.341	0.280	3.07E-81	y
HDL	1:182,168,885	G/A	0.35	0.47	0.08	3.18E-10	0.349	0.334	0.085	9.34E-05	y
LDL	1:220,970,593	T/G	0.32	1.09	0.2	5.62E-11	0.297	1.416	0.279	3.79E-07	y
TC	1:220,970,593	T/G	0.32	1.38	0.22	4.90E-13	0.297	1.613	0.269	1.89E-09	y
HDL	1:230,295,691	G/A	0.4	0.61	0.07	3.66E-21	0.418	0.700	0.092	2.77E-14	y
TG	1:230,305,312	G/A	0.39	-2.76	0.38	2.09E-14	0.426	-0.017	0.003	9.43E-08	y
LDL	1:234,858,597	A/T	0.48	1.13	0.18	9.38E-12	0.450	1.429	0.234	9.61E-10	y
TC	1:234,858,597	A/T	0.48	1.36	0.2	5.37E-14	0.453	1.643	0.231	1.02E-12	y
HDL	2:21,225,281	C/T	0.22	-0.9	0.09	1.22E-30	0.222	-0.969	0.099	1.76E-22	y
TG	2:21,225,281	C/T	0.22	5.99	0.45	1.36E-45	0.219	0.048	0.004	5.76E-38	y
LDL	2:21,263,900	A/G	0.3	-4.05	0.19	4.48E-114	0.303	-4.412	0.255	3.34E-67	y
TC	2:21,263,900	A/G	0.3	-4.16	0.22	4.08E-96	0.308	-4.144	0.249	4.30E-62	y
TC	2:27,730,940	T/C	0.41	-1.91	0.19	7.31E-27	0.388	-2.143	0.235	8.13E-20	y
TG	2:27,730,940	T/C	0.41	-8.76	0.4	5.68E-133	0.382	-0.064	0.003	9.19E-86	y
LDL	2:44,072,576	G/T	0.3	-2.75	0.2	1.73E-47	0.291	-2.914	0.265	3.20E-28	y
TC	2:44,072,576	G/T	0.3	-3.01	0.22	4.03E-45	0.300	-2.654	0.256	3.25E-25	y
TC	2:136,322,676	T/G	0.31	-1.18	0.22	1.39E-08	0.374	-1.180	0.292	5.34E-05	y
TG	2:165,513,091	C/T	0.4	2.01	0.38	1.63E-10	0.452	0.014	0.003	2.24E-05	y
HDL	2:165,540,800	C/T	0.13	-0.68	0.12	2.72E-10	0.131	-0.784	0.121	8.19E-11	y
TG	2:227,099,180	C/T	0.37	1.89	0.38	2.35E-08	0.365	0.016	0.003	3.14E-07	y
HDL	2:227,128,917	C/A	0.37	-0.46	0.08	2.01E-09	0.389	-0.444	0.090	7.48E-07	y
TC	3:12,628,920	C/G	0.22	1.42	0.23	4.21E-09	0.224	1.168	0.269	1.41E-05	y
TG	3:135,926,622	G/T	0.22	2.22	0.45	2.52E-08	0.231	0.014	0.004	5.21E-04	n
TG	4:88,030,261	G/T	0.41	2.25	0.38	8.65E-12	0.422	0.018	0.003	6.51E-09	y
HDL	4:103,188,709	T/C	0.07	0.84	0.16	7.20E-11	0.080	0.825	0.174	2.03E-06	y
HDL	5:53,298,025	A/G	0.26	0.49	0.09	4.98E-08	0.265	0.165	0.092	7.24E-02	n
TG	5:55,861,786	T/C	0.2	-2.57	0.49	1.32E-10	0.201	-0.017	0.004	1.46E-05	y
LDL	5:74,656,539	C/T	0.39	-2.45	0.18	5.12E-45	0.387	-2.573	0.235	7.57E-28	y
TC	5:74,656,539	C/T	0.39	-2.84	0.2	8.79E-47	0.388	-2.735	0.233	9.60E-32	y
LDL	5:156,390,297	T/C	0.35	1.67	0.19	1.89E-22	0.391	1.902	0.235	5.68E-16	y
TC	5:156,390,297	T/C	0.35	1.98	0.2	7.46E-28	0.389	2.078	0.232	3.72E-19	y

TG	5:156,479,323	G/C	0.36	2.63	0.39	3.68E-12	0.385	0.023	0.003	3.24E-12	y
LDL	6:16,127,407	T/C	0.22	1.43	0.21	1.16E-11	0.238	1.262	0.271	3.09E-06	y
TC	6:16,127,407	T/C	0.22	1.46	0.24	2.78E-09	0.233	1.402	0.270	2.01E-07	y
LDL	6:26,093,141	A/G	0.06	2.22	0.39	6.07E-10	0.061	1.749	0.529	9.39E-04	n
TC	6:26,093,141	A/G	0.06	2.16	0.43	2.49E-08	0.067	2.004	0.499	5.91E-05	y
TG	6:31,265,490	T/C	0.25	2.99	0.42	1.60E-15	0.226	0.027	0.005	1.81E-08	y
LDL	6:32,412,435	A/G	0.16	-1.83	0.24	2.40E-15	0.139	-2.304	0.489	2.48E-06	y
TC	6:32,412,435	A/G	0.16	-2.31	0.27	3.96E-19	0.145	-2.890	0.454	1.97E-10	y
TC	6:34,546,560	T/C	0.11	1.86	0.33	4.68E-11	0.136	1.261	0.370	6.51E-04	n
HDL	6:34,552,797	A/G	0.16	0.49	0.1	3.81E-09	0.168	0.450	0.119	1.64E-04	y
TC	6:116,312,893	T/A	0.35	1.18	0.2	1.69E-10	0.357	1.267	0.237	9.06E-08	y
LDL	6:116,354,591	T/C	0.41	0.89	0.18	2.95E-09	0.399	0.972	0.248	9.07E-05	y
HDL	6:139,829,666	C/T	0.42	0.39	0.08	2.55E-08	0.435	0.339	0.083	4.53E-05	y
LDL	6:160,578,860	C/T	0.17	-1.95	0.24	1.70E-17	0.159	-2.115	0.335	2.73E-10	y
TC	6:160,578,860	C/T	0.17	-2.18	0.27	9.71E-17	0.163	-1.824	0.324	1.74E-08	y
HDL	6:161,089,817	A/G	0.16	0.56	0.1	2.97E-08	0.164	0.420	0.310	1.76E-01	n
TC	7:21,582,917	T/C	0.15	-1.7	0.28	6.55E-10	0.145	-1.566	0.338	3.53E-06	y
LDL	7:21,607,352	C/T	0.23	-1.26	0.2	6.88E-10	0.245	-0.730	0.266	6.13E-03	n
TC	7:44,579,180	C/G	0.25	-2.01	0.29	3.22E-11	0.238	-1.749	0.307	1.17E-08	y
LDL	7:44,600,695	A/G	0.43	1.17	0.19	4.25E-11	0.433	1.401	0.234	2.17E-09	y
TG	7:72,129,667	T/C	0.04	7.91	1.34	1.13E-09	0.035	0.024	0.018	1.70E-01	n
TG	7:72,934,510	G/A	0.19	7.91	0.5	9.06E-59	0.213	0.053	0.004	1.93E-41	y
HDL	7:72,982,874	T/C	0.12	-0.57	0.12	1.19E-09	0.125	-0.612	0.135	5.66E-06	y
HDL	7:130,433,384	T/C	0.48	-0.59	0.07	1.21E-15	0.475	-0.600	0.082	2.20E-13	y
HDL	8:9,183,358	A/G	0.09	1.21	0.13	6.40E-25	0.105	1.333	0.140	1.94E-21	y
LDL	8:9,185,146	T/C	0.1	2.22	0.29	7.43E-15	0.109	2.531	0.376	1.78E-11	y
TC	8:9,185,146	T/C	0.1	3.14	0.32	8.98E-24	0.108	3.729	0.372	1.23E-23	y
TG	8:10,683,929	C/G	0.37	-2.01	0.39	1.30E-08	0.404	-0.010	0.003	1.31E-03	n
TC	8:18,255,709	G/A	0.32	-1.07	0.21	1.68E-09	0.305	-1.093	0.245	7.80E-06	y
TG	8:18,273,300	G/C	0.22	-2.97	0.42	4.11E-14	0.242	-0.021	0.004	9.96E-08	y
HDL	8:19,844,222	G/A	0.12	-2.25	0.12	9.71E-98	0.100	-2.116	0.135	2.99E-55	y
TG	8:19,844,222	G/A	0.12	13.64	0.65	1.50E-115	0.101	0.084	0.005	1.20E-61	y
LDL	8:59,311,697	A/G	0.35	-0.95	0.18	3.86E-09	0.316	-0.793	0.251	1.62E-03	n
TC	8:59,311,697	A/G	0.35	-1.26	0.2	8.79E-13	0.318	-1.195	0.248	1.45E-06	y
HDL	8:116,599,199	T/G	0.41	0.44	0.08	5.77E-11	0.405	0.402	0.085	2.44E-06	y
TC	8:116,648,565	C/A	0.3	1.11	0.21	2.45E-08	0.324	1.007	0.250	5.63E-05	y
LDL	8:126,482,621	A/C	0.46	1.84	0.17	2.59E-29	0.457	1.824	0.225	5.54E-16	y
TC	8:126,482,621	A/C	0.46	2.3	0.19	5.02E-36	0.458	2.368	0.222	1.69E-26	y
TG	8:126,490,972	T/A	0.47	5.64	0.39	3.29E-55	0.454	0.041	0.003	3.05E-39	y
HDL	8:126,495,818	T/C	0.44	-0.61	0.07	6.35E-19	0.429	-0.545	0.082	3.53E-11	y
LDL	8:145,043,543	G/A	0.4	-1.4	0.21	4.44E-13	0.374	-1.143	0.255	7.16E-06	y
TC	8:145,043,543	G/A	0.4	-1.34	0.24	8.96E-10	0.374	-0.972	0.249	9.39E-05	y
HDL	9:15,296,034	C/A	0.14	0.72	0.1	1.30E-13	0.135	0.680	0.128	9.80E-08	y
TC	9:15,305,378	G/C	0.18	1.57	0.26	3.08E-09	0.227	1.335	0.285	2.92E-06	y
HDL	9:107,664,301	T/C	0.25	0.94	0.09	1.75E-33	0.263	0.938	0.094	1.99E-23	y

TC	9:107,664,301	T/C	0.25	2.24	0.24	3.39E-27	0.264	2.539	0.258	7.86E-23	y
TC	9:136,153,875	T/C	0.21	-2.3	0.25	8.66E-21	0.205	-1.983	0.299	3.33E-11	y
LDL	9:136,154,304	T/C	0.22	-2.05	0.21	7.85E-22	0.207	-1.867	0.284	4.60E-11	y
TG	10:65,027,610	T/A	0.43	2.38	0.38	3.48E-12	0.409	0.015	0.003	4.68E-06	y
TG	10:94,839,642	A/G	0.47	2.28	0.38	2.38E-08	0.451	0.020	0.003	2.88E-10	y
LDL	10:113,910,721	A/G	0.29	-1.08	0.2	2.14E-09	0.290	-0.925	0.272	6.85E-04	n
TC	10:113,933,886	A/G	0.3	-1.14	0.2	2.03E-10	0.275	-1.021	0.255	6.37E-05	y
HDL	11:10,388,782	G/A	0.17	0.41	0.1	4.62E-08	0.217	0.283	0.110	9.97E-03	n
TC	11:18,664,241	T/G	0.29	1.06	0.22	2.52E-08	0.316	1.113	0.264	2.43E-05	y
HDL	11:46,743,247	C/T	0.15	-0.78	0.1	3.48E-18	0.160	-0.608	0.123	8.23E-07	y
TG	11:61,569,830	T/C	0.34	-3.82	0.38	5.41E-24	0.322	-0.030	0.004	2.43E-18	y
TC	11:61,571,478	C/T	0.34	1.78	0.2	2.08E-22	0.327	1.900	0.249	2.31E-14	y
LDL	11:61,609,750	T/C	0.35	1.71	0.19	1.17E-21	0.340	1.758	0.260	1.34E-11	y
HDL	11:61,623,140	T/C	0.36	0.73	0.08	1.50E-22	0.408	0.606	0.089	1.00E-11	y
HDL	11:116,648,917	G/C	0.13	1.5	0.11	5.21E-47	0.147	1.377	0.124	1.40E-28	y
LDL	11:116,648,917	G/C	0.13	-2.85	0.27	1.47E-26	0.145	-2.706	0.352	1.48E-14	y
TC	11:116,648,917	G/C	0.13	-4.68	0.29	6.21E-57	0.143	-4.329	0.344	2.08E-36	y
TG	11:116,648,917	G/C	0.13	-16.95	0.48	6.71E-240	0.148	-0.119	0.005	3.38E-141	y
TC	11:122,522,375	C/T	0.38	-0.97	0.19	1.52E-10	0.385	-1.041	0.230	5.79E-06	y
HDL	11:122,530,591	G/C	0.37	-0.31	0.08	2.66E-08	0.380	-0.230	0.084	6.16E-03	n
LDL	11:126,243,952	A/G	0.14	-1.95	0.26	1.20E-15	0.146	-1.938	0.333	5.58E-09	y
TC	11:126,248,211	T/A	0.11	-2.01	0.33	2.12E-11	0.141	-1.567	0.332	2.38E-06	y
HDL	12:20,473,758	A/C	0.42	-0.4	0.08	3.84E-08	0.428	-0.210	0.084	1.23E-02	n
TG	12:57,792,580	T/C	0.23	2.7	0.43	4.43E-10	0.236	0.018	0.004	1.70E-06	y
HDL	12:57,844,049	T/C	0.24	-0.46	0.09	1.64E-08	0.230	-0.549	0.103	1.02E-07	y
HDL	12:110,000,193	C/T	0.47	0.44	0.07	6.88E-15	0.456	0.566	0.082	4.65E-12	y
LDL	12:112,072,424	G/A	0.42	0.97	0.18	1.51E-09	0.418	0.799	0.254	1.67E-03	n
TC	12:112,072,424	G/A	0.42	0.96	0.2	6.77E-12	0.421	1.171	0.249	2.45E-06	y
LDL	12:121,416,650	C/A	0.33	-1.42	0.19	1.13E-15	0.321	-1.450	0.254	1.16E-08	y
TC	12:121,416,650	C/A	0.33	-1.45	0.2	1.48E-14	0.320	-1.674	0.251	2.53E-11	y
HDL	12:123,796,238	T/C	0.06	-0.86	0.16	7.50E-09	0.121	-0.616	0.135	5.12E-06	y
HDL	12:124,460,167	T/G	0.34	-0.44	0.08	2.89E-10	0.342	-0.448	0.092	1.11E-06	y
TG	12:124,486,678	G/A	0.34	2.42	0.41	1.21E-08	0.337	0.012	0.003	2.55E-04	y
HDL	12:125,261,593	C/T	0.31	-0.61	0.09	2.58E-14	0.354	-0.453	0.094	1.32E-06	y
LDL	14:24,883,058	T/C	0.48	-1.17	0.19	4.41E-11	0.442	-1.068	0.254	2.53E-05	y
TG	15:42,683,787	A/G	0.02	-7	1.49	1.87E-08	0.038	-0.025	0.010	1.05E-02	n
TG	15:44,245,931	T/A	0.05	-5.13	0.86	1.63E-11	0.163	-0.029	0.006	1.10E-06	y
HDL	15:58,683,366	A/G	0.39	-1.45	0.08	2.92E-96	0.388	-1.341	0.084	6.38E-58	y
TC	15:58,683,366	A/G	0.39	-1.54	0.2	8.83E-20	0.391	-1.566	0.231	1.13E-11	y
TG	15:58,731,153	G/C	0.22	-2.99	0.45	2.42E-13	0.304	-0.021	0.004	6.77E-09	y
HDL	15:63,396,867	A/G	0.2	0.39	0.1	8.75E-09	0.217	0.498	0.100	6.25E-07	y
TG	16:30,918,487	G/C	0.4	2.13	0.39	3.35E-08	0.400	0.006	0.004	1.06E-01	n
LDL	16:56,989,590	T/C	0.32	1.45	0.2	9.25E-13	0.318	1.332	0.245	5.70E-08	y
HDL	16:56,993,324	A/C	0.32	-3.39	0.09	7.10E-380	0.326	-3.242	0.086	7.27-311	y
TC	16:56,993,324	A/C	0.32	-1.67	0.23	6.67E-14	0.326	-1.624	0.239	9.96E-12	y

TG	16:57,004,889	A/G	0.45	2.88	0.38	1.15E-12	0.416	0.017	0.003	9.46E-08	y
HDL	16:67,928,042	A/G	0.12	-1.27	0.11	8.39E-33	0.133	-1.098	0.123	3.97E-19	y
LDL	16:72,108,093	A/G	0.2	-2	0.22	1.75E-22	0.193	-2.306	0.293	3.32E-15	y
TC	16:72,108,093	A/G	0.2	-2.34	0.24	3.22E-24	0.190	-2.695	0.291	2.31E-20	y
HDL	16:81,534,790	T/C	0.3	0.45	0.08	2.09E-11	0.306	0.467	0.089	1.81E-07	y
HDL	17:37,810,218	C/G	0.34	0.51	0.08	2.84E-14	0.379	0.385	0.087	9.67E-06	y
LDL	17:45,391,804	T/C	0.35	0.87	0.18	3.92E-09	0.349	0.794	0.236	7.74E-04	n
TC	17:45,425,115	A/G	0.49	-1.01	0.2	1.05E-08	0.492	-1.051	0.239	1.12E-05	y
HDL	17:66,875,294	G/C	0.32	0.42	0.08	1.79E-10	0.348	0.381	0.087	1.14E-05	y
HDL	17:76,377,482	T/G	0.48	0.4	0.08	4.98E-09	0.488	0.369	0.085	1.44E-05	y
HDL	18:47,160,953	G/T	0.17	1.31	0.1	2.73E-49	0.162	1.035	0.113	5.21E-20	y
TC	18:47,164,717	A/G	0.17	1.94	0.26	2.03E-19	0.166	1.544	0.307	4.85E-07	y
HDL	18:57,849,023	A/G	0.23	0.42	0.09	6.58E-09	0.235	0.392	0.096	4.91E-05	y
HDL	19:8,433,196	C/A	0.47	0.45	0.08	3.25E-08	0.472	0.361	0.084	1.81E-05	y
LDL	19:11,202,306	T/G	0.11	6.99	0.3	4.28E-117	0.111	7.917	0.432	4.30E-75	y
TC	19:11,202,306	T/G	0.11	7.09	0.34	6.65E-97	0.111	7.744	0.410	9.29E-80	y
HDL	19:11,347,493	C/T	0.08	0.64	0.14	3.10E-09	0.175	1.036	0.133	8.41E-15	y
LDL	19:19,407,718	C/T	0.07	3.11	0.38	6.69E-22	0.090	3.196	0.466	6.81E-12	y
TC	19:19,407,718	C/T	0.07	4.74	0.42	2.90E-38	0.088	4.258	0.454	7.02E-21	y
TG	19:19,407,718	C/T	0.07	7.83	0.82	1.61E-29	0.094	0.045	0.006	3.00E-13	y
TG	19:45,414,451	T/C	0.36	5.5	0.44	1.14E-30	0.362	0.029	0.004	7.91E-15	y
HDL	19:45,422,946	G/A	0.17	1.06	0.12	4.40E-21	0.178	0.804	0.124	8.81E-11	y
LDL	19:45,422,946	G/A	0.17	-7.14	0.29	8.72E-147	0.178	-6.348	0.346	2.40E-75	y
TC	19:45,422,946	G/A	0.17	-6.83	0.32	5.20E-111	0.180	-6.429	0.334	1.10E-82	y
TC	19:49,206,417	G/A	0.49	-1.27	0.21	2.01E-10	0.490	-1.413	0.237	2.58E-09	y
HDL	19:54,792,761	C/G	0.2	-0.83	0.11	4.29E-16	0.251	-0.737	0.106	4.14E-12	y
TC	20:34,152,782	T/C	0.15	1.19	0.27	3.82E-10	0.152	1.356	0.314	1.62E-05	y
TC	20:39,091,487	G/A	0.29	1.38	0.21	6.08E-11	0.329	0.967	0.240	5.67E-05	y
LDL	20:39,091,514	G/A	0.33	0.98	0.19	1.11E-08	0.382	0.645	0.241	7.36E-03	n
TC	20:39,811,275	C/G	0.47	-1.52	0.19	2.76E-17	0.472	-1.549	0.242	1.55E-10	y
LDL	20:39,936,815	T/C	0.47	-1.41	0.17	3.18E-19	0.498	-1.335	0.227	3.97E-09	y
HDL	20:43,042,364	T/C	0.03	1.88	0.24	1.05E-15	0.032	1.541	0.259	2.47E-09	y
TC	20:43,042,364	T/C	0.03	4.73	0.66	5.72E-13	0.033	4.143	0.696	2.67E-09	y
TG	20:44,545,048	C/T	0.24	-3.32	0.42	4.69E-18	0.288	-0.025	0.004	2.96E-13	y
HDL	20:44,554,015	C/T	0.18	0.93	0.1	1.90E-22	0.181	0.852	0.107	1.34E-15	y
HDL	22:21,932,068	T/C	0.2	0.46	0.09	1.11E-08	0.255	0.413	0.101	3.97E-05	y
TG	22:38,546,033	C/T	0.4	1.54	0.38	3.82E-08	0.352	0.011	0.003	9.88E-04	n

Supplemental table 4. Replication of the variants of GLGC[32]

Trait	Chr:Position	A1/A2	GLGC			This study				
			MAF	β_{A1}	*p*-value	MAF	β_{A1}	SE_{β}	*p*-value	replicated
TC	1:23,766,233	C/T	0.15	-0.03	6.00E-09	0.192	1.631	0.328	6.72E-07	y
HDL	1:27,138,393	T/C	0.09	-0.051	1.00E-15	0.079	0.773	0.166	3.34E-06	y
LDL	1:27,138,393	T/C	0.09	0.05	3.00E-12	0.082	-0.400	0.460	3.85E-01	n
TG	1:27,138,393	T/C	0.09	0.037	1.00E-09	0.083	-0.018	0.006	4.31E-03	n
LDL	1:150,958,836	G/A	0.16	-0.033	5.00E-09	0.145	0.836	0.335	1.26E-02	n
HDL	1:156,700,651	G/T	0.34	0.02	2.00E-08	0.340	-0.208	0.096	2.95E-02	n
HDL	1:178,515,312	G/A	0.49	0.021	7.00E-09	0.499	-0.329	0.088	1.95E-04	y
LDL	2:63,149,557	G/A	0.35	-0.024	6.00E-09	0.332	1.264	0.243	1.89E-07	y
LDL	2:118,835,841	A/G	0.08	-0.051	2.00E-12	0.074	1.778	0.447	7.06E-05	y
TC	2:118,835,841	A/G	0.08	0.042	6.00E-09	0.078	1.582	0.435	2.74E-04	y
LDL	2:121,309,488	T/C	0.4	0.021	9.00E-09	0.418	-0.629	0.239	8.44E-03	n
TC	2:121,309,488	T/C	0.4	0.02	4.00E-08	0.419	-0.476	0.234	4.17E-02	n
TC	2:169,830,155	G/A	0.41	0.027	4.00E-12	0.399	-0.650	0.243	7.39E-03	n
TC	2:203,532,304	G/A	0.25	0.028	2.00E-09	0.243	-1.339	0.284	2.49E-06	y
HDL	2:211,540,507	A/C	0.33	-0.027	9.00E-10	0.324	0.333	0.091	2.53E-04	y
LDL	2:216,304,384	T/C	0.27	-0.024	3.00E-08	0.257	0.659	0.265	1.28E-02	n
LDL	2:234,679,384	T/C	0.12	0.034	5.00E-08	0.163	-1.276	0.364	4.49E-04	y
TC	2:234,679,384	T/C	0.12	0.037	1.00E-09	0.159	-1.008	0.360	5.06E-03	n
HDL	3:11,400,249	C/T	0.39	0.025	5.00E-08	0.400	-0.116	0.084	1.71E-01	n
LDL	3:32,533,010	T/C	0.09	-0.039	1.00E-08	0.122	1.028	0.422	1.49E-02	n
TC	3:32,533,010	T/C	0.09	-0.038	1.00E-08	0.118	0.888	0.411	3.08E-02	n
HDL	3:47,061,183	A/G	0.2	-0.03	4.00E-09	0.172	0.449	0.123	2.49E-04	y
HDL	3:50,129,399	C/T	0.5	0.025	9.00E-12	0.481	-0.361	0.082	1.07E-05	y
HDL	3:52,532,118	A/G	0.21	0.029	9.00E-11	0.221	-0.344	0.102	6.97E-04	n
TC	3:58,381,287	A/G	0.1	-0.036	4.00E-08	0.086	1.034	0.406	1.10E-02	n
HDL	3:119,560,606	T/C	0.39	0.02	1.00E-08	0.414	-0.061	0.092	5.06E-01	n
HDL	3:132,163,200	T/G	0.14	0.028	5.00E-09	0.134	-0.232	0.132	7.93E-02	n
LDL	3:132,163,200	T/G	0.14	-0.034	2.00E-09	0.125	0.892	0.378	1.83E-02	n
LDL	4:3,473,139	G/A	0.42	0.025	2.00E-08	0.456	-0.871	0.238	2.48E-04	y
TC	4:3,473,139	G/A	0.42	-0.022	1.00E-10	0.451	-1.140	0.233	9.71E-07	y
TG	4:3,473,139	G/A	0.42	0.026	2.00E-12	0.458	-0.009	0.003	4.70E-03	n
HDL	4:26,062,990	G/A	0.18	-0.027	5.00E-08	0.175	0.412	0.111	2.01E-04	y
HDL	4:89,741,269	A/G	0.46	-0.025	4.00E-12	0.479	0.242	0.082	3.20E-03	n
HDL	4:100,014,805	A/G	0.44	0.019	5.00E-08	0.443	-0.184	0.089	3.88E-02	n
LDL	5:122,855,416	G/A	0.46	-0.028	4.00E-12	0.435	0.590	0.231	1.05E-02	n
TC	5:122,855,416	G/A	0.46	-0.023	2.00E-09	0.437	0.502	0.229	2.80E-02	n
TC	6:39,250,837	A/G	0.3	0.023	3.00E-08	0.286	-0.587	0.249	1.85E-02	n
HDL	6:43,757,896	A/C	0.49	-0.026	2.00E-11	0.466	0.385	0.097	6.57E-05	y
TG	6:43,757,896	A/C	0.49	0.029	3.00E-15	0.457	-0.016	0.004	3.67E-05	y

HDL	6:127,436,064	C/T	0.49	0.02	3.00E-10	0.488	-0.430	0.082	1.43E-07	y
TG	6:127,436,064	C/T	0.49	-0.02	3.00E-08	0.483	0.009	0.003	2.54E-03	n
TC	6:135,411,228	C/T	0.28	-0.025	3.00E-09	0.248	-0.847	0.269	1.67E-03	n
TC	7:1,083,777	G/A	0.16	0.033	3.00E-10	0.152	-1.483	0.324	4.68E-06	y
HDL	7:6,449,272	G/A	0.45	0.024	7.00E-12	0.483	-0.166	0.083	4.62E-02	n
HDL	7:17,919,258	T/G	0.38	-0.026	9.00E-12	0.428	0.341	0.090	1.47E-04	y
LDL	7:25,991,826	C/T	0.2	0.039	4.00E-14	0.156	-1.737	0.342	3.68E-07	y
TC	7:25,991,826	C/T	0.2	0.023	7.00E-09	0.157	-1.255	0.331	1.49E-04	y
TG	7:25,991,826	C/T	0.2	0.029	9.00E-11	0.154	0.010	0.005	3.02E-02	n
HDL	7:50,305,863	G/T	0.32	0.022	1.00E-08	0.310	-0.165	0.096	8.57E-02	n
TG	7:116,358,044	G/A	0.47	-0.019	2.00E-08	0.449	0.008	0.003	1.52E-02	n
HDL	7:150,529,449	C/T	0.12	-0.036	2.00E-08	0.083	0.391	0.151	9.46E-03	n
LDL	8:55,421,614	A/G	0.21	0.032	4.00E-11	0.190	-1.275	0.288	9.63E-06	y
TC	8:55,421,614	A/G	0.21	0.03	5.00E-11	0.194	-1.302	0.282	3.94E-06	y
LDL	9:2,640,759	G/A	0.08	-0.044	2.00E-09	0.100	1.419	0.443	1.37E-03	n
TC	9:2,640,759	G/A	0.08	-0.044	7.00E-10	0.098	1.651	0.430	1.21E-04	y
TG	10:5,254,847	G/A	0.18	-0.033	2.00E-12	0.148	0.016	0.005	2.52E-04	y
TC	10:17,260,290	G/A	0.43	0.025	3.00E-11	0.426	-0.281	0.247	2.54E-01	n
HDL	10:46,013,277	C/A	0.26	0.026	2.00E-10	0.243	-0.328	0.095	5.35E-04	y
TC	10:46,013,277	C/A	0.26	-0.026	8.00E-09	0.242	-0.633	0.261	1.53E-02	n
HDL	11:51,512,090	C/T	0.15	0.034	2.00E-10	0.125	-0.530	0.138	1.29E-04	y
HDL	11:65,391,317	A/G	0.23	0.024	3.00E-08	0.223	-0.360	0.107	8.07E-04	n
HDL	11:75,455,021	A/C	0.19	-0.026	1.00E-08	0.199	0.394	0.112	4.12E-04	y
TC	11:118,486,067	T/C	0.42	0.022	1.00E-08	0.432	-0.447	0.228	5.03E-02	n
TC	12:9,082,581	G/A	0.12	-0.035	2.00E-09	0.110	1.549	0.374	3.45E-05	y
LDL	13:32,953,388	T/C	0.48	0.024	2.00E-11	0.483	-0.858	0.243	4.22E-04	y
HDL	14:105,277,209	G/A	0.4	0.02	1.00E-07	0.417	-0.272	0.090	2.43E-03	n
TG	16:15,129,940	T/C	0.43	-0.02	2.00E-08	0.392	0.009	0.004	1.21E-02	n
HDL	16:53,809,247	A/G	0.43	-0.02	7.00E-09	0.432	0.242	0.088	5.91E-03	n
TG	16:53,809,247	A/G	0.43	-0.021	3.00E-08	0.432	-0.003	0.003	3.05E-01	n
LDL	17:7,091,650	C/T	0.37	-0.024	3.00E-10	0.350	0.772	0.258	2.78E-03	n
TC	17:7,091,650	C/T	0.37	-0.023	3.00E-10	0.350	0.847	0.251	7.32E-04	n
TG	17:41,878,166	C/A	0.22	0.025	1.00E-08	0.205	-0.004	0.004	3.77E-01	n
LDL	17:64,210,580	C/A	0.04	0.103	1.00E-11	0.035	-2.189	0.816	7.35E-03	n
TG	19:7,224,431	A/G	0.42	-0.022	5.00E-10	0.398	0.015	0.003	5.51E-06	y
HDL	19:33,899,065	G/A	0.35	-0.022	3.00E-09	0.351	0.307	0.086	3.46E-04	y
TG	19:33,899,065	G/A	0.35	0.022	3.00E-09	0.345	-0.011	0.003	1.06E-03	n
HDL	19:52,324,216	A/G	0.26	-0.029	2.00E-13	0.253	0.451	0.095	2.07E-06	y
LDL	20:12,962,718	A/G	0.38	-0.025	4.00E-10	0.370	1.201	0.237	3.79E-07	y
LDL	20:17,845,921	C/A	0.21	0.03	6.00E-09	0.189	-1.823	0.310	4.23E-09	y
LDL	22:30,378,703	T/C	0.04	0.077	1.00E-08	0.042	-1.512	0.733	3.92E-02	n
TC	22:35,711,098	A/G	0.36	0.021	5.00E-08	0.381	-0.624	0.237	8.58E-03	n
LDL	22:46,627,603	T/C	0.11	-0.031	3.00E-08	0.106	-0.985	0.383	1.01E-02	n
TC	22:46,627,603	T/C	0.11	0.032	1.00E-08	0.108	-1.284	0.372	5.58E-04	y

Supplemental table 5. The results for testing the heterogeneity of the nineteen variants after the meta-analysis of all discovery cohorts, of all replication cohorts and of all cohorts combined. A1 is allele 1 and A2 is allele 2, HetISq is the I^2 statistic which measures heterogeneity on scale of 0-100%, HetChiSq is the chi-squared statistic in simple test of heterogeneity, df is the degrees of freedom for heterogeneity statistic and HetPVal is the *p*-value for heterogeneity statistic. The variants marked *, are the significantly replicated variants.

Trait	rs identifier	A1	A2	Discovery				Replication				Combined			
				HetISq	HetChiSq	df	HetPVal	HetISq	HetChiSq	df	HetPVal	HetISq	HetChiSq	df	HetPVal
HDL	rs75909755	T	C	11.7	20.376	18	0.3121	6.7	19.293	18	0.374	49.7	73.495	37	0.0003313
HDL	rs60839105	T	C	72.5	10.918	3	0.01218	0.0	0.321	2	0.8519	57.4	14.091	6	0.02863
HDL	rs77697917*	T	C	24.0	15.781	12	0.2015	74.6	66.844	17	7.482E-08	75.0	119.982	30	1.027E-12
LDL	rs9266229	C	G	0.0	8.242	10	0.6053	40.8	30.416	18	0.03359	63.1	78.540	29	1.891E-06
LDL	rs186696265*	T	C	53.5	34.415	16	0.004775	63.6	35.677	13	0.0006659	79.7	148.084	30	1.464E-17
LDL	rs146369471	T	C	0.0	10.753	11	0.4642	0.0	6.911	9	0.6464	59.3	51.574	21	0.0002195
TC	rs6457374*	T	C	0.0	9.452	13	0.738	44.2	30.451	17	0.02327	63.6	85.079	31	6.192E-07
TC	rs186696265*	T	C	45.2	31.013	17	0.0199	70.3	50.580	15	9.675E-06	78.3	151.978	33	3.406E-17
TC	rs151198427	A	G	0.0	2.433	4	0.6567	30.1	1.431	1	0.2316	63.4	16.410	6	0.01172
TC	rs146369471	T	C	0.0	11.722	12	0.4683	0.5	11.057	11	0.4385	55.9	54.369	24	0.0003805
TC	rs829112	A	G	45.6	27.577	15	0.02437	20.2	25.053	20	0.1994	57.0	83.649	36	1.162E-05
TC	rs8065026	T	C	27	20.656	15	0.1482	47.1	37.807	20	0.009349	59.6	89.152	36	2.111E-06
TC	rs2618566	T	G	0.0	16.183	19	0.645	52.9	46.709	22	0.001601	58.2	100.441	42	1.079E-06
TG	-	CAG	C	0.0	15.345	18	0.6382	0.0	9.600	17	0.9195	0.0	33.792	36	0.5741
TG	rs608736	C	G	0.0	13.109	18	0.7851	41.9	34.424	20	0.02339	26.9	53.367	39	0.06242
TG	rs376563	T	C	0.0	7.527	14	0.9125	21.4	25.439	20	0.1851	28.6	49.053	35	0.05779
TG	rs7140110	T	C	12.6	18.313	16	0.3059	26.4	24.450	18	0.1408	28.7	49.106	35	0.05721
TG	rs150844304	A	C	0.0	7.461	17	0.9768	55.4	35.898	16	0.002989	36.4	53.420	34	0.01822
TG	rs116843064*	A	G	53.0	25.537	12	0.01248	64.8	34.110	12	0.006481	59.6	61.890	25	5.711E-05

Supplemental table 6. The results for the nineteen variants after the meta-analysis of all European samples, African samples or Asian samples of this study. A1 is allele 1 and A2 is allele 2, Freq is the frequency of A1, β is the effect of A1. The *p*-values in bold are those *p*-values below $2.63 \cdot 10^{-3}$ (Bonferroni correction based on nineteen variants). The variants marked *, are the significantly replicated variants.

Trait	rs identifier	A1	A2	European					African					Asian				
				Freq	*N*	β	SE_β	*p*-value	Freq	*N*	β	SE_β	*p*-value	Freq	*N*	β	SE_β	*p*-value
HDL	rs75909755	T	C	0.038	130,874	0.022	0.040	5.85E-01	0.007	7,087	0.154	1.932	9.366E-01	0.028	9,491	-0.033	0.050	5.12E-01
HDL	rs60839105	T	C	0.006	3,574	-4.022	12.729	7.52E-01	0.072	7,872	2.742	0.527	**1.97E-07**	-	-	-	-	-
HDL	rs77697917*	T	C	0.036	98,151	-0.265	0.042	**1.78E-10**	0.004	3,345	-7.912	4.231	6.147E-02	0.018	9,992	-0.172	0.068	1.11E-02
LDL	rs9266229	C	G	0.572	80,819	-0.041	0.029	1.56E-01	0.456	6,945	-1.655	0.796	3.758E-02	0.360	10,418	-0.024	0.016	1.31E-01
LDL	rs186696265*	T	C	0.012	94,175	0.337	0.082	**3.96E-05**	0.010	6,840	4.981	3.856	1.965E-01	0.003	6,322	0.096	0.200	6.32E-01
LDL	rs146369471	T	C	0.993	85,587	0.048	0.125	6.99E-01	0.999	603	-41.350	44.930	3.574E-01	0.995	7,194	0.235	0.180	1.91E-01
TC	rs6457374*	T	C	0.712	103,240	0.114	0.028	**5.08E-05**	0.906	5,902	0.241	1.305	8.537E-01	0.853	10,702	0.036	0.020	6.38E-02
TC	rs186696265*	T	C	0.012	120,628	0.316	0.081	**9.74E-05**	0.010	7,092	4.037	3.973	3.095E-01	0.003	6,548	0.059	0.192	7.58E-01
TC	rs151198427	A	G	0.001	9,469	12.861	10.634	2.27E-01	0.116	7,899	4.748	1.058	**7.143E-06**	-	-	-	-	-
TC	rs146369471	T	C	0.993	115,456	0.034	0.118	7.72E-01	0.999	612	-42.600	45.720	3.515E-01	0.997	6,548	0.124	0.207	5.50E-01
TC	rs829112	A	G	0.662	128,447	0.024	0.016	1.24E-01	0.788	6,136	3.091	0.932	**9.075E-04**	0.840	10,000	-0.008	0.019	7.00E-01
TC	rs8065026	T	C	0.796	117,102	-0.048	0.019	9.70E-03	0.690	6,735	-2.435	0.826	3.209E-03	0.820	10,000	-0.009	0.019	6.29E-01
TC	rs2618566	T	G	0.650	130,945	-0.044	0.016	5.99E-03	0.584	9,187	-1.585	0.726	2.895E-02	0.556	10,702	-0.011	0.015	4.60E-01
TG	-	CAG	C	0.427	91,344	-0.014	0.003	**1.57E-06**	0.767	8,997	-0.012	0.009	1.952E-01	0.527	10,687	-0.002	0.014	8.75E-01
TG	rs608736	C	G	0.503	105,838	-0.013	0.002	**2.23E-07**	0.168	8,997	-0.022	0.010	2.420E-02	0.566	10,687	-0.025	0.014	7.02E-02
TG	rs376563	T	C	0.474	103,335	-0.011	0.002	**6.67E-06**	0.261	7,231	-0.008	0.009	4.04E-01	0.495	9,982	0.013	0.014	3.58E-01
TG	rs7140110	T	C	0.717	90,045	-0.015	0.003	**3.29E-06**	0.756	7,013	0.004	0.010	7.333E-01	0.637	10,186	-0.030	0.014	3.26E-02
TG	rs150844304	A	C	0.960	98,308	-0.064	0.008	**1.94E-14**	0.995	6,899	-0.100	0.066	1.287E-01	0.988	9,982	-0.084	0.070	2.34E-01
TG	rs116843064*	A	G	0.031	66,684	-0.088	0.012	**7.98E-13**	0.007	3,149	0.001	0.101	9.948E-01	0.019	8,589	-0.072	0.069	2.98E-01

Supplemental table 7. The results for the random-effect meta-analysis of the nineteen variants after the meta-analysis of all cohorts combined. A1 is allele 1 and A2 is allele 2, Freq is the frequency of A1, β is the effect of A1. The *p*-values in bold are those *p*-values below $2.63 \cdot 10^{-3}$ (Bonferroni correction based on nineteen variants). The variants marked *, are the significantly replicated variants.

Trait	rs identifier	A1	A2	Freq	β	SE_β	*p*-value	*N*
HDL	rs75909755	T	C	0.031	0.099	0.080	2.11E-01	149,357
HDL	rs60839105	T	C	0.007	1.494	0.606	1.37E-02	122,590
HDL	rs77697917*	T	C	0.028	-0.952	0.151	**2.81E-10**	138,562
LDL	rs9266229	G	C	0.501	0.062	0.047	1.86E-01	117,477
LDL	rs186696265*	T	C	0.025	1.116	0.319	**4.69E-04**	114,847
LDL	rs146369471	C	T	0.006	-0.227	0.230	3.22E-01	114,847
TC	rs6457374*	T	C	0.763	0.129	0.052	1.33E-02	145,883
TC	rs186696265*	T	C	0.009	1.012	0.298	**7.02E-04**	141,869
TC	rs151198427	A	G	0.011	0.416	0.502	4.07E-01	115,601
TC	rs146369471	C	T	0.007	-0.148	0.224	5.11E-01	141,868
TC	rs829112	G	A	0.290	-0.036	0.035	3.02E-01	150,956
TC	rs8065026	C	T	0.194	0.046	0.046	2.56E-01	140,899
TC	rs2618566	T	G	0.635	-0.060	0.035	9.03E-02	152,242
TG	-	CAG	C	-	-	-	-	-
TG	rs608736	C	G	0.483	-0.015	0.003	**6.36E-07**	126,936
TG	rs376563	C	T	0.541	0.011	0.003	**1.74E-04**	126,934
TG	rs7140110	C	T	0.284	0.014	0.004	**1.69E-04**	126,932
TG	rs150844304	C	A	0.030	0.075	0.012	**3.97E-10**	116,600
TG	rs116843064*	A	G	0.026	-0.088	0.020	**8.18E-06**	117,515

Supplemental Figures

Figure S1: The standard error per cohort against the sample size.

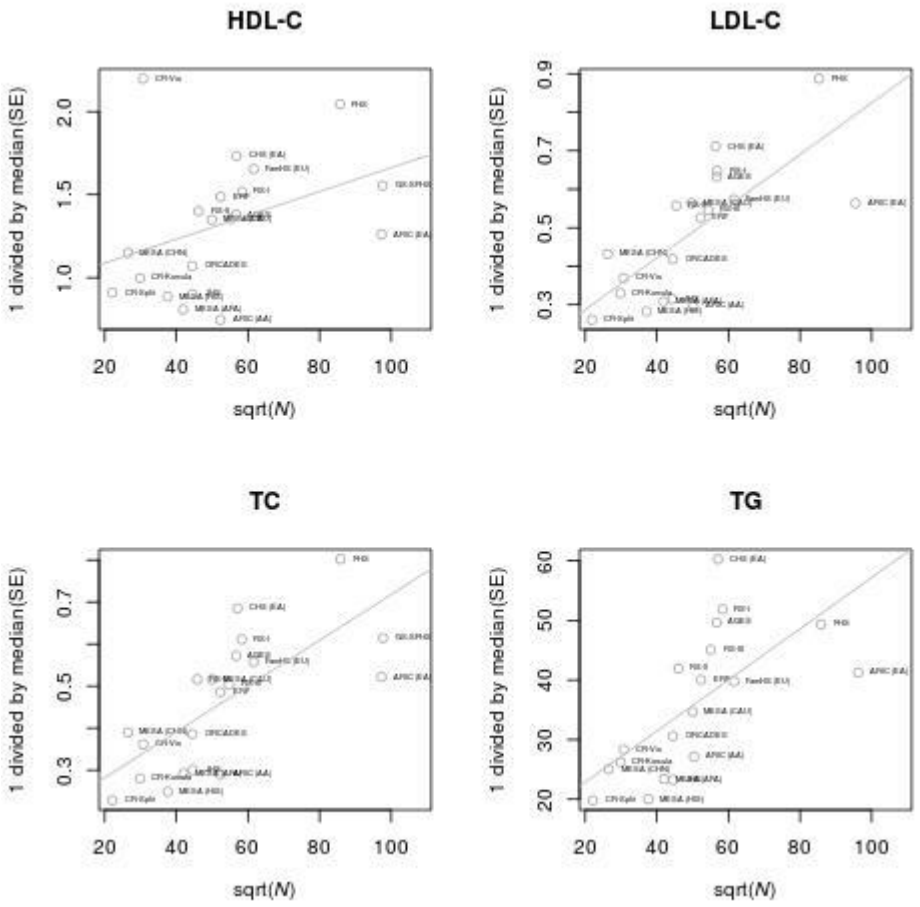


Figure S2: The variance in the β per cohort for chromosome 22.

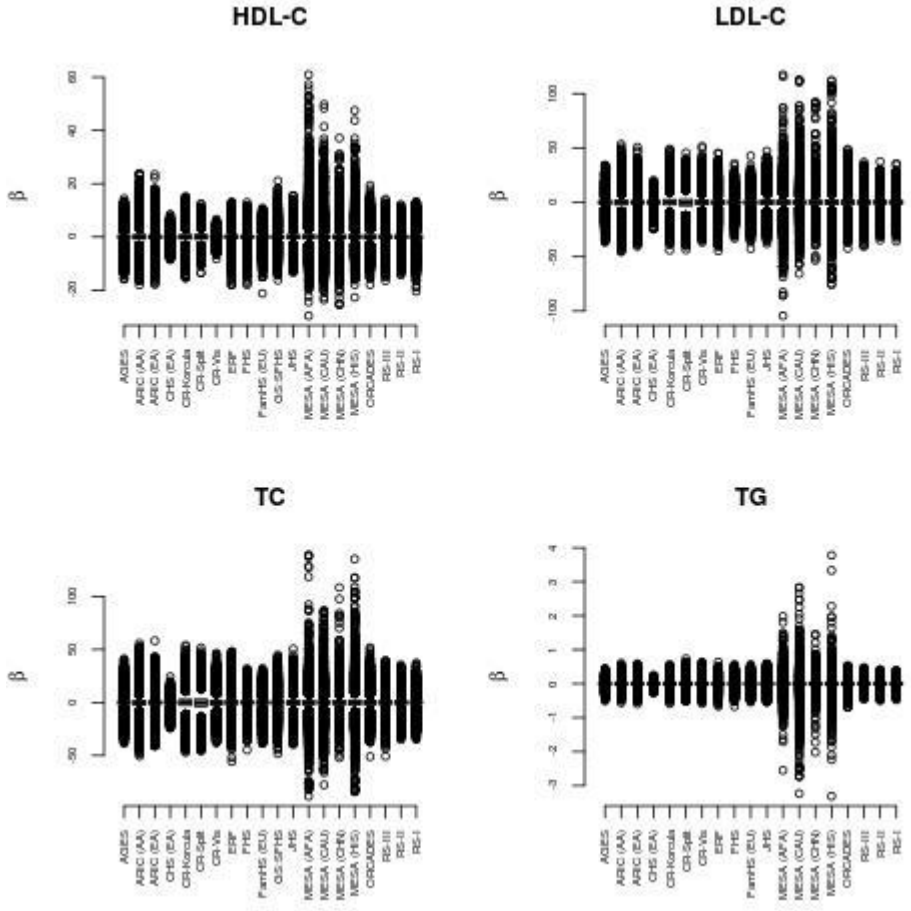
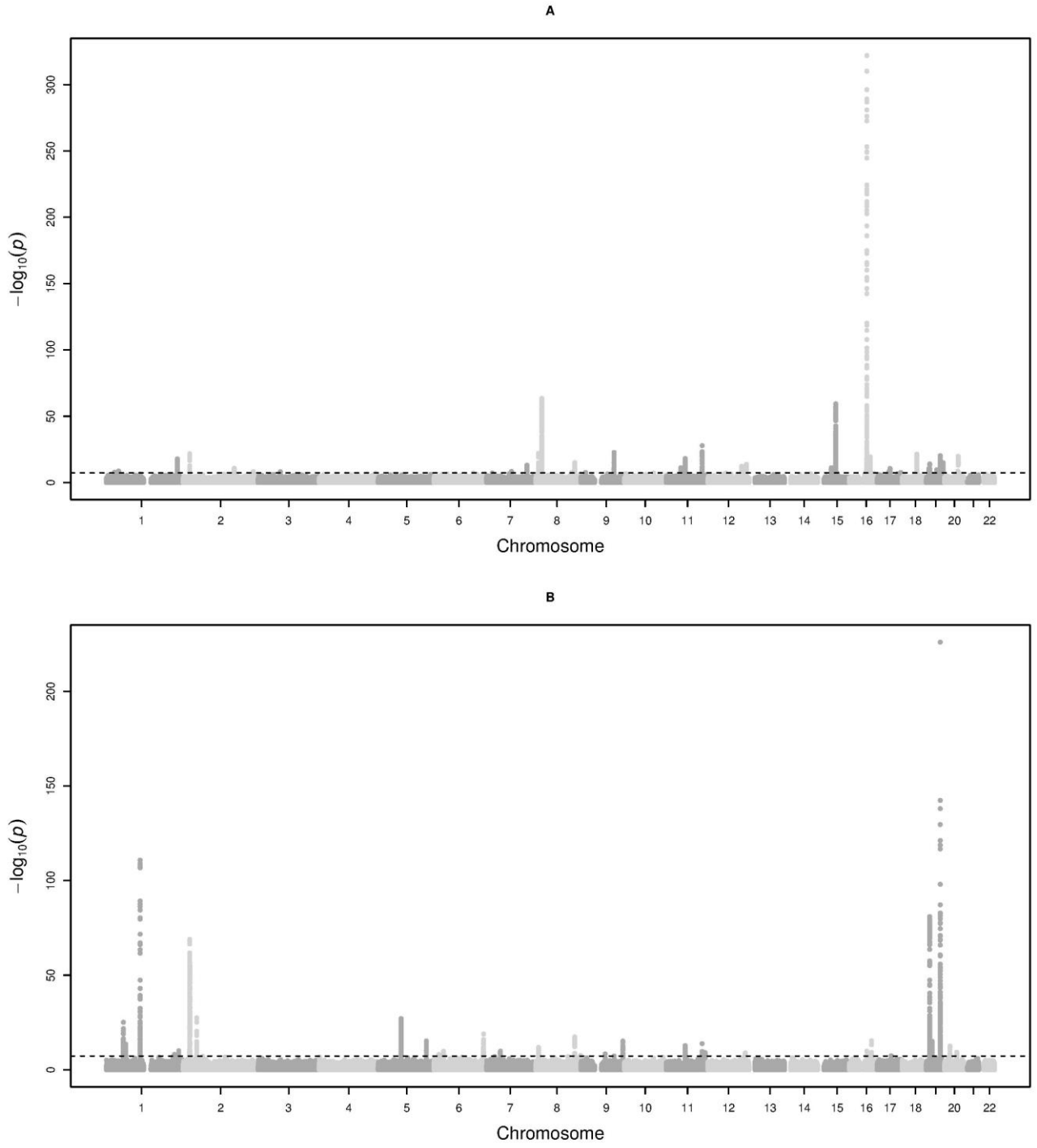
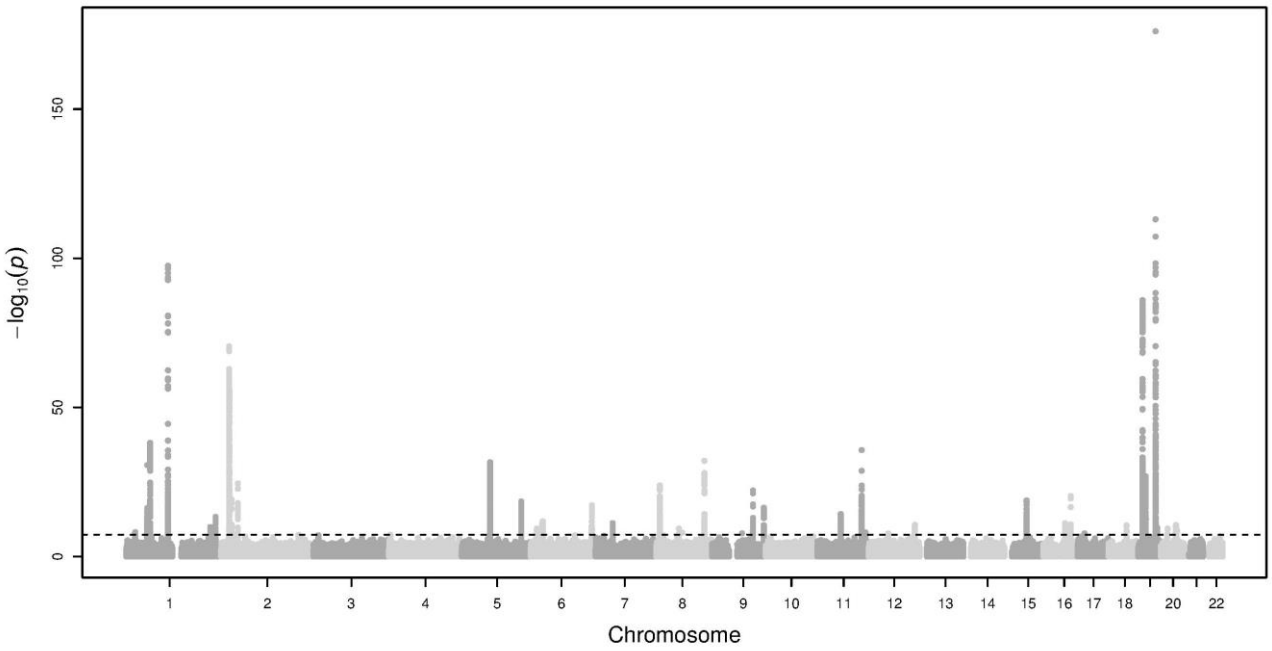


Figure S3: Manhattan plots for HDL-C (A), LDL-C (B), TC (C) and TG (D) after the meta-analysis of all discovery cohorts after exclusion of those variant that were not present in at least 4 cohorts.



C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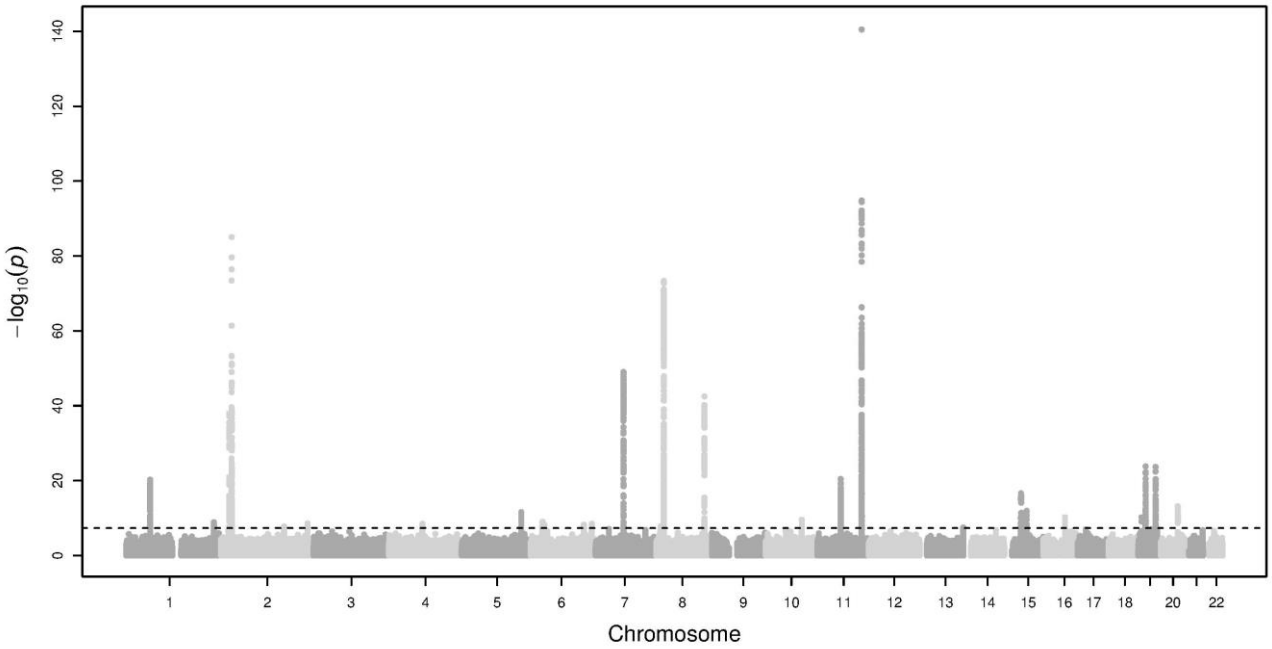
50
100
150
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
20
22
Chromosome

D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60
80
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140
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11
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22
Chromosome

Figure S4: QQ-plot for HDL-C (A), LDL-C (B), TC (C) and TG (D) after the meta-analysis of all discovery cohorts after exclusion of those variant that were not present in at least 4 cohorts.

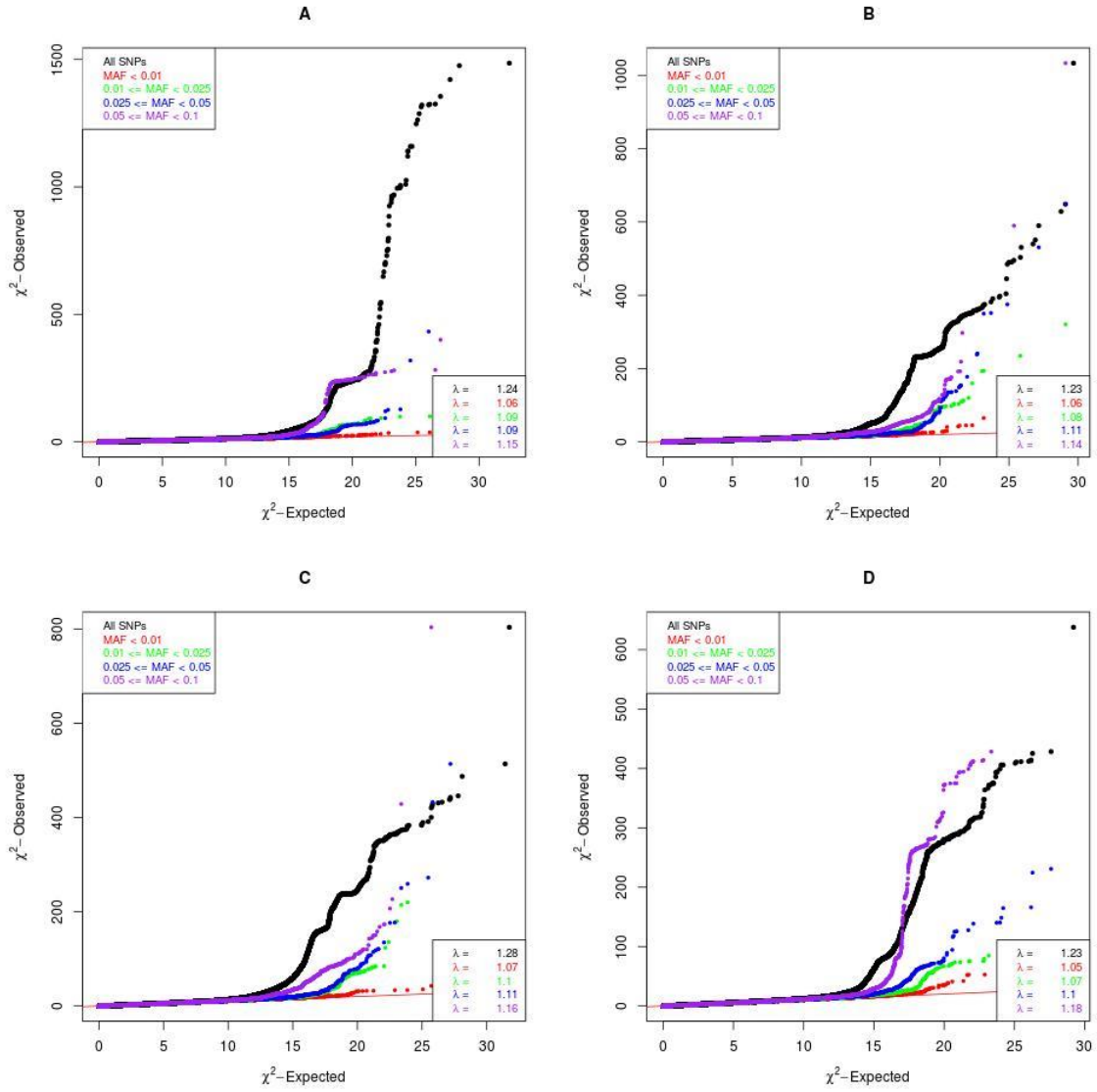


Figure S5: The comparison of the results of Teslovich *et al.* with the meta-analysis of the discovery cohorts. Panel (A) shows the comparison of β values, panel (B) shows the comparison of MAF values and panel (C) shows the comparison of p-values. The red circles are the HDL-C loci, the blue circles are the LDL-C loci, the green circles are the TC loci and the purple circles are the TG loci.

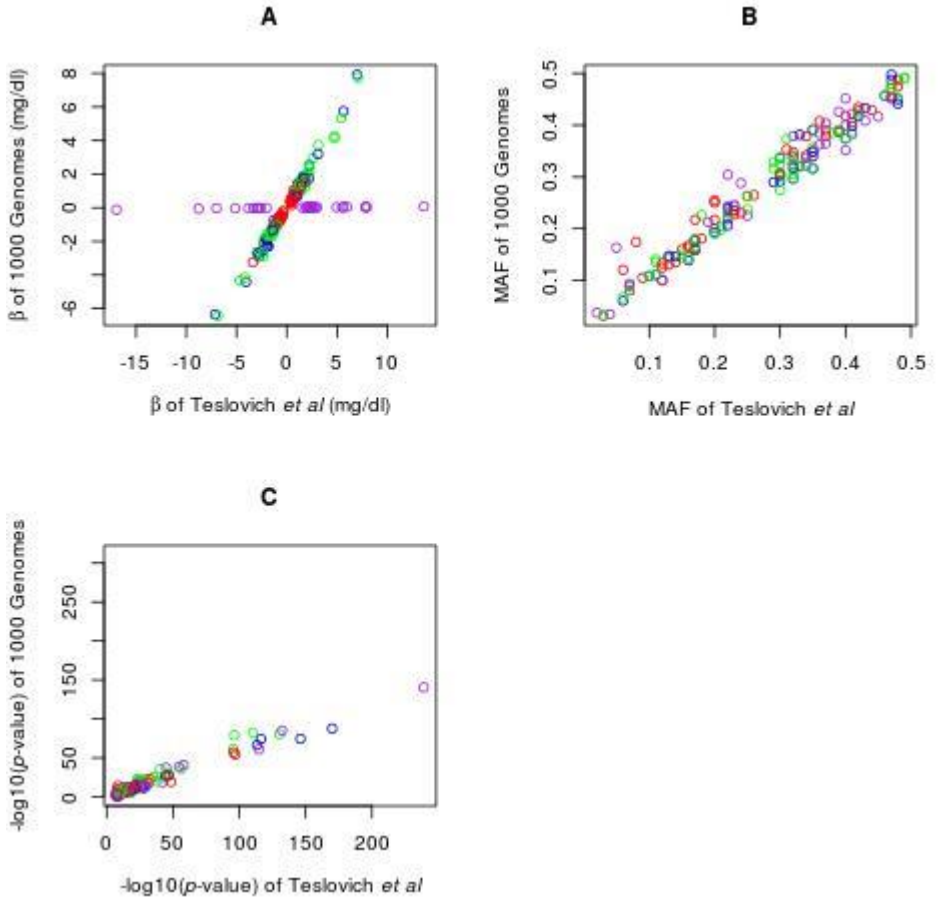


Figure S6: The comparison of the results of GLGC with the meta-analysis of the discovery cohorts. Panel (A) shows the comparison of MAF values and panel (B) shows the comparison of p-values. The red circles are the HDL-C loci, the blue circles are the LDL-C loci, the green circles are the TC loci and the purple circles are the TG loci.

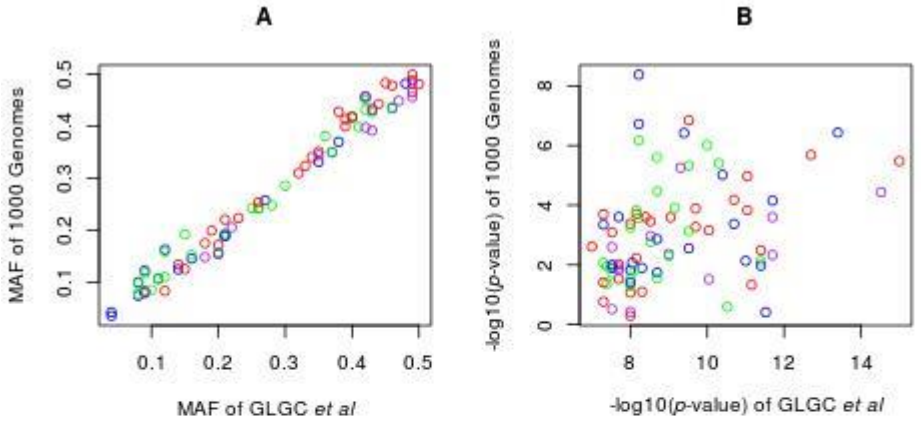
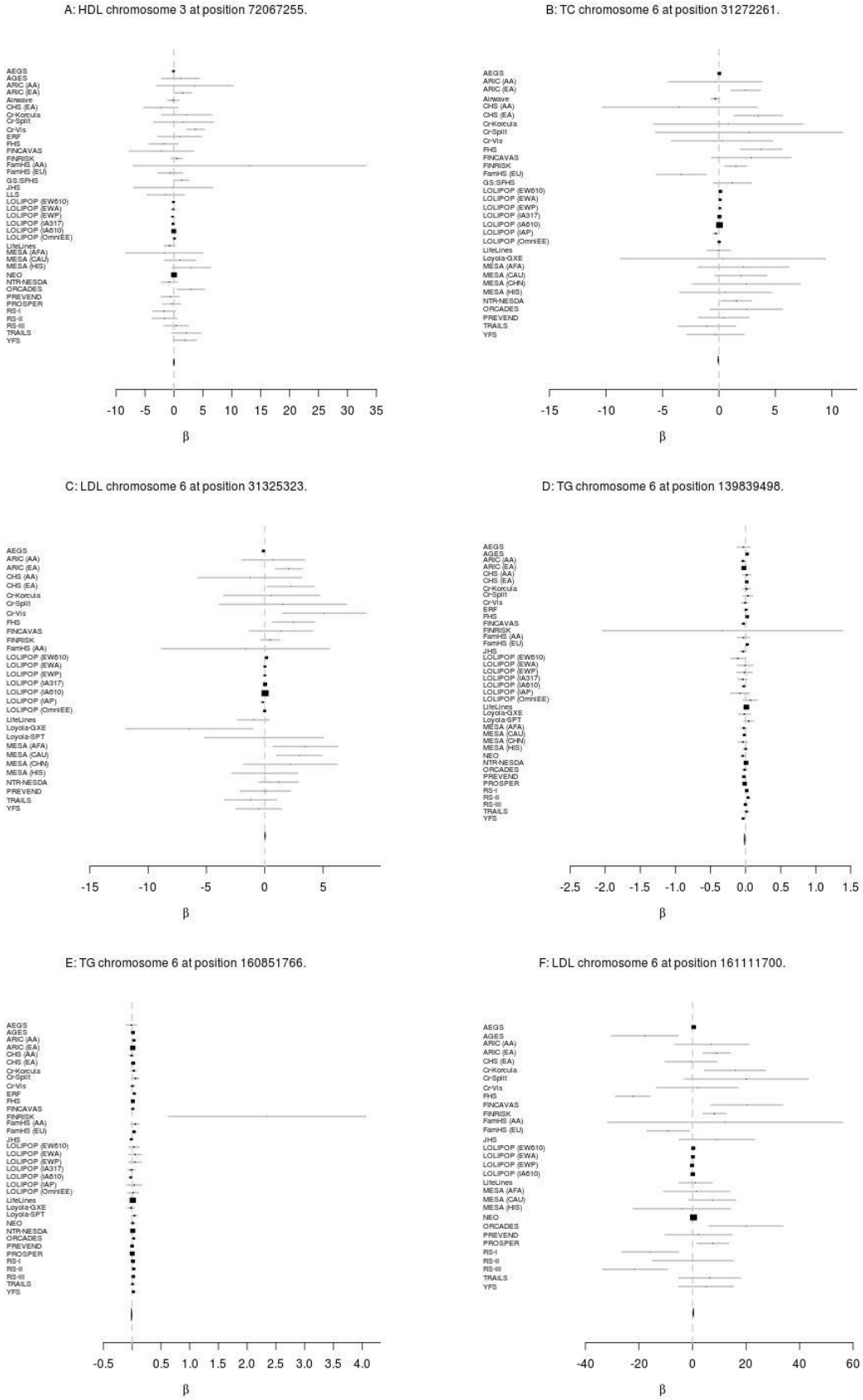
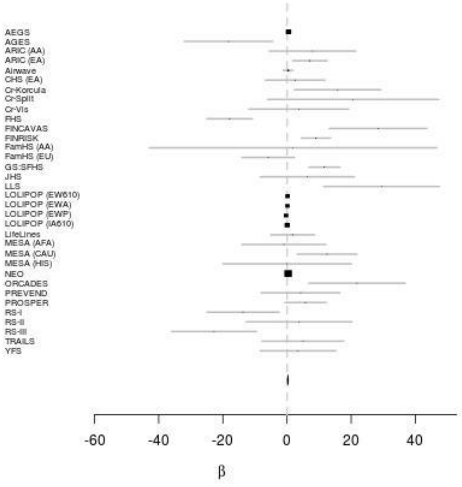


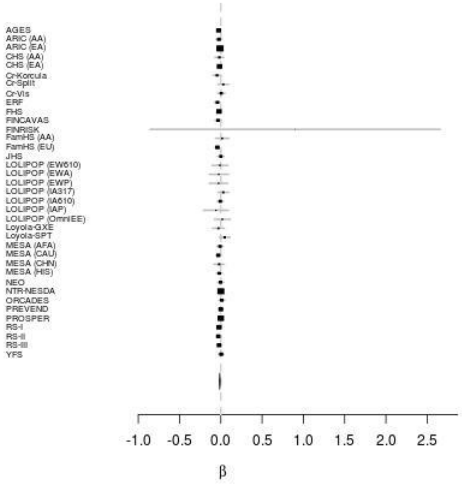
Figure S7: Forest plot for the 19 variants after quality control.



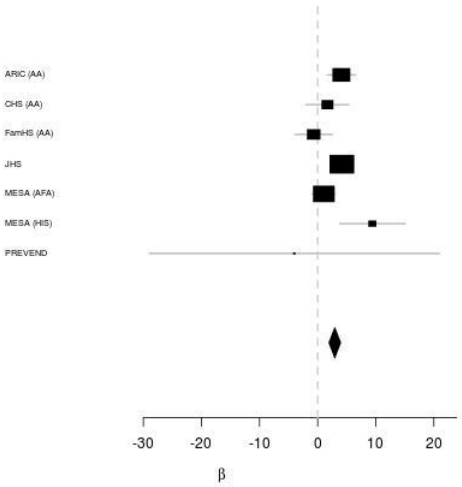
G: TC chromosome 6 at position 161111700.



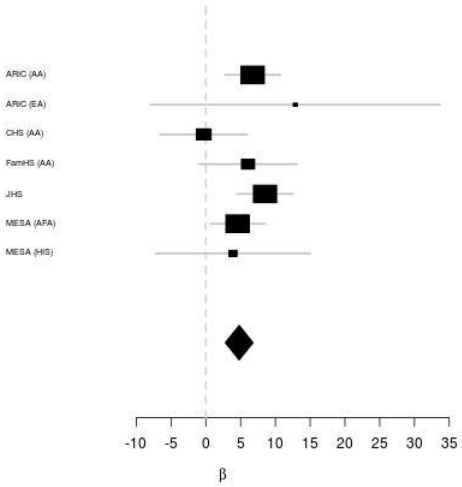
H: TG chromosome 6 at position 36648275.



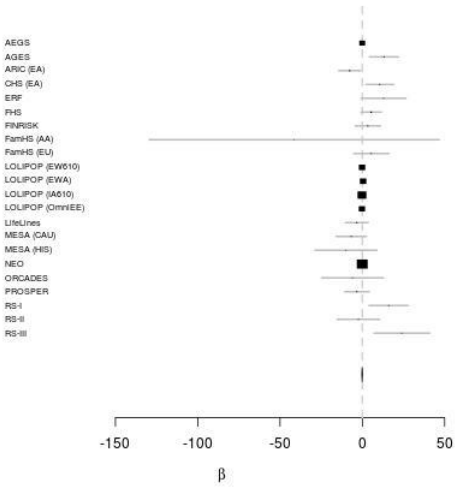
I: HDL chromosome 7 at position 80492357.



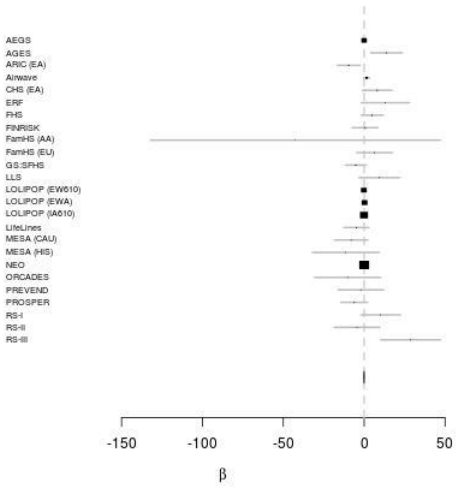
J: TC chromosome 8 at position 68351787.



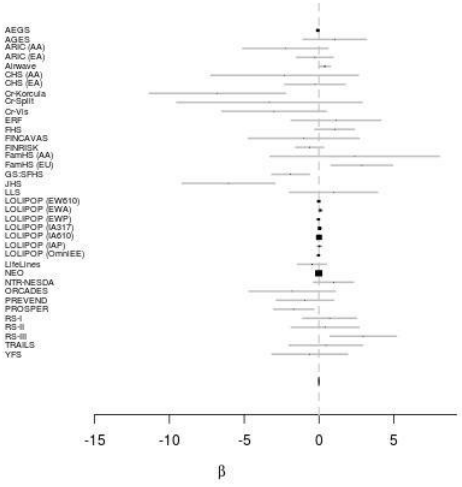
K: LDL chromosome 9 at position 78728065.



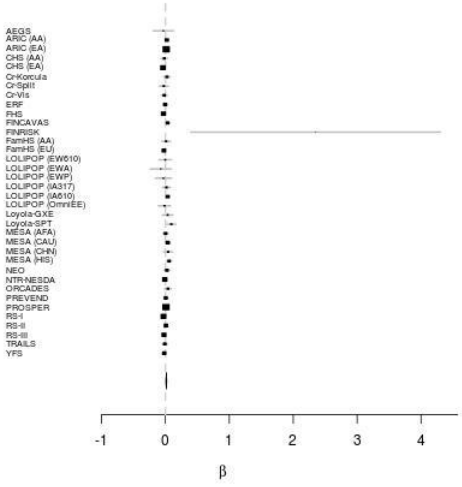
L: TC chromosome 9 at position 78728065.



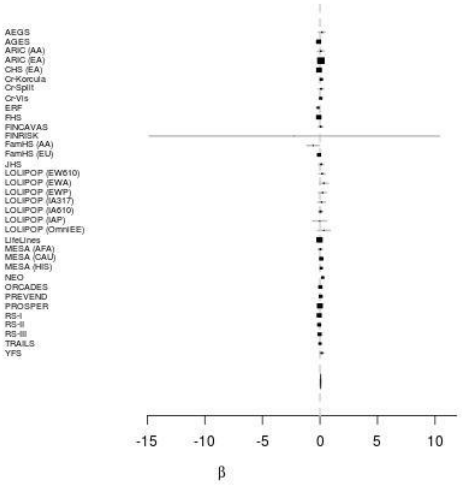
M: TC chromosome 12 at position 51207704.



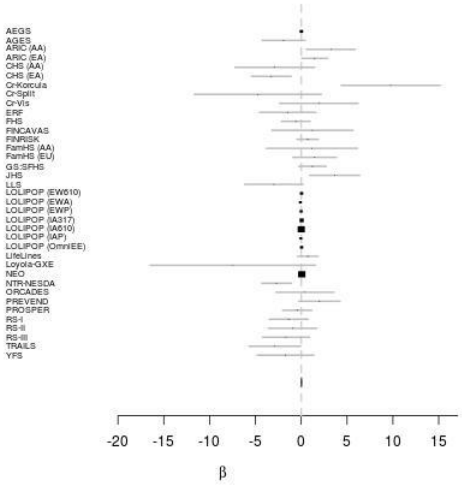
N: TG chromosome 13 at position 114544024.



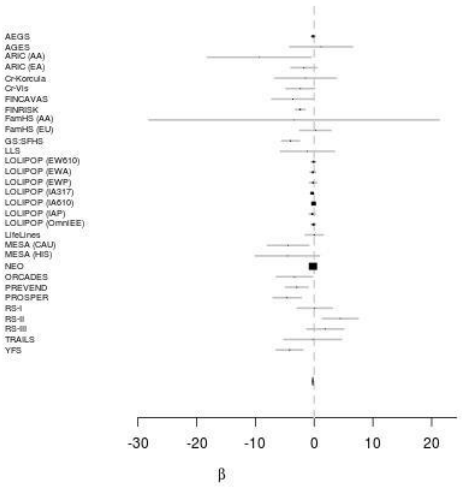
O: TG chromosome 15 at position 43726625.



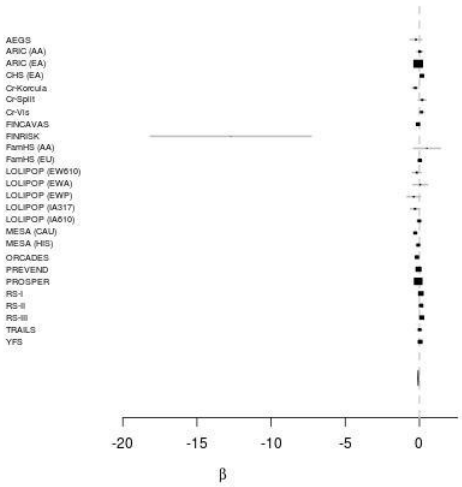
P: TC chromosome 17 at position 18046290.



Q: HDL chromosome 17 at position 41840849.



R: TG chromosome 19 at position 8429323.



S: TC chromosome 20 at position 17844684.