

DATA SUPPLEMENT

Insights from a Large-Scale Whole-Genome Sequencing Study of Systolic Blood Pressure, Diastolic Blood Pressure, and Hypertension

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Table of Contents

Expanded Methods.....	3
Supplemental References.....	11
Table S1.....	12
Table S2.....	13
Table S3.....	19
Table S4.....	22
Table S5.....	24
Table S6.....	27
Table S7.....	29
Table S8.....	30
Table S9.....	33
Table S10.....	35
Table S11.....	39
Table S12.....	43
Table S13.....	45
Table S14.....	46
Table S15.....	50
Table S16.....	54
Table S17.....	57
Table S18.....	62
Table S19.....	65
Table S20.....	66
Table S21.....	69
Table S22.....	70
Table S23.....	72
Figure S1.....	73
Figure S2.....	80
Figure S3.....	82
Author Affiliations.....	83
TOPMed Acknowledgements.....	85
Study Specific Acknowledgements and Funding Sources.....	87
Disclosures.....	91
Million Veteran Program: Consortium Acknowledgement For Manuscripts.....	92

EXPANDED METHODS

Stage-1 Studies

The Amish Complex Disease Research Program (Amish)

(<http://www.medschool.umaryland.edu/endocrinology/Amish-Research-Program/>): The Amish study includes a set of large community-based studies focused largely on cardiometabolic health carried out in the Old Order Amish (OOA) community of Lancaster County, Pennsylvania. Over 7,000 Amish have been recruited to date. This Amish community is a founder population who immigrated to Pennsylvania from Western Europe in the early 1700's, later expanding into other regions of the U.S. The Amish cohort participating in the Trans-Omics for Precision Medicine (TOPMed) Consortium BP analyses comprises 1,111 subjects ≥ 18 years of age from large multigenerational families who were recruited for specific protocols between 2001 and 2006. Subjects have been extensively phenotyped for a range of cardiometabolic traits, including anthropometry, lipids, blood pressure (BP), glucose and related measures, vascular imaging, and a range of other phenotypes. BP was measured at baseline in triplicate using a standard sphygmomanometer. All BP measures were taken with participants in the sitting position after 5 minutes of rest. For the current analysis, the average of the second and third blood pressure measurements was used for analysis. DNA samples have been collected and serum and plasma samples biobanked. The TOPMed Program has provided whole genome sequencing (WGS) data to complement genome-wide association study (GWAS) array data already collected in >5,000 Amish study participants. Due to their ancestral history, the OOA are enriched for rare exonic variants that arose in the population from a single founder (or small number of founders) and propagated through genetic drift. Many of these variants have large effect sizes and identifying them can lead to new biological insights about health and disease. A major goal of the TOPMed WGS sequencing efforts is to identify functional variants that underlie some of the large effect associations observed in this unique population.

Atherosclerosis Risk in Communities (ARIC) Study: The ARIC study is a population-based prospective cohort study of cardiovascular disease sponsored by the National Heart, Lung, and Blood Institute (NHLBI). ARIC included 15,792 individuals, predominantly European American and African American, aged 45-64 years at baseline (1987-89), chosen by probability sampling from four US communities. Cohort members completed three additional triennial follow-up examinations, a fifth exam in 2011-2013, a sixth exam in 2016-2017, and a seventh exam in 2018-2019. BP measures and medication use at the baseline exam were used in this study, which included 6,545 ARIC participants with WGS data from TOPMed and the CCDG programs. BP was measured using a standardized Hawksley random-zero mercury column sphygmomanometer with participants in a sitting position after a resting period of 5 minutes. The size of the cuff was chosen according to the arm circumference. Three sequential recordings for systolic and diastolic BP were obtained; the mean of the last two measurements was used in this analysis, discarding the first reading. BP lowering medication use was recorded from the medication history.

The Cardiovascular Health Study (CHS): The CHS is a population-based cohort study of risk factors for coronary heart disease and stroke in adults ≥ 65 years conducted across four field centers. The original predominantly European ancestry cohort of 5,201 persons was recruited in 1989-1990 from random samples of the Medicare eligibility lists; subsequently, an additional predominantly African-American cohort of 687 persons was enrolled for a total sample of 5,888. A subset of 3,622 CHS participants were selected for the TOPMed sequencing program which included African Americans participants, cases of idiopathic venous thromboembolism, myocardial infarction, coronary heart disease or stroke and a

random sample of “healthy elderly”. Blood samples were drawn from all participants at their baseline examination and DNA was subsequently extracted from available samples. Research staff with central training in BP measurement assessed two right-arm systolic and diastolic BP levels at baseline with a Hawksley random-zero sphygmomanometer. Measures were taken after five minutes of seated rest, with BP measurements taken one minute apart. Means of the two repeated BP measurements from the baseline examination were used for the analyses. CHS was approved by institutional review committees at each field center and the 2,839 individuals in the present analysis had available DNA and gave informed consent including consent to use of genetic information for the study of cardiovascular disease.

The Cleveland Family Study (CFS): The CFS is a family-based cohort study that aims to examine the genetic and familial basis of sleep apnea. The total cohort consists of 2,534 African- and European-American individuals from 356 families. 275 index probands with confirmed sleep apnea diagnoses were recruited from northern Ohio sleep centers. Neighborhood control probands with at least two living relatives available for study were also selected at random from a list provided by the index family. The spouses and relatives of the cases and controls were also recruited if available. Data was collected from up to four visits made from 1990 to 2006, and a final laboratory visit at a clinical research center between 2000 and 2006. Blood samples were obtained from individuals who participated in the final two exam cycles, and DNA was extracted from samples that passed quality control. When the current analysis was performed, WGS data was available for a total of 990 CFS participants through the TOPMed program. Two to three measurements of systolic and diastolic BP were obtained from the last available examination for each participant. BP measurements were taken in the sitting (n=350) or supine (n=640) positions following standardized guidelines and using a calibrated sphygmomanometer. The average of two BP measures were used in the current analyses. When three BP measures were available for a study participant, the first measure was discarded and the final two measures were averaged.

Coronary Artery Risk Development in Young Adults (CARDIA): CARDIA is a prospective multicenter study with 5,115 adults Caucasian and African American participants of the age group 18-30 years, recruited from four centers at the baseline examination in 1985-1986. The recruitment was done from the total community in Birmingham, AL, from selected census tracts in Chicago, IL and Minneapolis, MN; and from the Kaiser Permanente health plan membership in Oakland, CA. Details about study design for CARDIA have been previously published. Nine examinations have been completed since initiation of the study, respectively in the years 0, 2, 5, 7, 10, 15, 20, 25, and 30, with a tenth examination underway. Written informed consent was obtained from participants at each examination and all study protocols were approved by the institutional review boards of the participating institutions. Systolic and diastolic BP was measured in triplicate on the right arm using a random-zero sphygmomanometer with the participant seated and following a 5-min. rest. The average of the second and third measurements was taken as the BP value. BP medication use was obtained by questionnaire. WGS data is available for a subset of the cohort who provided informed consent and had genome-wide genotyping (N=2,930).

Framingham Heart Study (FHS): FHS is a community-based longitudinal study designed for cardiovascular diseases and heart-disease-related risk factors using family-based study design (<https://theframinghamheartstudy.org>). The FHS sample are Caucasians, including family members of three generations, the original, offspring and the Third-Generation, who have completed their first on-site clinical examinations in 1948, 1971, and 2002, respectively. Participants maintain on-site follow-up examinations an average of every 4 years and have consented for genetic studies, as well as the annual well-being survey. At each on-site examination, participants undergo a physician-administered physical examination, a face-to-face interview with research staff, and a self-administered questionnaire process.

Through the on-site examination researchers collect information on medical history, anthropometry, health status, medical and sociodemographic countenances, lifestyle characteristics, and blood or urine samples.

Examining physicians followed a standardized protocol for measuring BP among seated FHS participants. Specifically, they used a mercury column sphygmomanometer to collect two repeated measures of BP taken from the left arm. For the current analysis, the mean value of the two systolic and diastolic BP measures were used. In addition, we used BP values obtained at participants' first FHS examination to minimize medication-alteration. Information on anti-hypertension medication use was self-reported by the FHS participants at on-site examination. Fifteen mmHg was added to systolic BP and 10 mmHg was added to diastolic BP for participants who reported medication use for hypertension. In the late 1980s and through the 1990s, DNA was collected from living study participants of the original and offspring cohorts. DNA samples are available for participants of the Third-Generation cohort. A total of 3,615 TOPMed WGS participants who met the inclusion criteria for the BP analysis contributed to the current study.

Genetic Epidemiology Network of Arteriopathy (GENOA): The GENOA study consists of hypertensive sibships that were recruited for linkage and association studies in order to identify genes that influence BP and its target organ damage. In the initial phase of the GENOA study (Phase I: 1996-2001), all members of sibships containing ≥ 2 individuals with essential hypertension clinically diagnosed before age 60 were invited to participate, including both hypertensive and normotensive siblings. A total of 1,583 non-Hispanic whites from Rochester, MN, and 1,854 African Americans from Jackson, MS, were examined. Sitting systolic BP (SBP) (mmHg) and diastolic BP (DBP) (mmHg) were measured three times with a random zero sphygmomanometer. The average of the last two measurements at Phase I was used in this study. For subjects taking any anti-hypertensive (BP lowering) medications, 15 mmHg was added to SBP and 10 mmHg was added to DBP. A physician specializing in hypertension reviewed all medications and made the final determination of whether a medication was considered an anti-hypertensive. Only African Americans were sequenced through the TOPMed project, and participants who were also in the ARIC or Jackson Heart Study (JHS) were excluded from analysis. A total of 1,214 African American participants were included in the current analysis.

Genetic Epidemiology Network of Salt-Sensitivity (GenSalt): The GenSalt study is a unique NHLBI-sponsored family feeding-study designed to examine the interaction between genes and dietary sodium and potassium intake on BP. A total of 3,142 participants from 633 Han families from rural, north China were ascertained through a proband with untreated pre-hypertension or stage-1 hypertension identified from a population-based BP screening. A total of 1,906 GenSalt probands and their siblings, spouses, and offspring were eligible. Among them, 1,818 took part in the TOPMed WGS program and had BP and covariable data available for the current analysis.

All BP readings were measured by trained and certified observers using a random-zero sphygmomanometer and a standard protocol. BP was measured with the participant in the sitting position after 5 minutes of rest. In addition, participants were advised to avoid alcohol, cigarette smoking, coffee/tea, and exercise for at least 30 minutes prior to their BP measurements. Systolic and diastolic BP measures were taken in triplicate during each day of a three-day baseline observation. After throwing out the first measure, the subsequent two measures obtained on the first day of baseline observation were averaged and used in this analysis.

Genetics of Lipid Lowering Drugs and Diet Network (GOLDN): GOLDN is a family-based study of European descent individuals recruited in Minneapolis and Salt Lake City (two of the NHLBI Family Heart Study sites). It aims to uncover genetic predictors of variability in lipid phenotypes, which include both fasting and postprandial lipids quantified using traditional methods, NMR, and high-throughput lipidomics. During the initial screening of ~1,350 individuals, the following criteria were used for exclusion: age < 18 years; fasting triglycerides ≥ 1500 mg/dL; recent history of myocardial infarction, coronary bypass surgery, or coronary angioplasty; self-report of a positive history of liver, kidney, pancreas, or gallbladder disease, or a history of nutrient malabsorption; current use of insulin; abnormal liver or kidney function; in women of childbearing potential, pregnancy, breastfeeding, not using an acceptable form of contraception. Of those who enrolled, 1,048 individuals consented to the use of their DNA in research; 942 participants with data on all exposures, outcomes, and covariates were included in the current study. All participants had two repeated measures of blood pressure which were obtained using a standard protocol and an automated oscillometric device. Resting BP was measured in the morning while participants were in a sitting position. The average of the two BP measurements were used in this analysis.

Genetic Studies of Atherosclerosis Risk (GeneSTAR): GeneSTAR is an ongoing family-based prospective study designed to determine environmental, phenotypic, and genetic causes of premature cardiovascular disease. GeneSTAR was conducted originally in healthy adult European- and African-American siblings of probands with documented early onset coronary disease under 60 years of age at the time of hospitalization in any of 10 Baltimore area hospitals from 1982-2006. Participants were screened for traditional coronary disease and stroke risk factors and have been followed regularly to ascertain incident cardiovascular disease. Commencing in 2003, the siblings, their offspring, and the coparent of the offspring who were free of cardiovascular disease participated in a 2 week trial of aspirin 81 mg/day with pre and post ex vivo platelet function assessed using multiple agonists and were screened for traditional coronary disease and stroke risk factors. Of the total 3949 participants, 2142 had complete measures of platelet function; of those, 1786 were selected for TOPMed based on (1) participation in later GeneSTAR studies and (2) largest family size.

Data on medication use was obtained from a standardized interview, where information on medication name, dosage, indication, and frequency of use was collected. Participants who reported current use of any medication classified as an anti-hypertensive agent were coded as 'yes' for anti-hypertensive use. BP was measured using a standard mercury or aneroid sphygmomanometer, following the American Heart Association and JNC Guidelines. The mean of the second two resting BP readings taken during the baseline screening visit was used to characterize BP. A total of 1,735 GeneSTAR participants with WGS and BP data were included in the current analysis.

Hispanic Community Health Study-Study of Latinos (HCHS-SOL): HCHS/SOL is a prospective, population-based cohort study of 16,415 Hispanics/Latino adults (ages 18-74 years) recruited from randomly selected households in four US communities (Chicago, IL; Miami, FL; Bronx, NY; San Diego, CA) between 2008 and 2011. At baseline clinic examination, sitting BP was measured on the right arm using an OMRON HEM-907XL (Omron Healthcare, Inc., Lake Forest, IL) automatic sphygmomanometer by certified staff. Three sets of systolic and diastolic BPs were measured 1 minute apart after an initial 5-minute rest period, and the average of the last two measurements was used in the study. For those taking antihypertensive medication, 15mmHg was added to systolic BP and 10 mmHg was added to diastolic BP. A total of 1,590 participants with WGS data through TOPMed program were included in the current analysis.

Hypertension Genetic Epidemiology Network (HyperGEN): The HyperGEN study is one of the four networks in the Family Blood Pressure Program (FBPP) supported by the NHLBI to identify genetic contributors to hypertension. HyperGEN is a family-based study with a sib-pair design. Hypertensive African American sibships were recruited from Forsyth County, NC and from the community-at-large in Birmingham, AL from 1995 to 2000. Sib-pairs with hypertension onset before age 60 were recruited in the first phase. The study was subsequently extended to siblings and the offspring of the hypertensive probands who were unmedicated adults. BP was measured with an automated oscillometric device using a standard protocol. After a 5-minute resting period, BP was measured 6 times, with each BP measurement taken two minutes apart. The average of the second and third BP measurements was averaged and used in this analysis. In addition, we added 15 mm Hg to the SBP values and 10 mmHg to DBP values for subjects taking antihypertensive or BP-lowering medications. A total of 1,880 HyperGEN participants were included in the current analysis.

Jackson Heart Study (JHS): The JHS (<https://www.jacksonheartstudy.org>) is a large, population-based observational study evaluating the etiology of cardiovascular, renal, and respiratory diseases 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 5306 participants, including a nested family cohort of 1498 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. Participants provided medical and social history and had an array of physical and biochemical measures and diagnostic procedures during a baseline examination (2000-2004) and two follow-up examinations (2005-2008 and 2009-2012). Samples for genomic DNA were collected during the first two examinations. Consent for genetic studies and broad sharing of genetic data was provided by 3,482 participants. After quality control, WGS data are available for 3,307 participants. 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, and preparation for a fourth examination is in progress. SBP and DBP were measured twice after the participant had been seated for 5 minutes. BP was measured using a Hawksley random-zero sphygmomanometer (Hawksley and Sons Ltd, Lancing, UK). The random-zero BP measurements were calibrated to an oscillometric device using robust regression. The average of the two BP measures were used for the current analysis.

The Mount Sinai BioMe Biobank (BioMe): The BioMe Biobank is an ongoing, prospective, hospital- and outpatient- based population research program operated by The Charles Bronfman Institute for Personalized Medicine (IPM) at Mount Sinai. BioMe has enrolled over 50,000 participants between September 2007 and July 2019. BioMe is an Electronic Medical Record (EMR)-linked biobank that integrates research data and clinical care information for consented patients at The Mount Sinai Medical Center, which serves diverse local communities of upper Manhattan with broad health disparities. IPM BioMe populations include 25% of African American ancestry (AA), 36% of Hispanic Latino ancestry (HL), 30% of white European ancestry (EA), and 9% of other ancestry. The BioMe disease burden is reflective of health disparities in the local communities. BioMe operations are fully integrated in clinical care processes, including direct recruitment from clinical sites waiting areas and phlebotomy stations by dedicated BioMe recruiters independent of clinical care providers, prior to or following a clinician standard of care visit. Recruitment currently occurs at a broad spectrum of over 30 clinical care sites. Information on anthropometrics, demographics, BP and use of BP-lowering medication was derived from participants' EMR. Full genetic and phenotype data for 3,155 individuals was available for analyses.

Multi-ethnic Study of Atherosclerosis (MESA): MESA is a study of the characteristics of subclinical cardiovascular disease and the risk factors that predict progression to clinically overt cardiovascular

disease or progression of the subclinical disease. MESA consisted of a diverse, population-based sample of an initial 6,814 asymptomatic men and women aged 45-84. Thirty-eight percent of the recruited participants were white, 28 percent African American, 22 percent Hispanic, and 12 percent Asian, predominantly of Chinese descent. 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 first examination took place over two years, from July 2000 - July 2002. BP was measured after a 5-minute rest during clinical visits. BP was measured three times at 1 minute intervals using a Dinamap PRO 100 automated oscillometric device (Critikon, Tampa, FL) with the subject in seated, and the average of the second and third BP measurements was recorded for each visit. Antihypertensive medication use was recorded. Participants have been contacted every 9 to 12 months throughout the study to assess clinical morbidity and mortality. It was followed by four examination periods that were 17-20 months in length, and a sixth exam is currently taking place. A total of 4,526 MESA participants with available WGS and BP data were included in the current analysis.

Samoan Study: Genome-wide Association Study of Adiposity in Samoans. The parent Samoan study is a population-based GWAS of adiposity and cardiometabolic phenotypes among adults, 25-65 years of age, from the independent nation of Samoa in the South Pacific. The research goal of this study is to identify genetic variation that increases susceptibility to obesity and cardiometabolic phenotypes. Biomarker and questionnaire data were collected to assess cardiometabolic phenotypes. DNA was collected and the Affymetrix 6.0 chip used for SNP genotyping. After quality control checks on genotyping and excluding individuals with key missing data we have a final sample of 3,122 adults with high-quality genome-wide marker data. Participation in TOPMed provided WGS data for 1,284 individuals from the GWAS sample chosen for maximal informativity for our Samoan-specific imputation panel. BP was measured after a 10-minute seated rest period three times, with 3-minute rest periods between measurements, using an Omron HEM907 XL digital blood pressure monitor (Omron Healthcare, IL). Results of the second and third blood pressure measurements were averaged for used for the current analyses. A total of 1,261 participants with available WGS and phenotype data were included in this analysis.

Taiwan Study of Hypertension using Rare Variants (THRIV): THRIV proposed to identify rare and low frequency genetic variants for BP and hypertension through whole exome sequencing of a subset of highly enriched Taiwan Chinese hypertensive families and as many matched controls. The Taiwan Chinese families (N=1,200) were previously recruited as part of the NHLBI-sponsored SAPPHIRE Network which is part of the FBPP. The SAPPHIRE families were recruited to have multiple hypertensive sibs and some of them also included one normotensive/hypotensive sib. The matched controls (N=1,200) were selected from the large population-based HALST Study and a Hospital-based population, both in Taipei, Taiwan. Resting BP was measured in triplicate using a standard protocol and automated DINAMAP device. The average of the second and third BP readings were averaged and used in the current analysis.

WHI (Women's Health Initiative): WHI is a long-term national health study that focuses on strategies for preventing common diseases such as heart disease, cancer and fracture in postmenopausal women. A total of 161,808 women aged 50–79 years old were recruited from 40 clinical centers in the US between 1993 and 1998. WHI consists of an observational study, two clinical trials of postmenopausal hormone therapy (HT, estrogen alone or estrogen plus progestin), a calcium and vitamin D supplement trial, and a dietary modification trial. The WHI contribution of TOPMed was designed as a case-control study of stroke and venous thromboembolism (VTE). Approximately 5,000 stroke and 1,000 VTE cases and 5,000 controls were selected for WGS. The controls were selected to frequency match the cases by age at

recruitment, ethnicity, and membership in the WHI hormone therapy trial. Study protocols and consent forms were approved by the IRB at all participating institutions. Self-reported medications were collected using standardized questionnaires at the screening visit and BP was measured in a clinical visit by certified staff using standardized procedures and instruments. Two BP measures were recorded after 5 minutes rest using a mercury sphygmomanometer. Appropriate cuff bladder size was determined at each visit based on arm circumference. Diastolic BP was taken from the phase V Korotkoff measures. The average of the two measurements, obtained 30 seconds apart, was used in analyses. We added a constant to measured BP for individuals taking anti-hypertensive medications. A total of 10,860 WHI participants with WGS and BP data were included in the current analysis.

Stage-1 Quality Control of TOPMed Freeze 6 Data

A detailed description of WGS methods have been reported previously.¹ Briefly, WGS at a mean depth of at least 30X was conducted using Illumina HiSeq X Ten instruments at six sequencing centers. Variant discovery and genotype calling were conducted jointly across the 18 discovery stage studies using the GotCloud pipeline at the University of Michigan Informatics Research Center.² This procedure resulted in a single, multi-study genotype call set that underwent rigorous variant, genotype, and sample quality control procedures. After setting genotypes with read depth less than 10X to missing, additional quality control included the removal of variants failing the support vector machine filter, with excess heterozygosity or Mendelian inconsistencies, overlapping centromeric or other low complexity regions, or with missingness greater than 5%. Sample quality filtering excluded duplicate samples from the same individual, samples with sex discrepancies, misidentified samples, or consent issues, and those of poor quality based on concordance of WGS and array data.

Stage-1 Phenotype Harmonization

Quality control and harmonization of SBP, DBP, and hypertension phenotypes across studies followed a standard protocol developed by the TOPMed BP Working Group. All participants included in the discovery stage analysis had at least two sitting measures of blood pressure at a single clinical study visit and information on current use of antihypertension medication. Prior to harmonization, each study removed unlikely BP values, such as SBP<60 mmHg, SBP>300 mmHg, or DBP>SBP. Phenotype harmonization involved using the mean of two BP measures from a study visit to estimate SBP and DBP for each participant. For longitudinal studies, we used BP measures obtained at the first visit, which optimized sample size and minimized the percent of participants taking antihypertension medications. If a participant was taking antihypertension medication, SBP and DBP values were imputed by adding 15 and 10 mmHg, respectively, to observed values.³ Hypertension was defined as mean SBP≥140 mmHg, mean DBP≥90 mmHg, or current use of anti-hypertension medication. The systolic and diastolic BP thresholds selected are consistent with the definition of stage-2 hypertension, according to the American College of Cardiology and American Heart Association guidelines. A stringent hypertension definition was used to enrich cases for disease causing variants. Continuous SBP and DBP phenotypes were transformed within each ancestry strata by first regressing BP on age, sex, body mass index (BMI), study, and the first 11 ancestry principal components (PCs). BP residuals then underwent rank-based inverse normal transformation and were subsequently rescaled by multiplying the transformed value by the standard deviation of the original harmonized BP phenotype, an approach that allowed subsequent effect size estimates to reflect clinically meaningful values in mmHg.

Stage-2 Studies

In UK Biobank, genome-wide array-based genotypes were phased using Eagle v2.4,⁴ converted from GRCh37 to GRCh38 using LiftOver,⁵ and imputed using the TOPMed freeze 5 reference panel with Minimac4.¹ Whole exomes were captured using a modified version of the IDT xGen probe library and

sequenced using on the Illumina NovaSeq 6000 platform. Resting BP was measured twice during a clinical visit using a standardized protocol and Omron electronic BP monitor. The SBP, DBP, and hypertension phenotypes were harmonized and transformed using the same protocol that was implemented in stage-1. Individual SNVs identified in stage-1 were tested for association with the continuous and binary BP phenotypes using respective linear and logistic mixed models implemented in SAIGE.⁶ These models adjusted for age, sex, BMI, and ancestry PCs and accounted known and cryptic relatedness, in this instance, using a genetic relatedness matrix. Stage-1 gene-based signals from aggregate rare variant analyses were tested in stage-2 using an optimized sequence kernel association test (SKAT-O) implemented in our mixed model framework in SAIGE-Gene.

REGARDS participants were genotyped using Illumina Infinium Multi-Ethnic AMR/AFR BeadChip arrays (MEGA chip; Illumina, Inc., San Diego, CA). BP was measured during the in-home baseline study visit twice using aneroid sphygmomanometers following a standardized protocol by trained examiners. Participants were asked to sit for five minutes with both feet on the floor prior to the first BP measurement and there was a 30 second rest between measurements. The average of the two measurements was recorded. Among those taking antihypertension medication, 15 mmHg and 10 mmHg were added to SBP and DBP values, respectively. Hypertension was defined as SBP>140 mmHg, DBP>90 mmHg, or use of anti-hypertension medication. GWAS of the continuous BP and binary hypertension phenotypes were performed using linear and logistic regression models, respectively, with adjustment for age, sex, BMI, and ancestry PCs. These analyses were performed using PLINK2 software.

MVP participants were genotyped using the Affymetrix Axiom Biobank array. These data were phased using Eagle v2.3⁴ and imputed to the 1KG Project⁷ phase 3, version 5 reference panel using Minimac3. Multiple measures of SBP over time were derived from electronic health records. GWAS analyses used the median SBP value, along with DBP and covariable information derived from the same time-point. Among those taking antihypertension medication, 15 mmHg and 10 mmHg were added to SBP and DBP values, respectively. Hypertension was defined as SBP>140 mmHg, DBP>90 mmHg, or use of anti-hypertension medication. GWAS of the continuous BP and binary hypertension phenotypes were performed using linear and logistic regression models, respectively, with adjustment for age, age², sex, BMI, and ancestry PCs. These analyses were performed using SNPTEST-v2.5.4-beta.

Conditional and Gene-Tissue Expression (GTEx) Analyses

Conditional analyses were conducted to fine map and verify the independence of potentially novel signals from previously reported BP loci by conditioning the variant signal on all previously reported variants at the locus. Furthermore, identified variants were tested for association with expression of genes in *cis* (defined as genes with a transcription start site within 1 Mb of the variant) using Gene-Tissue Expression (GTEx) v8 WGS (dbGaP phs000424.v8.p2) and gene expression data from 49 tissues (including 2 cell lines) in up to 838 participants (<https://www.gtexportal.org/home/documentationPage#staticTextAnalysisMethods>).

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Table S1. Characteristics of 51,456 participants included in the stage-1 WGS study, according to ancestry.

Ancestry	N	Mean age* (s.d.)	Women, %	Mean BMI† (s.d.)	Mean SBP‡ (s.d.)	Mean DBP‡ (s.d.)	HTN§, %	Anti-HTN medicine, %
African	13,836	51.9 (15.8)	66.5	30.7 (7.3)	128.8 (20.8)	75.7 (11.2)	56.3	46.0
Asian	3,796	47.1 (13.4)	52.2	24.1 (3.5)	123.4 (20.8)	75.1 (12.1)	36.2	22.1
European	28,390	55.8 (15.7)	68.0	27.2 (5.5)	124.0 (19.1)	72.3 (10.4)	37.8	25.9
Hispanic	4,173	55.4 (14.5)	64.6	30.0 (6.4)	127.2 (21.6)	73.1 (11.4)	48.2	35.8
Samoaan	1,261	44.6 (11.3)	60.3	33.6 (6.7)	128.4 (19.1)	82.0 (13.0)	32.0	7.2

BMI, body mass index; DBP, diastolic blood pressure (BP); HTN, hypertension; SBP, systolic BP.

*Age in years. †Measurements in kg/m². ‡Measurements in mmHg. §Defined as SBP≥140, DBP≥90 or use of anti-HTN medication.

Table S2. Novel lead variants achieving $P < 1E-06$ in single marker analyses of the multi-ancestry TOPMed sample.

Chr	Position (B38)	rsID	Ref	Alt	AAF	Loc	Phe	TOPMed			UKBB			MVP			REGARDS			Meta-Analysis		
								Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
<i>Novel Loci</i>																						
1	53004394	rs4926583	A	C	0.13	1	SBP	-0.89	0.18	6.93E-07	-0.01	0.06	8.32E-01	0.00	0.06	9.54E-01	NA	NA	NA	-0.06	0.04	1.82E-01
1	71055350	rs1396751049	A	G	0.0002	2	SBP	-21.55	4.16	2.29E-07	-4.43	29.80	8.82E-01	NA	NA	NA	NA	NA	NA	-21.22	4.12	2.67E-07
1	160906765	rs889484496	C	T	0.0002	3	HTN	3.16	0.56	1.26E-08	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
2	7653714*	rs1462610506	G	A	0.0001	4	SBP	-32.57	5.97	4.99E-08	-59.79	37.28	1.09E-01	NA	NA	NA	NA	NA	NA	-33.25	5.90	1.73E-08
2	141889431	rs990096779	A	C	0.0001	5	SBP	-27.26	5.54	8.73E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
2	214211381	rs574793711	A	T	0.0004	6	HTN	-1.96	0.38	2.01E-07	-1.82	8.26	8.26E-01	NA	NA	NA	0.25	0.48	6.07E-01	-1.13	0.30	1.48E-04
3	380679	rs932205533	C	T	0.0001	7	DBP	17.01	3.38	4.89E-07	61.07	22.42	6.44E-03	NA	NA	NA	NA	NA	NA	17.99	3.34	7.42E-08
3	60081049	rs2630149	C	A	0.37	8	SBP	-0.66	0.13	3.15E-07	-0.13	0.05	1.10E-02	-0.03	0.04	4.88E-01	NA	NA	NA	-0.10	0.03	1.36E-03
3	60090146	rs4679628	C	A	0.68	8	DBP	0.38	0.08	9.36E-07	0.04	0.03	1.78E-01	0.03	0.03	3.92E-01	0.11	0.16	4.84E-01	0.06	0.02	3.88E-03
3	62426785	rs189713255	C	T	0.004	9	HTN	-0.69	0.13	3.03E-08	0.51	0.71	4.72E-01	0.02	0.08	8.47E-01	0.06	0.17	7.22E-01	-0.15	0.06	1.42E-02
4	14112599	rs991813513	C	T	0.0001	10	SBP	-27.72	5.45	3.59E-07	-3.35	3.29	3.08E-01	NA	NA	NA	NA	NA	NA	-9.87	2.82	4.58E-04
4	32295377	rs563161224	C	T	0.0001	11	DBP	-16.47	3.25	4.01E-07	-0.14	1.16	9.05E-01	NA	NA	NA	NA	NA	NA	-2.00	1.10	6.85E-02
4	44148142 [†]	rs142082332	T	A	0.0011	12	DBP	-5.83	1.18	8.44E-07	1.67	7.34	8.20E-01	NA	NA	NA	NA	NA	NA	-5.64	1.17	1.40E-06
4	71695559	rs146985843	T	G	0.001	13	HTN	-1.01	0.20	4.74E-07	0.07	0.13	6.02E-01	NA	NA	NA	0.40	0.42	3.42E-01	-0.20	0.10	5.43E-02
4	135102674	rs763094728	G	A	0.000	14	SBP	16.86	3.40	7.25E-07	0.06	0.99	9.55E-01	NA	NA	NA	NA	NA	NA	1.37	0.95	1.50E-01
5	25019911	rs6874667	G	C	0.06	15	DBP	-0.83	0.17	7.98E-07	-0.57	0.28	4.53E-02	0.07	0.09	4.10E-01	0.24	0.21	2.53E-01	-0.11	0.07	1.30E-01
5	30143572	rs148958561	C	T	0.006	16	HTN	-0.50	0.10	8.19E-07	-0.50	0.81	5.36E-01	0.01	0.06	8.58E-01	0.13	0.12	2.96E-01	-0.09	0.05	6.54E-02
5	81811929	rs181227642	C	T	0.0001	17	SBP	31.09	6.11	3.61E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
7	9276283	rs892358621	C	T	0.0001	18	HTN	3.86	0.75	2.69E-07	-0.25	0.56	6.57E-01	NA	NA	NA	NA	NA	NA	1.21	0.45	6.70E-03
7	86352300 [‡]	rs1009138170	G	A	0.0003	19	SBP	19.70	3.92	5.06E-07	NA	NA	NA	-2.97	2.38	2.12E-01	NA	NA	NA	3.14	2.04	1.23E-01
7	86389044	rs370834859	C	A	0.0003	19	DBP	10.87	2.06	1.39E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
7	93871514	rs1166654114	T	C	0.0001	20	HTN	-3.63	0.72	4.32E-07	-31.22	22.47	1.65E-01	NA	NA	NA	NA	NA	NA	-3.66	0.72	3.47E-07
7	120623195	rs959927014	A	T	0.0001	21	DBP	14.12	2.86	7.96E-07	49.71	38.11	1.92E-01	NA	NA	NA	NA	NA	NA	14.32	2.85	5.17E-07
7	120907812	rs578061109	T	A	0.0001	21	HTN	3.77	0.74	3.17E-07	-0.20	0.26	4.45E-01	NA	NA	NA	NA	NA	NA	0.24	0.25	3.21E-01
7	142607166	rs56349639	G	A	0.07	22	DBP	0.67	0.14	8.31E-07	0.02	0.04	6.32E-01	NA	NA	NA	0.24	0.46	6.11E-01	0.09	0.04	4.17E-02
8	8373964	rs575133860	C	T	0.0001	23	SBP	-25.24	5.13	8.64E-07	2.47	2.64	3.49E-01	NA	NA	NA	NA	NA	NA	-3.34	2.35	1.55E-01
8	87524937	rs533133339	T	C	0.002	24	DBP	-3.87	0.77	4.55E-07	0.13	0.23	5.84E-01	0.16	0.47	7.39E-01	-2.97	3.42	3.86E-01	-0.15	0.20	4.60E-01
8	87524937	rs533133339	T	C	0.002	24	SBP	-6.48	1.32	9.18E-07	0.43	0.40	2.86E-01	0.45	0.63	4.69E-01	5.78	5.85	3.24E-01	0.03	0.33	9.34E-01
8	107340941	rs538833666	T	C	0.002	25	HTN	0.88	0.18	6.88E-07	0.03	0.05	5.13E-01	NA	NA	NA	-0.13	0.61	8.31E-01	0.08	0.04	6.39E-02
8	135907343	rs191358526	A	T	0.001	26	HTN	1.15	0.23	6.27E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

8	137338862	rs569370277	AT	A	0.007	27	DBP	2.22	0.45	8.00E-07	-0.25	3.46	9.41E-01	0.28	0.27	2.96E-01	-0.33	0.60	5.88E-01	0.64	0.21	2.81E-03
9	5567352	rs749617638	G	A	0.0001	28	DBP	16.70	3.34	5.83E-07	1.96	1.94	3.13E-01	NA	NA	NA	NA	NA	NA	5.68	1.68	7.19E-04
9	72031527	rs531405529	C	T	0.0007	29	HTN	-1.39	0.28	9.90E-07	0.06	0.09	5.36E-01	NA	NA	NA	0.98	1.14	3.90E-01	-0.07	0.09	3.92E-01
9	77018488	rs907073171	G	C	0.0009	30	DBP	6.07	1.22	6.51E-07	NA	NA	NA	NA	NA	NA	-2.17	1.77	2.20E-01	3.42	1.01	6.68E-04
9	80991323	rs373277444	T	C	0.0001	31	HTN	-3.23	0.65	7.56E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
9	101019274	rs1829803343	CT	C	0.0003	32	SBP	19.86	3.88	3.01E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
10	23308387	rs11013376	C	G	0.08	33	SBP	-1.39	0.26	6.98E-08	0.26	0.22	2.26E-01	-0.10	0.09	2.97E-01	NA	NA	NA	-0.18	0.08	3.06E-02
12	11216526	rs535260317	C	T	0.0001	34	SBP	29.17	5.25	2.74E-08	4.48	4.69	3.40E-01	NA	NA	NA	NA	NA	NA	15.43	3.50	1.01E-05
13	52274686	rs548695515	G	A	0.0005	35	DBP	8.28	1.62	3.23E-07	NA	NA	NA	-0.94	0.82	2.52E-01	NA	NA	NA	0.94	0.73	1.98E-01
13	98785378	rs575544397	C	T	0.0007	36	DBP	6.97	1.41	7.82E-07	NA	NA	NA	-0.70	0.95	4.61E-01	-3.21	1.82	7.78E-02	0.91	0.72	2.06E-01
14	58479635	rs760711883	TAG ^A	T	0.02	37	DBP	-1.14	0.22	4.03E-07	-0.01	0.06	8.85E-01	-0.04	0.09	6.30E-01	-0.04	0.66	9.56E-01	-0.08	0.05	1.23E-01
14	59185891	rs371613755	G	A	0.0001	38	SBP	-27.78	5.36	2.21E-07	-6.85	4.45	1.23E-01	NA	NA	NA	NA	NA	NA	-15.38	3.42	6.99E-06
14	87679583	rs150713962	T	A	0.0004	39	HTN	-1.93	0.36	8.09E-08	NA	NA	NA	NA	NA	NA	-0.22	0.46	6.27E-01	-1.29	0.28	5.95E-06
15	28094070	rs528063737	T	C	0.0009	40	SBP	9.90	2.02	8.94E-07	-0.86	0.67	2.03E-01	NA	NA	NA	NA	NA	NA	0.22	0.64	7.30E-01
15	35547150	rs565076535	CAAC	C	0.006	41	SBP	4.18	0.84	7.17E-07	-43.88	33.93	1.96E-01	0.32	0.42	4.38E-01	NA	NA	NA	1.08	0.37	3.98E-03
17	10736438	rs138965752	A	G	0.003	42	HTN	-0.79	0.15	8.19E-08	-0.01	0.07	8.46E-01	-0.06	0.37	8.80E-01	-1.42	1.16	2.23E-01	-0.15	0.06	1.37E-02
18	67293512	rs11877435	A	G	0.09	43	HTN	-0.13	0.03	2.34E-07	0.01	0.01	1.25E-01	0.00	0.01	7.61E-01	-0.02	0.08	8.35E-01	0.00	0.01	9.70E-01
18	69556248	rs568824589	C	A	0.0007	44	DBP	-7.17	1.44	5.96E-07	-19.60	22.65	3.87E-01	-1.40	1.46	3.38E-01	0.65	1.87	7.29E-01	-3.21	0.90	3.45E-04
20	14356827	rs752530366	C	A	0.0009	45	SBP	-10.36	1.99	1.88E-07	-2.77	1.33	3.74E-02	NA	NA	NA	NA	NA	NA	-5.11	1.10	3.74E-06
20	45220398	rs8183137	C	A	0.007	46	DBP	-2.37	0.47	6.07E-07	3.18	5.04	5.28E-01	0.00	0.64	9.94E-01	NA	NA	NA	-1.50	0.38	7.75E-05
20	56748383	rs375606398	G	A	0.001	47	HTN	1.13	0.21	1.24E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
21	38363851	rs187484456	C	T	0.0006	48	HTN	1.60	0.33	9.54E-07	-1.52	0.79	5.33E-02	NA	NA	NA	NA	NA	NA	1.14	0.30	1.56E-04
22	21877466	rs538476214	G	T	0.0002	49	DBP	-11.92	2.42	8.17E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Novel variants from previously reported loci

1	5806611	rs74049495	C	T	0.04	1	HTN	-0.20	0.04	9.12E-07	NA	NA	NA	-0.01	0.02	6.17E-01	0.08	0.05	1.16E-01	-0.04	0.02	3.58E-02
1	10429054	rs148861708	G	A	0.0002	2	SBP	-23.82	4.69	3.88E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
1	36845873	rs966779519	T	C	0.0003	3	HTN	-2.48	0.49	4.66E-07	-0.75	2.83	7.90E-01	NA	NA	NA	NA	NA	NA	-2.43	0.48	5.42E-07
1	112064726	rs550856031	G	C	0.0003	4	SBP	-20.48	3.94	2.00E-07	-32.57	75.69	6.67E-01	NA	NA	NA	NA	NA	NA	-20.51	3.93	1.84E-07
1	150513095	rs12031974	T	C	0.999	5	SBP	12.46	2.37	1.44E-07	NA	NA	NA	NA	NA	NA	4.68	3.31	1.58E-01	9.82	1.93	3.40E-07
1	171639054	rs41263718	C	T	0.12	6	DBP	-0.55	0.11	6.31E-07	-0.03	0.04	4.48E-01	-0.06	0.04	1.72E-01	0.21	0.22	3.47E-01	-0.08	0.03	8.72E-03
2	35187494 [§]	rs1572465247	GA	G	0.002	7	HTN	-1.01	0.20	2.61E-07	-22.00	10.91	4.38E-02	0.02	0.19	9.11E-01	-0.63	0.23	7.49E-03	-0.51	0.12	1.28E-05
2	71882926	rs889387219	G	A	0.0003	8	DBP	11.93	2.43	8.81E-07	-35.34	26.17	1.77E-01	NA	NA	NA	NA	NA	NA	11.53	2.42	1.84E-06
2	214824553	rs912831463	T	G	0.0003	9	DBP	-11.79	2.41	9.69E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
2	237894197	rs140263198	C	T	0.0006	10	HTN	1.56	0.32	8.75E-07	-1.17	2.29	6.08E-01	NA	NA	NA	NA	NA	NA	1.51	0.31	1.58E-06

2	241963149	rs567873302	T	C	0.0003	11	DBP	-11.33	2.23	3.67E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
3	123913288	rs186997509	C	G	0.001	12	HTN	-1.37	0.27	4.54E-07	0.05	0.28	8.47E-01	-0.09	0.25	7.22E-01	-0.22	0.35	5.28E-01	-0.42	0.14	3.03E-03
3	159745965	rs146308569	T	A	0.003	13	DBP	-3.49	0.68	3.01E-07	-3.76	5.12	4.63E-01	0.04	0.35	9.12E-01	NA	NA	NA	-0.70	0.31	2.29E-02
4	23985590	rs536671665	T	C	0.0004	14	HTN	1.94	0.39	6.78E-07	0.14	0.37	7.11E-01	0.14	0.38	7.04E-01	NA	NA	NA	0.71	0.22	1.27E-03
4	76564270	rs115879419	G	A	0.0004	15	DBP	-9.19	1.87	8.38E-07	109.67	60.75	7.10E-02	-0.21	0.91	8.16E-01	-0.36	2.39	8.82E-01	-1.75	0.77	2.34E-02
5	4261835	rs116759517	G	A	0.004	16	HTN	-0.59	0.12	9.22E-07	0.35	0.44	4.22E-01	0.02	0.07	7.31E-01	0.05	0.15	7.35E-01	-0.10	0.06	8.17E-02
5	159633157	rs1044263121	T	C	0.0002	17	DBP	15.96	3.04	1.58E-07	-6.90	3.65	5.83E-02	NA	NA	NA	NA	NA	NA	6.57	2.34	4.94E-03
5	172024835	rs779225390	A	G	0.0001	18	DBP	-14.72	2.86	2.67E-07	0.01	0.69	9.89E-01	NA	NA	NA	NA	NA	NA	-0.81	0.67	2.31E-01
6	33005486	rs3128936	A	T	0.60	19	HTN	0.08	0.02	6.39E-07	0.00	0.01	7.46E-01	0.00	0.01	7.29E-01	0.00	0.03	9.76E-01	0.01	0.00	1.74E-01
6	43409521	rs1214755	G	A	0.90	20	HTN	-0.13	0.03	1.51E-07	-0.02	0.01	6.73E-03	-0.02	0.01	1.16E-01	-0.09	0.06	1.24E-01	-0.03	0.01	7.04E-06
6	95514748	rs186696749	G	A	0.0003	21	DBP	-10.52	2.10	5.79E-07	4.16	34.41	9.04E-01	NA	NA	NA	NA	NA	NA	-10.46	2.10	6.31E-07
6	169255785	rs149346837	T	C	0.002	22	HTN	-0.94	0.18	2.54E-07	-1.29	1.54	4.01E-01	NA	NA	NA	0.09	0.28	7.36E-01	-0.64	0.15	2.75E-05
7	18813701	rs564948273	C	T	0.0003	23	HTN	-2.36	0.46	2.81E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
7	27247464	rs186177734	C	G	0.003	24	HTN	0.70	0.14	4.90E-07	-1.20	0.79	1.26E-01	NA	NA	NA	-0.11	0.17	5.27E-01	0.35	0.11	1.04E-03
7	73727423	rs530529907	C	A	0.0005	25	DBP	-8.76	1.73	4.04E-07	-8.53	6.73	2.05E-01	NA	NA	NA	NA	NA	NA	-8.74	1.67	1.76E-07
7	76931441	rs188780722	C	T	0.0008	26	HTN	-1.35	0.27	5.24E-07	-11.30	16.00	4.80E-01	NA	NA	NA	-0.06	0.35	8.71E-01	-0.88	0.21	3.96E-05
7	106438072	rs1013536627	G	A	0.0002	27	DBP	12.43	2.50	6.52E-07	0.32	0.62	6.12E-01	NA	NA	NA	NA	NA	NA	1.02	0.60	9.01E-02
7	151027237	rs6953514	T	C	0.09	28	SBP	1.15	0.23	4.00E-07	0.14	0.10	1.64E-01	0.15	0.07	3.65E-02	NA	NA	NA	0.21	0.06	2.17E-04
8	52941509	rs565101557	A	G	0.0005	29	DBP	-8.40	1.71	8.83E-07	NA	NA	NA	-0.79	1.18	5.00E-01	1.39	1.87	4.57E-01	-2.26	0.86	8.67E-03
8	140001243	rs578246850	G	T	0.001	30	SBP	9.39	1.86	4.53E-07	0.66	0.62	2.86E-01	NA	NA	NA	-4.37	8.26	5.97E-01	1.51	0.59	1.02E-02
9	134415900	rs188233102	G	A	0.0008	31	SBP	-10.58	2.16	9.57E-07	0.82	0.80	3.04E-01	NA	NA	NA	NA	NA	NA	-0.55	0.75	4.62E-01
10	21363678	rs115722966	G	C	0.01	32	DBP	1.72	0.35	8.08E-07	1.07	0.53	4.16E-02	0.10	0.20	6.18E-01	0.94	0.48	4.92E-02	0.61	0.16	1.09E-04
10	28836801	rs187784229	C	T	0.005	33	DBP	2.40	0.49	8.95E-07	-0.11	0.16	4.85E-01	NA	NA	NA	-3.37	1.84	6.69E-02	0.11	0.15	4.63E-01
10	73511521	rs529232710	G	T	0.0005	34	HTN	1.96	0.39	6.87E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
10	93038333	rs541185854	T	TA	0.007	35	DBP	2.28	0.43	1.01E-07	-0.06	0.18	7.13E-01	0.81	1.92	6.73E-01	-0.06	1.75	9.74E-01	0.27	0.16	9.05E-02
11	30758017	rs759526273	G	A	0.0005	36	SBP	-12.80	2.56	5.95E-07	-9.19	6.62	1.65E-01	NA	NA	NA	NA	NA	NA	-12.33	2.39	2.51E-07
11	63656287	rs181639791	T	G	0.0003	37	SBP	18.27	3.48	1.49E-07	-0.09	2.80	9.73E-01	-2.25	2.09	2.80E-01	NA	NA	NA	2.23	1.51	1.39E-01
12	12607733	rs118057078	C	A	0.002	38	HTN	-0.94	0.18	1.63E-07	2.63	3.98	5.09E-01	NA	NA	NA	NA	NA	NA	-0.93	0.18	1.97E-07
12	14176419	rs557148731	G	A	0.002	39	HTN	-0.90	0.18	5.13E-07	0.15	0.54	7.75E-01	0.21	0.11	5.47E-02	-0.22	0.21	2.97E-01	-0.11	0.08	2.08E-01
12	19446565	rs574863317	T	C	0.0002	40	SBP	22.24	4.45	5.61E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
12	53249550	rs145405677	G	A	0.0009	41	DBP	-5.83	1.16	5.12E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
12	55408999	rs958667188	T	C	0.0002	42	SBP	-18.57	3.79	9.83E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
12	89929715	rs796212487	G	A	0.02	43	SBP	-1.98	0.40	7.15E-07	NA	NA	NA	NA	NA	NA	-1.07	1.24	3.91E-01	-1.89	0.38	6.28E-07
13	29924833	rs182650574	G	A	0.0001	44	DBP	-15.34	3.09	6.65E-07	9.50	10.03	3.44E-01	-0.24	1.53	8.77E-01	NA	NA	NA	-2.98	1.36	2.82E-02

13	96399768	rs9516682	A	G	0.38	45	SBP	0.62	0.13	8.33E-07	0.12	0.05	1.49E-02	0.00	0.04	9.81E-01	-0.08	0.29	7.88E-01	0.07	0.03	1.08E-02
13	96399768	rs9516682	A	G	0.38	45	HTN	0.08	0.02	6.29E-07	0.02	0.01	4.13E-03	0.00	0.01	6.16E-01	0.06	0.03	7.13E-02	0.01	0.00	6.71E-04
13	111403978	rs1056873364	G	C	0.0006	46	SBP	-12.08	2.41	5.51E-07	-1.34	1.73	4.38E-01	NA	NA	NA	NA	NA	NA	-4.99	1.41	3.89E-04
14	22811645	rs141077504	T	C	0.005	47	SBP	-5.19	0.97	7.85E-08	-4.87	6.86	4.78E-01	0.05	0.36	8.98E-01	0.06	1.12	9.57E-01	-0.54	0.32	9.34E-02
14	23304280	rs927479517	A	G	0.0003	47	HTN	-2.03	0.40	4.42E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
14	59509859	rs374539360	C	T	0.0001	48	SBP	-29.27	5.60	1.74E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
14	89608947	rs117378667	C	A	0.01	49	HTN	-0.33	0.06	3.46E-07	0.01	0.02	5.60E-01	-0.04	0.04	3.38E-01	0.21	0.23	3.58E-01	-0.02	0.02	2.04E-01
15	26628999	rs990895163	C	T	0.0001	50	SBP	-26.84	5.47	9.46E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
15	74439850	rs1019875382	C	T	0.0001	51	DBP	14.92	2.85	1.68E-07	-1.07	0.99	2.75E-01	NA	NA	NA	NA	NA	NA	0.63	0.93	4.98E-01
15	96338035	rs34353956	C	AAC	0.25	52	DBP	-0.46	0.09	1.30E-07	NA	NA	NA	-0.04	0.04	3.18E-01	-0.07	0.31	8.19E-01	-0.12	0.04	1.17E-03
16	10510935	rs188073931	C	T	0.0002	53	SBP	26.76	5.34	5.31E-07	NA	NA	NA	-4.13	1.48	5.43E-03	NA	NA	NA	-1.91	1.43	1.82E-01
16	49743010	rs375915281	T	G	0.0003	54	HTN	2.95	0.55	9.27E-08	-2.30	1.96	2.40E-01	NA	NA	NA	NA	NA	NA	2.56	0.53	1.42E-06
16	59640176	rs999280636	G	A	0.0001	55	HTN	-4.06	0.71	1.02E-08	-0.57	0.94	5.44E-01	NA	NA	NA	NA	NA	NA	-2.79	0.57	7.82E-07
17	78431329	rs376726828	G	A	0.0003	56	SBP	-20.28	4.05	5.36E-07	7.01	3.86	6.92E-02	NA	NA	NA	NA	NA	NA	-5.99	2.79	3.19E-02
17	81131161	rs144434820	C	T	0.003	57	DBP	-3.32	0.68	9.04E-07	0.13	0.22	5.54E-01	NA	NA	NA	4.76	3.26	1.44E-01	-0.17	0.20	4.05E-01
19	7325055	rs36136513	A	G	0.45	58	DBP	-0.36	0.07	4.18E-07	-0.28	0.03	3.24E-22	NA	NA	NA	-0.57	0.17	1.11E-03	-0.30	0.03	2.32E-29
19	10221104	rs563785784	C	T	0.0005	59	SBP	-13.30	2.70	8.73E-07	0.80	1.10	4.69E-01	NA	NA	NA	NA	NA	NA	-1.20	1.02	2.37E-01
19	17071566	rs1026811864	C	T	0.0002	60	DBP	13.95	2.81	6.57E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
19	33403836	rs932829441	T	TG	0.0001	61	DBP	18.17	3.63	5.70E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
19	33460006	rs963318995	C	T	0.0001	61	HTN	3.60	0.73	7.73E-07	-2.06	2.44	3.99E-01	NA	NA	NA	NA	NA	NA	3.13	0.70	6.93E-06
19	40205764	rs528766533	C	T	0.0006	62	SBP	-13.02	2.66	9.52E-07	NA	NA	NA	0.51	1.01	6.15E-01	NA	NA	NA	-1.21	0.95	2.02E-01
20	10405335	rs372944937	A	C	0.0001	63	DBP	-16.17	3.07	1.40E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
21	36123658	rs192304372	G	A	0.0005	64	HTN	-1.78	0.35	3.81E-07	NA	NA	NA	NA	NA	NA	0.06	0.51	9.02E-01	-1.19	0.29	3.86E-05

Previously reported variants

1	10736490	rs17035646	G	A	0.32	1	SBP	0.88	0.14	1.02E-10	0.57	0.05	5.22E-29	0.39	0.04	3.33E-23	0.73	0.34	2.97E-02	0.48	0.03	9.99E-57
1	10736809	rs880315	T	C	0.32	1	HTN	0.10	0.02	9.33E-09	0.05	0.01	3.78E-16	0.06	0.01	4.61E-15	0.06	0.04	1.30E-01	0.05	0.00	8.75E-36
1	10736809	rs880315	T	C	0.32	1	DBP	0.40	0.08	3.48E-07	NA	NA	NA	0.27	0.03	4.76E-20	0.28	0.19	1.44E-01	0.28	0.03	1.18E-25
1	11823674	rs12567136	C	T	0.13	2	DBP	-0.54	0.10	2.26E-07	-0.64	0.04	1.36E-68	-0.36	0.04	6.88E-21	-0.37	0.24	1.20E-01	-0.51	0.03	5.89E-88
1	11845794	rs61764044	A	G	0.04	2	SBP	-1.65	0.31	1.44E-07	-1.77	0.11	1.48E-63	-0.98	0.09	1.42E-27	-1.33	0.74	7.26E-02	-1.33	0.07	1.32E-88
2	26689211	rs1275986	C	A	0.49	3	DBP	-0.41	0.08	5.43E-08	-0.33	0.03	5.97E-33	-0.27	0.03	1.35E-19	-0.16	0.18	3.73E-01	-0.31	0.02	2.72E-56
2	26696221	rs1275982	C	T	0.47	3	SBP	-0.79	0.13	1.92E-09	-0.66	0.05	1.54E-40	-0.49	0.04	4.79E-35	-0.39	0.32	2.28E-01	-0.57	0.03	1.40E-79
2	26700227	rs1275978	C	T	0.47	3	HTN	-0.10	0.02	9.46E-10	-0.05	0.01	1.41E-21	-0.06	0.01	1.60E-15	-0.07	0.04	4.94E-02	-0.06	0.00	7.40E-43
3	27521497	rs2643826	C	T	0.55	4	SBP	0.74	0.14	4.53E-08	0.49	0.05	3.20E-24	0.37	0.04	2.17E-18	0.00	0.40	9.94E-01	0.44	0.03	2.38E-45
3	27521497	rs2643826	C	T	0.55	4	DBP	0.41	0.08	1.82E-07	0.14	0.03	2.00E-07	0.19	0.03	1.66E-09	-0.21	0.23	3.62E-01	0.18	0.02	1.07E-18

3	41996388	rs77014899	T	C	0.15	5	DBP	0.54	0.10	6.22E-08	0.45	0.04	6.59E-30	0.16	0.04	2.28E-05	-0.24	0.23	2.95E-01	0.31	0.03	4.02E-32
3	169405049	rs17485157	G	A	0.17	6	DBP	-0.53	0.09	2.00E-08	-0.30	0.03	2.50E-20	-0.15	0.03	1.97E-05	-0.70	0.29	1.70E-02	-0.25	0.02	1.04E-27
3	169447385	rs1918973	A	G	0.58	6	SBP	-0.72	0.13	1.79E-08	-0.46	0.05	2.47E-21	-0.14	0.04	1.06E-04	-0.19	0.28	5.00E-01	-0.28	0.03	5.61E-23
4	80259918	rs10857147	A	T	0.25	7	HTN	0.10	0.02	3.32E-08	0.10	0.01	6.96E-66	0.12	0.01	4.99E-51	0.02	0.05	6.22E-01	0.11	0.00	3.80E-121
4	80263187	rs16998073	A	T	0.25	7	DBP	0.55	0.08	7.83E-11	0.56	0.03	2.17E-78	0.38	0.03	4.10E-34	-0.03	0.23	8.83E-01	0.47	0.02	5.51E-115
4	80263187	rs16998073	A	T	0.25	7	SBP	0.84	0.14	4.95E-09	1.06	0.05	1.02E-90	0.49	0.04	3.29E-32	-0.58	0.40	1.44E-01	0.71	0.03	5.34E-111
4	102267552	rs13107325	C	T	0.05	8	DBP	-0.99	0.16	1.06E-09	-0.80	0.05	1.27E-53	-0.47	0.06	1.32E-17	-0.66	0.52	2.06E-01	-0.66	0.04	6.24E-73
5	158560240	rs2963481	C	T	0.29	9	SBP	0.68	0.14	5.36E-07	0.42	0.05	1.16E-15	0.27	0.04	3.79E-11	NA	NA	NA	0.34	0.03	3.35E-28
6	43388113	rs2396004	A	G	0.45	10	HTN	-0.09	0.02	1.26E-08	-0.03	0.01	1.86E-07	-0.04	0.01	1.07E-08	-0.04	0.04	3.85E-01	-0.04	0.00	8.00E-19
6	43388113	rs2396004	A	G	0.45	10	SBP	-0.96	0.13	5.46E-13	-0.30	0.05	9.03E-10	-0.33	0.04	1.32E-15	-0.69	0.36	5.58E-02	-0.35	0.03	6.93E-31
6	126805001	rs13196855	T	C	0.36	11	DBP	0.38	0.08	7.32E-07	0.30	0.03	2.92E-28	0.18	0.03	8.82E-10	0.21	0.20	2.99E-01	0.25	0.02	3.38E-39
6	165767459	rs6932812	C	G	0.16	12	DBP	-0.67	0.11	3.86E-10	-0.37	0.05	7.96E-12	-0.21	0.05	2.97E-06	-0.01	0.17	9.77E-01	-0.30	0.03	1.00E-20
6	165767459	rs6932812	C	G	0.16	12	SBP	-0.95	0.19	2.75E-07	-0.61	0.10	3.37E-10	-0.17	0.06	3.65E-03	-0.32	0.30	2.84E-01	-0.34	0.05	2.27E-12
8	11466488	rs2618484	C	A	0.23	13	SBP	-0.76	0.15	3.08E-07	-0.28	0.05	5.17E-08	-0.12	0.04	6.46E-03	NA	NA	NA	-0.21	0.03	4.77E-11
10	18431916	rs11014204	C	T	0.20	14	SBP	-0.77	0.15	5.05E-07	-0.78	0.05	2.38E-47	-0.35	0.04	1.13E-14	0.17	0.42	6.90E-01	-0.53	0.03	1.82E-56
10	18448045	rs11014267	G	A	0.25	14	HTN	-0.10	0.02	5.20E-08	-0.07	0.01	1.71E-29	-0.05	0.01	2.27E-10	-0.04	0.04	3.91E-01	-0.06	0.00	2.19E-43
11	16327586	rs7127937	C	A	0.17	15	HTN	0.10	0.02	5.97E-07	0.05	0.01	1.50E-13	0.04	0.01	1.72E-04	0.08	0.06	1.54E-01	0.05	0.01	1.18E-20
11	16331652	rs34610248	TA	T	0.16	15	DBP	0.68	0.10	3.20E-12	0.28	0.03	5.67E-16	0.22	0.04	5.78E-09	0.77	0.28	6.00E-03	0.28	0.02	8.75E-31
11	16331652	rs34610248	TA	T	0.16	15	SBP	1.08	0.17	1.12E-10	0.47	0.06	1.98E-14	0.26	0.05	1.90E-07	1.01	0.48	3.65E-02	0.39	0.04	1.16E-24
11	61510774	rs751984	T	C	0.16	16	DBP	-0.52	0.10	3.19E-07	-0.46	0.04	2.83E-27	-0.19	0.04	1.71E-05	-0.50	0.21	1.67E-02	-0.34	0.03	7.73E-33
11	65799248	rs557675	T	G	0.43	17	SBP	-0.63	0.13	5.98E-07	-0.30	0.05	5.50E-10	-0.18	0.04	2.47E-06	NA	NA	NA	-0.25	0.03	1.81E-17
12	20025130	rs4762917	C	T	0.69	18	SBP	0.81	0.14	1.10E-08	0.23	0.06	5.23E-05	0.11	0.04	1.07E-02	0.23	0.28	4.20E-01	0.19	0.03	1.11E-08
12	20043911	rs12829468	A	C	0.59	18	DBP	0.47	0.08	1.65E-09	0.36	0.03	9.55E-33	0.19	0.03	1.02E-10	0.17	0.17	3.10E-01	0.29	0.02	2.18E-45
12	50149639	rs10783336	T	C	0.36	19	SBP	-0.67	0.13	5.81E-07	-0.41	0.05	3.05E-14	-0.15	0.04	1.91E-04	-0.44	0.28	1.19E-01	-0.27	0.03	9.93E-18
12	50217528	rs10747572	T	A	0.30	19	HTN	-0.11	0.02	1.48E-10	-0.03	0.01	4.93E-07	-0.02	0.01	8.67E-03	-0.03	0.03	4.17E-01	-0.03	0.00	8.97E-13
12	89632746	rs11105354	A	G	0.16	20	DBP	-0.60	0.10	1.29E-09	-0.44	0.04	7.26E-34	-0.28	0.04	9.98E-14	0.06	0.25	8.13E-01	-0.37	0.03	3.66E-50
12	89632746	rs11105354	A	G	0.16	20	SBP	-1.11	0.17	4.12E-11	-1.06	0.06	9.13E-62	-0.53	0.05	1.31E-25	-0.70	0.43	1.03E-01	-0.75	0.04	3.04E-85
12	89696964	rs11105378	C	T	0.16	20	HTN	-0.11	0.02	4.35E-07	-0.09	0.01	3.82E-32	-0.08	0.01	2.15E-17	-0.08	0.05	1.20E-01	-0.09	0.01	8.94E-54
12	111466567	rs4766578	T	A	0.67	21	DBP	-0.43	0.08	2.46E-07	-0.59	0.03	5.58E-105	-0.23	0.03	7.88E-15	0.07	0.25	7.76E-01	-0.43	0.02	2.62E-106
12	114914926	rs2384550	G	A	0.32	22	DBP	-0.44	0.08	1.04E-08	-0.14	0.03	3.59E-07	-0.06	0.03	3.28E-02	0.01	0.16	9.57E-01	-0.12	0.02	2.11E-10
12	114914926	rs2384550	G	A	0.32	22	SBP	-0.68	0.13	2.20E-07	-0.31	0.05	8.47E-10	-0.13	0.04	8.92E-04	-0.25	0.28	3.70E-01	-0.22	0.03	1.17E-13
12	115118002	rs1579381	C	G	0.17	22	HTN	-0.11	0.02	5.19E-07	-0.04	0.01	7.98E-06	-0.05	0.01	4.75E-06	-0.08	0.04	2.33E-02	-0.05	0.01	3.77E-15
13	29563691	rs7338758	T	C	0.54	23	DBP	-0.43	0.08	2.54E-07	-0.19	0.03	1.30E-09	-0.13	0.03	1.06E-04	-0.25	0.20	2.08E-01	-0.19	0.02	1.10E-16
17	1674897	rs8073857	A	G	0.30	24	DBP	0.43	0.08	2.84E-07	0.07	0.03	3.51E-02	0.11	0.03	1.10E-03	0.27	0.16	1.02E-01	0.12	0.02	1.68E-07

17	58775664 [¶]	rs12950119	C	T	0.24	25	SBP	0.81	0.15	5.71E-08	0.18	0.05	4.61E-04	0.23	0.04	1.32E-07	NA	NA	NA	0.24	0.03	2.46E-13
22	19999679	rs7285377	G	T	0.21	26	SBP	0.78	0.15	2.68E-07	0.27	0.05	4.20E-07	0.17	0.05	1.22E-04	NA	NA	NA	0.24	0.03	6.49E-13

AAF, alternative allele frequency; Alt, alternative allele; Chr, chromosome; DBP, diastolic blood pressure (BP); HTN, hypertension; MVP, Million Veteran Program; NA, not available; Ref, reference allele; SBP, systolic BP; TOPMed, Trans-Omics for Precision Medicine; UKBB, UK Biobank.

*An SNV at 2:7701061 was used as a proxy for 2:7653714 in UK Biobank ($r^2=0.87$); †An SNV at 4:44156061 was used as a proxy for 4:44148142 in UK Biobank ($r^2=1.0$). ‡An SNV at 7:86389044 was used as a proxy for 7:86352300 in MVP ($r^2=0.83$); §An SNV at 2:35260112 was used as a proxy for 2:35187494 in MVP ($r^2=0.98$). ¶An SNV at 4:76567636 was used as a proxy for 4:76564270 in UK Biobank ($r^2=1.0$); ¶An SNV at 17:58783892 was used as a proxy for 17:58775664 in UK Biobank ($r^2=0.99$)

Table S3. Novel lead variants achieving $P < 1E-06$ in single marker analyses of participants of African ancestry.

Chr	Position (B38)	rsID	Ref	Alt	AAF	Locus (1MB)	Pheno	TOPMed			MVP			REGARDS			Meta-Analysis			Identified in Multi-ancestry Analyses
								Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P	
<i>Novel Loci</i>																				
2	214211381	rs574793711	A	T	0.002	1	HTN	-2.16	0.40	5.65E-08	NA	NA	NA	0.25	0.48	6.07E-01	-1.19	0.31	1.09E-04	Y
2	223786791	rs111623545	A	G	0.30	2	HTN	-0.16	0.03	8.70E-07	NA	NA	NA	0.02	0.04	6.09E-01	-0.09	0.03	6.87E-04	N
3	511367	rs751672976	C	T	0.0004	3	DBP	18.28	3.60	3.74E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	N
3	62420681	rs144748865	T	C	0.02	4	HTN	-0.61	0.11	6.15E-08	0.02	0.06	7.61E-01	0.08	0.13	5.30E-01	-0.10	0.05	5.03E-02	Y
3	129950737	rs1033675304	C	T	0.0007	5	HTN	-2.66	0.54	9.80E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	N
3	175462935	rs184866027	T	G	0.0006	6	DBP	-15.51	3.07	4.40E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	N
4	30091023	rs80299918	A	C	0.002	7	DBP	7.40	1.50	7.41E-07	-0.41	2.13	8.49E-01	3.79	2.08	6.88E-02	4.56	1.06	1.54E-05	N
4	125543541	rs530987100	C	G	0.001	8	HTN	-2.59	0.53	8.99E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	N
4	160911462	rs4525929	T	G	0.43	9	HTN	0.15	0.03	4.12E-07	0.03	0.02	1.50E-01	-0.10	0.04	3.21E-03	0.03	0.01	2.13E-02	N
5	30143572	rs148958561	C	T	0.02	10	HTN	-0.54	0.11	8.57E-07	0.01	0.06	8.58E-01	0.13	0.12	2.96E-01	-0.08	0.05	9.69E-02	Y
6	23864406	rs187127066	G	A	0.0007	11	SBP	-23.58	4.74	6.60E-07	-0.64	2.59	8.06E-01	NA	NA	NA	-5.91	2.27	9.32E-03	N
7	86369352	rs891244454	G	C	0.0009	12	DBP	12.27	2.41	3.65E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	Y
7	103975616	rs192963752	G	A	0.003	13	HTN	-1.50	0.30	6.80E-07	NA	NA	NA	0.52	0.44	2.37E-01	-0.85	0.25	6.42E-04	N
7	118992150	rs191868039	A	G	0.002	14	DBP	-9.75	1.82	8.79E-08	NA	NA	NA	1.98	2.51	4.29E-01	-5.70	1.47	1.12E-04	N
7	142172215	rs183009842	C	T	0.0009	15	DBP	-12.38	2.42	3.23E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	Y
8	137338862	rs569370277	AT	A	0.02	16	DBP	2.55	0.51	6.93E-07	0.31	0.27	2.58E-01	-0.33	0.60	5.88E-01	0.65	0.22	3.83E-03	Y
10	8686705	rs144076023	C	T	0.001	17	HTN	-2.14	0.43	6.37E-07	NA	NA	NA	-0.36	0.50	4.77E-01	-1.38	0.33	2.20E-05	N
11	127059794	rs192393392	G	A	0.0006	18	HTN	-3.51	0.68	2.07E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	N
11	133891929	rs148370253	C	T	0.003	19	DBP	6.87	1.37	5.37E-07	NA	NA	NA	-0.73	1.73	6.73E-01	3.94	1.07	2.44E-04	N
12	70961942	rs56338775	C	T	0.19	20	HTN	-0.20	0.04	2.54E-07	-0.02	0.02	3.95E-01	-0.03	0.04	4.37E-01	-0.05	0.02	1.16E-03	N
12	75745873	rs12427271	G	A	0.14	21	HTN	0.22	0.04	6.11E-07	-0.02	0.02	3.27E-01	0.00	0.05	9.30E-01	0.03	0.02	1.52E-01	N
13	52274686*	rs548695515	G	A	0.002	22	DBP	8.52	1.64	2.07E-07	-0.94	0.82	2.52E-01	1.79	1.92	3.52E-01	1.06	0.69	1.22E-01	Y
14	87679583	rs150713962	T	A	0.002	23	HTN	-1.83	0.37	7.23E-07	NA	NA	NA	-0.22	0.46	6.27E-01	-1.20	0.29	3.00E-05	N
15	97980174	rs28562538	C	T	0.35	24	SBP	1.30	0.26	8.80E-07	0.05	0.10	6.33E-01	-0.10	0.31	7.58E-01	0.18	0.09	4.66E-02	N
17	15224226	rs116416972	G	C	0.07	25	DBP	1.47	0.30	9.08E-07	0.37	0.14	6.63E-03	-0.41	0.35	2.46E-01	0.45	0.12	1.11E-04	N
17	51779485	rs1526189	C	A	0.18	26	DBP	-1.06	0.20	8.96E-08	NA	NA	NA	-0.02	0.24	9.42E-01	-0.63	0.15	3.51E-05	N
20	22968267	rs148725323	G	A	0.0004	27	HTN	-4.10	0.82	5.34E-07	0.38	0.38	3.26E-01	-0.06	0.52	9.12E-01	-0.31	0.29	2.76E-01	N
<i>Novel Variants from Previously Reported Loci</i>																				
1	36845873	rs966779519	T	C	0.001	1	HTN	-2.46	0.50	8.05E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	Y

1	150513095	rs12031974	T	C	0.997	2	SBP	12.59	2.39	1.39E-07	NA	NA	NA	4.68	3.31	1.58E-01	9.88	1.94	3.46E-07	Y
1	201168587	rs12096352	C	T	0.03	3	SBP	3.90	0.76	2.44E-07	0.25	0.28	3.73E-01	0.15	0.89	8.67E-01	0.65	0.25	1.02E-02	N
2	37301487	rs927593440	G	C	0.0004	4	HTN	-3.66	0.74	6.80E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	N
2	241963149	rs567873302	T	C	0.001	5	DBP	-11.26	2.27	7.32E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	N
5	22756610	rs539642938	A	G	0.002	6	SBP	-13.04	2.63	7.36E-07	NA	NA	NA	4.42	3.05	1.48E-01	-5.60	1.99	5.01E-03	N
5	108627449	rs943034543	TA	T	0.85	7	DBP	1.03	0.21	8.08E-07	NA	NA	NA	-0.09	0.24	7.26E-01	0.55	0.16	4.47E-04	N
6	7715354	rs1575291	A	G	0.86	8	SBP	1.89	0.37	3.43E-07	0.39	0.13	3.72E-03	0.49	0.42	2.47E-01	0.56	0.12	3.93E-06	N
6	95514748	rs186696749	G	A	0.001	9	DBP	-10.53	2.11	5.87E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	Y
6	169255785	rs149346837	T	C	0.006	10	HTN	-1.00	0.19	1.54E-07	NA	NA	NA	0.09	0.28	7.36E-01	-0.65	0.16	3.39E-05	Y
7	18813701	rs564948273	C	T	0.001	11	HTN	-2.33	0.46	4.77E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	Y
9	3353211	rs542476106	G	T	0.0004	12	HTN	-4.34	0.87	6.08E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	N
10	125494847	rs746384383	C	T	0.0004	13	HTN	-4.02	0.82	9.92E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	N
11	64639661	rs528476366	G	A	0.0005	14	SBP	28.99	5.73	4.29E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	Y
12	14176419	rs557148731	G	A	0.006	15	HTN	-0.95	0.19	3.27E-07	0.21	0.11	5.47E-02	-0.22	0.21	2.97E-01	-0.11	0.09	1.97E-01	Y
12	41910349	rs11181238	A	G	0.52	16	DBP	0.74	0.15	5.87E-07	0.14	0.07	4.07E-02	0.16	0.17	3.64E-01	0.24	0.06	5.06E-05	Y
13	73178219	rs9543252	T	C	0.24	17	SBP	1.45	0.29	8.58E-07	-0.05	0.10	6.13E-01	-0.24	0.35	4.94E-01	0.09	0.10	3.46E-01	N
14	22811645	rs141077504	T	C	0.02	18	SBP	-5.16	1.02	4.44E-07	-0.03	0.37	9.34E-01	0.06	1.12	9.57E-01	-0.55	0.33	9.22E-02	Y
14	23304280	rs927479517	A	G	0.001	18	HTN	-2.39	0.46	2.37E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	Y
14	100851073	rs112924824	G	A	0.0009	19	HTN	-2.77	0.57	9.88E-07	NA	NA	NA	0.81	0.65	2.10E-01	-1.22	0.43	4.10E-03	N
16	68384745	rs7200932	C	G	0.30	20	SBP	-1.44	0.27	1.45E-07	-0.14	0.10	1.84E-01	-0.47	0.33	1.49E-01	-0.31	0.09	7.49E-04	Y
16	83121771	rs61113216	A	T	0.14	21	HTN	-0.21	0.04	9.15E-07	NA	NA	NA	-0.09	0.05	6.43E-02	-0.16	0.03	8.95E-07	N
16	86509951	rs117935802	G	A	0.01	22	DBP	-3.17	0.62	3.39E-07	0.34	0.28	2.36E-01	0.21	0.73	7.69E-01	-0.22	0.24	3.74E-01	N
17	57156920	rs12936510	A	G	0.92	23	DBP	1.42	0.29	8.26E-07	0.40	0.13	2.18E-03	0.14	0.33	6.87E-01	0.53	0.11	2.78E-06	N
18	46016131	rs145337022	A	G	0.007	24	DBP	-4.30	0.88	9.70E-07	NA	NA	NA	0.49	1.06	6.43E-01	-2.35	0.68	5.11E-04	N
19	17071566	rs1026811864	C	T	0.0007	25	DBP	13.96	2.81	6.82E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	N
19	33403836	rs932829441	T	TG	0.0004	26	DBP	18.21	3.64	5.75E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	Y
19	39043568	rs190692784	C	T	0.0005	27	DBP	16.24	3.12	1.96E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	N
20	7306301	rs6085986	C	A	0.62	28	HTN	-0.16	0.03	5.20E-07	-0.01	0.02	4.33E-01	0.01	0.04	8.84E-01	-0.04	0.01	3.61E-03	N
20	8474254	rs1035041462	C	G	0.0009	29	DBP	-11.84	2.40	7.75E-07	NA	NA	NA	0.90	2.24	6.87E-01	-5.04	1.64	2.08E-03	N
20	10405335	rs372944937	A	C	0.0004	30	DBP	-17.75	3.47	3.11E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	Y
20	49368981	rs542440171	C	T	0.0005	31	DBP	16.44	3.33	7.81E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	N
21	36123658	rs192304372	G	A	0.002	32	HTN	-1.95	0.37	1.87E-07	NA	NA	NA	0.06	0.51	9.02E-01	-1.25	0.30	3.57E-05	Y

AAF, alternative allele frequency; Alt, alternative allele; Chr, chromosome; DBP, diastolic blood pressure (BP); HTN, hypertension; MVP, Million Veteran Program; NA, not available; Pheno, phenotype; Ref, reference allele; SBP, systolic BP; TOPMed, Trans-Omics for Precision Medicine; UKBB, UK Biobank.

*An SNV at 13:52412945 was used as a proxy for 13:52274686 in REGARDS ($r^2=0.89$).

Table S4. Novel variants achieving $P < 1E-06$ in single marker analyses of participants of Asian ancestry.

Chr	Position (B38)	rsID	Ref	Alt	AAF	Locus (1MB)	Pheno	TOPMed			MVP			Meta-analysis			Identified in Multi-ancestry Analyses
								Beta	SE	P	Beta	SE	P	Beta	SE	P	
<i>Novel Loci</i>																	
1	20034935	rs78952711	G	A	0.002	1	DBP	15.06	3.00	4.94E-07	NA	NA	NA	NA	NA	NA	N
1	71055350	rs1396751049	A	G	0.003	2	SBP	-21.96	4.25	2.43E-07	NA	NA	NA	NA	NA	NA	Y
2	7653714	rs1462610506	G	A	0.002	3	SBP	-32.29	5.92	4.91E-08	NA	NA	NA	NA	NA	NA	Y
5	27033039	rs183826057	T	C	0.004	4	DBP	10.90	2.08	1.66E-07	NA	NA	NA	NA	NA	NA	N
5	105976684	rs1465366879	G	C	0.002	5	DBP	13.65	2.77	8.34E-07	NA	NA	NA	NA	NA	NA	N
6	77907910	rs983348260	C	T	0.002	6	DBP	15.23	2.87	1.15E-07	NA	NA	NA	NA	NA	NA	N
7	147057965	rs59454844	C	A	0.02	7	SBP	-9.50	1.92	7.44E-07	NA	NA	NA	NA	NA	NA	N
8	3512422	rs928576052	T	A	0.001	8	HTN	3.93	0.78	4.07E-07	NA	NA	NA	NA	NA	NA	N
9	80991323	rs373277444	T	C	0.002	9	HTN	-3.25	0.65	6.24E-07	NA	NA	NA	NA	NA	NA	Y
13	18251702	rs1369784734	G	A	0.003	10	SBP	22.19	4.22	1.49E-07	NA	NA	NA	NA	NA	NA	N
14	90802718	rs57506024	G	T	0.002	11	SBP	23.52	4.74	6.84E-07	NA	NA	NA	NA	NA	NA	N
17	33851243	rs377109	C	T	0.51	12	HTN	-0.30	0.06	7.60E-07	NA	NA	NA	NA	NA	NA	N
20	45265366	rs8115076	A	G	0.04	13	SBP	-5.85	1.17	5.21E-07	NA	NA	NA	NA	NA	NA	Y
<i>Novel Variants at Previously Reported Loci</i>																	
1	42140873	rs895048624	C	T	0.002	1	DBP	-15.41	3.03	3.59E-07	NA	NA	NA	NA	NA	NA	N
1	112064726	rs550856031	G	C	0.004	2	SBP	-20.75	3.90	1.00E-07	NA	NA	NA	NA	NA	NA	Y
4	118304240	rs372614646	T	C	0.002	3	DBP	-14.53	2.91	5.71E-07	NA	NA	NA	NA	NA	NA	N
4	124603162	rs62324576	A	G	0.21	4	SBP	-2.95	0.57	2.29E-07	NA	NA	NA	NA	NA	NA	N
5	159688603	rs1056949606	G	C	0.002	5	DBP	16.11	3.02	9.50E-08	NA	NA	NA	NA	NA	NA	Y
6	78578616	rs1771129668	AAGG	A	0.002	6	DBP	17.48	3.28	9.75E-08	NA	NA	NA	NA	NA	NA	N
10	122776836	rs869742	A	G	0.29	7	SBP	2.59	0.53	8.83E-07	-0.15	0.45	7.46E-01	1.01	0.34	3.14E-03	N
11	117539708	rs2509004	G	A	0.32	8	HTN	-0.34	0.06	7.55E-08	NA	NA	NA	NA	NA	NA	N
12	12635001	rs113998718	G	A	0.03	9	HTN	-0.93	0.18	2.81E-07	NA	NA	NA	NA	NA	NA	Y
13	49466684	rs148785348	G	A	0.008	10	HTN	1.63	0.33	6.52E-07	NA	NA	NA	NA	NA	NA	N
14	59506013	rs376505264	A	T	0.002	11	SBP	-29.41	5.57	1.29E-07	NA	NA	NA	NA	NA	NA	Y
15	26628999	rs990895163	C	T	0.002	12	SBP	-27.38	5.44	4.96E-07	NA	NA	NA	NA	NA	NA	Y
16	49743010	rs375915281	T	G	0.004	13	HTN	2.80	0.54	2.71E-07	NA	NA	NA	NA	NA	NA	Y
19	5502949	rs892681603	A	G	0.003	14	DBP	12.99	2.64	9.04E-07	NA	NA	NA	NA	NA	NA	N

AAF, alternative allele frequency; Alt, alternative allele; Chr, chromosome; DBP, diastolic blood pressure (BP); HTN, hypertension; MVP, Million Veteran Program; NA, not available; Pheno, phenotype; Ref, reference allele; SBP, systolic BP; TOPMed, Trans-Omics for Precision Medicine; UKBB, UK Biobank.

Table S5. Novel variants achieving $P < 1E-06$ in single marker analyses of participants of European ancestry.

Chr	Position (B38)	rsID	Ref	Alt	AAF	Loc	Phe	TOPMed			UKBB			MVP			REGARDS			Meta-analysis			Multi-ancestry Analyses
								Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P	
<i>Novel Loci</i>																							
1	62765101	rs76269172	C	A	0.03	1	DBP	1.42	0.27	1.61E-07	0.03	0.07	6.74E-01	0.11	0.09	2.22E-01	-1.77	1.23	1.52E-01	0.12	0.06	3.52E-02	N
2	129699875	rs540567720	A	G	0.0004	2	DBP	-12.61	2.42	1.95E-07	0.15	0.53	7.72E-01	NA	NA	NA	NA	NA	NA	-0.42	0.51	4.12E-01	N
2	194267770	rs1008983838	T	C	0.0003	3	DBP	12.95	2.64	9.69E-07	-1.45	1.69	3.91E-01	NA	NA	NA	NA	NA	NA	2.73	1.42	5.53E-02	N
3	25416500	rs149809786	C	T	0.006	4	SBP	5.07	1.02	6.82E-07	-0.29	0.29	3.24E-01	-0.43	0.31	1.60E-01	-4.75	4.27	2.67E-01	-0.14	0.21	4.92E-01	N
4	33007919	rs76192272	G	A	0.0006	5	SBP	-16.00	3.14	3.51E-07	-1.61	1.30	2.14E-01	NA	NA	NA	-11.27	7.89	1.53E-01	-3.87	1.18	1.07E-03	Y
4	66198983	rs561884114	A	C	0.0002	6	HTN	4.06	0.83	9.70E-07	-0.38	0.82	6.44E-01	NA	NA	NA	NA	NA	NA	1.81	0.58	1.88E-03	N
4	126021610	rs566516927	A	C	0.001	7	DBP	-6.94	1.38	4.51E-07	-0.68	0.46	1.38E-01	NA	NA	NA	NA	NA	NA	-1.31	0.43	2.66E-03	N
4	154348736	rs892714163	T	C	0.0005	8	HTN	2.32	0.47	9.05E-07	1.04	0.75	1.66E-01	NA	NA	NA	NA	NA	NA	1.95	0.40	9.86E-07	N
4	183700478	rs543591385	T	A	0.0008	9	DBP	7.91	1.59	6.87E-07	0.41	0.42	3.30E-01	NA	NA	NA	NA	NA	NA	0.91	0.41	2.64E-02	N
6	86561152	rs558889883	G	T	0.0009	10	SBP	-12.56	2.56	9.53E-07	-0.04	0.72	9.53E-01	NA	NA	NA	NA	NA	NA	-0.95	0.69	1.69E-01	N
7	120623195	rs959927014	A	T	0.0002	11	DBP	14.11	2.86	8.20E-07	49.71	38.11	1.92E-01	NA	NA	NA	NA	NA	NA	14.31	2.85	5.32E-07	Y
7	120907812	rs578061109	T	A	0.0002	11	HTN	3.86	0.74	2.05E-07	-0.20	0.26	4.45E-01	NA	NA	NA	NA	NA	NA	0.25	0.25	3.14E-01	Y
7	143976251	rs751854967	T	A	0.0003	12	HTN	3.06	0.62	7.46E-07	0.15	0.25	5.53E-01	NA	NA	NA	NA	NA	NA	0.56	0.23	1.60E-02	N
8	8373964	rs575133860	C	T	0.0002	13	SBP	-25.24	5.14	9.19E-07	2.47	2.64	3.49E-01	NA	NA	NA	NA	NA	NA	-3.32	2.35	1.58E-01	Y
9	89734572	rs958296179	T	G	0.0003	14	DBP	-13.28	2.70	8.83E-07	-0.46	1.07	6.68E-01	NA	NA	NA	NA	NA	NA	-2.19	0.99	2.75E-02	N
10	111787758	rs11816391	C	T	0.001	15	HTN	1.55	0.32	9.53E-07	0.13	0.13	3.28E-01	0.15	0.09	8.56E-02	1.42	1.10	1.99E-01	0.22	0.07	1.85E-03	N
11	60495718	rs117337046	A	G	0.01	16	DBP	1.92	0.38	5.72E-07	0.00	0.11	9.74E-01	0.23	0.14	9.80E-02	0.08	1.77	9.64E-01	0.17	0.08	3.83E-02	N
12	83815309	rs561552220	ACT1	A	0.0003	17	SBP	-22.82	4.63	8.17E-07	-16.17	12.26	1.87E-01	NA	NA	NA	NA	NA	NA	-21.99	4.33	3.79E-07	N
13	38675796	rs577492884	CAT1	A	0.003	18	HTN	-0.99	0.19	1.94E-07	0.04	0.05	3.87E-01	NA	NA	NA	-1.07	1.24	3.89E-01	-0.03	0.05	5.98E-01	N
13	101948434	rs141819525	T	C	0.007	19	DBP	2.79	0.55	3.92E-07	0.24	0.18	1.84E-01	0.24	0.26	3.54E-01	1.10	2.32	6.34E-01	0.42	0.14	3.53E-03	N
14	57988146	rs749207023	C	T	0.0003	20	DBP	12.42	2.52	8.36E-07	0.83	0.68	2.25E-01	NA	NA	NA	NA	NA	NA	1.62	0.66	1.40E-02	Y
15	28155119	rs372510625	T	C	0.001	21	SBP	10.60	2.10	4.50E-07	-0.80	0.67	2.38E-01	NA	NA	NA	NA	NA	NA	0.27	0.64	6.76E-01	Y
17	39044508	rs748270054	C	T	0.0002	22	SBP	-29.24	5.41	6.59E-08	3.53	1.58	2.54E-02	NA	NA	NA	NA	NA	NA	0.96	1.52	5.28E-01	N
19	54026925	rs400400	G	A	0.14	23	DBP	-0.68	0.13	3.28E-07	-0.09	0.04	3.11E-02	-0.03	0.05	5.78E-01	-0.10	0.60	8.63E-01	-0.09	0.03	1.97E-03	N
20	53496720	rs528746565	A	G	0.0007	24	HTN	2.02	0.40	3.76E-07	-0.12	0.11	2.75E-01	NA	NA	NA	NA	NA	NA	0.04	0.11	7.38E-01	N
<i>Novel Variants at Previously Reported Loci</i>																							
1	220559313	rs1444461605	G	A	0.005	1	DBP	3.18	0.63	4.37E-07	-0.01	0.20	9.48E-01	0.34	0.30	2.48E-01	3.74	3.61	2.99E-01	0.31	0.16	5.36E-02	N
1	242546033	rs12748137	T	G	0.66	2	DBP	0.48	0.10	5.85E-07	0.01	0.03	8.22E-01	0.02	0.03	5.91E-01	-0.72	0.40	6.76E-02	0.03	0.02	1.32E-01	N
3	185604045	rs541586343	C	T	0.001	3	DBP	-8.78	1.77	6.87E-07	1.80	1.47	2.21E-01	NA	NA	NA	NA	NA	NA	-2.53	1.13	2.54E-02	N

4	23985590	rs536671665	T	C	0.0005	4	DBP	10.09	2.05	8.33E-07	3.41	1.87	6.86E-02	-0.82	1.84	6.58E-01	NA	NA	NA	3.84	1.11	5.20E-04	N
4	23985590	rs536671665	T	C	0.0005	4	HTN	2.19	0.44	5.02E-07	0.14	0.37	7.11E-01	NA	NA	NA	NA	NA	NA	1.00	0.28	3.97E-04	N
4	102682904	rs191838284	G	C	0.01	5	SBP	-3.45	0.68	3.96E-07	-0.08	0.20	6.99E-01	0.47	0.39	2.33E-01	-1.02	2.90	7.24E-01	-0.20	0.17	2.63E-01	N
5	172024835	rs779225390	A	G	0.0002	6	DBP	-14.73	2.86	2.72E-07	0.01	0.69	9.89E-01	NA	NA	NA	NA	NA	NA	-0.81	0.67	2.32E-01	Y
5	172180433	rs150791232	C	T	0.001	6	SBP	14.15	2.83	5.57E-07	0.02	1.35	9.87E-01	NA	NA	NA	-9.01	8.07	2.64E-01	2.39	1.21	4.72E-02	Y
6	154480077	rs114764916	C	T	0.0002	7	DBP	-14.94	3.05	9.46E-07	5.24	2.92	7.28E-02	NA	NA	NA	NA	NA	NA	-4.42	2.11	3.61E-02	N
7	106438072	rs1013536627	G	A	0.0003	8	DBP	12.88	2.62	8.91E-07	0.32	0.62	6.12E-01	NA	NA	NA	NA	NA	NA	0.99	0.61	1.03E-01	Y
7	107735653	rs147635708	A	G	0.004	9	HTN	-0.75	0.15	6.13E-07	-0.14	0.05	9.41E-03	NA	NA	NA	0.68	0.76	3.73E-01	-0.20	0.05	6.04E-05	N
7	136718949	rs556650389	G	A	0.0004	10	DBP	-11.01	2.17	3.97E-07	0.07	1.12	9.52E-01	NA	NA	NA	NA	NA	NA	-2.26	1.00	2.32E-02	N
8	140001243	rs578246850	G	T	0.002	11	SBP	9.36	1.88	6.71E-07	0.66	0.62	2.86E-01	NA	NA	NA	-4.37	8.26	5.97E-01	1.49	0.59	1.15E-02	Y
8	144843317	rs559045193	T	C	0.004	12	HTN	0.81	0.16	6.28E-07	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	N
10	48254181	rs562935500	G	A	0.0004	13	SBP	18.60	3.75	7.19E-07	1.28	2.12	5.45E-01	NA	NA	NA	NA	NA	NA	5.47	1.85	3.03E-03	N
10	93065629	rs118003307	G	A	0.01	14	DBP	2.31	0.47	9.36E-07	-0.15	0.18	3.83E-01	0.32	0.24	1.87E-01	0.33	2.89	9.10E-01	0.21	0.14	1.34E-01	Y
10	132389085	rs183489999	C	G	0.005	15	HTN	0.72	0.14	1.24E-07	-0.02	0.04	6.25E-01	NA	NA	NA	0.31	0.50	5.35E-01	0.03	0.03	3.57E-01	N
11	30758017	rs759526273	G	A	0.001	16	SBP	-13.33	2.60	2.80E-07	-9.19	6.62	1.65E-01	NA	NA	NA	NA	NA	NA	-12.78	2.42	1.24E-07	Y
14	102002363	rs539350051	G	A	0.0002	17	HTN	4.15	0.83	6.44E-07	-0.93	0.45	4.06E-02	NA	NA	NA	NA	NA	NA	0.23	0.40	5.58E-01	N
15	74602739	rs900421386	T	C	0.0002	18	DBP	14.93	2.85	1.69E-07	-0.93	0.99	3.48E-01	NA	NA	NA	NA	NA	NA	0.77	0.93	4.09E-01	N
15	96338035	rs34353956	C	AAC	0.38	19	DBP	-0.47	0.09	5.14E-07	NA	NA	NA	-0.04	0.05	4.47E-01	0.06	0.53	9.16E-01	-0.12	0.04	3.56E-03	Y
17	41088764	rs184774589	A	G	0.003	20	HTN	0.83	0.17	5.09E-07	0.01	0.04	7.32E-01	0.00	0.06	9.55E-01	0.15	0.58	8.01E-01	0.04	0.03	1.93E-01	N

Previously Reported Loci

1	10736809	rs880315	T	C	0.34	1	SBP	0.89	0.17	1.13E-07	0.57	0.05	1.74E-28	0.38	0.05	7.99E-17	-0.41	0.69	5.47E-01	0.47	0.03	1.95E-46	Y
1	11798900	rs45553335	T	C	0.16	2	DBP	-0.76	0.13	2.39E-09	-0.63	0.04	5.08E-66	-0.33	0.04	8.48E-14	-1.40	0.50	5.48E-03	-0.52	0.03	3.50E-80	Y
3	169405049	rs17485157	G	A	0.23	3	SBP	-1.16	0.19	7.96E-10	-0.45	0.06	1.68E-15	-0.10	0.05	4.33E-02	-2.98	0.78	1.29E-04	-0.30	0.04	4.44E-16	Y
3	169405049	rs17485157	G	A	0.23	3	DBP	-0.63	0.11	7.28E-09	-0.30	0.03	2.50E-20	-0.13	0.04	7.34E-04	-1.09	0.46	1.68E-02	-0.25	0.02	2.30E-25	Y
4	102267552	rs13107325	C	T	0.07	4	DBP	-1.07	0.18	1.36E-09	-0.80	0.05	1.27E-53	-0.46	0.06	6.93E-15	0.21	0.73	7.75E-01	-0.67	0.04	2.24E-69	Y
5	128525056	rs6595835	C	T	0.29	5	SBP	0.88	0.17	4.09E-07	0.46	0.05	6.57E-19	0.30	0.05	2.35E-10	2.02	0.72	4.89E-03	0.40	0.03	4.20E-31	N
6	43388113	rs2396004	A	G	0.56	6	SBP	-0.94	0.16	4.43E-09	-0.30	0.05	9.03E-10	-0.31	0.04	3.48E-12	-1.06	0.66	1.10E-01	-0.33	0.03	5.93E-25	Y
6	43440728	rs2794264	C	G	0.77	6	HTN	-0.13	0.02	5.02E-08	-0.02	0.01	0.000228	-0.02	0.01	7.38E-02	0.05	0.09	5.85E-01	-0.03	0.01	3.83E-07	Y
8	11434264	rs34443092	C	G	0.22	7	SBP	-1.00	0.19	2.04E-07	-0.27	0.06	7.21E-06	-0.16	0.05	3.56E-03	-0.14	0.78	8.59E-01	-0.24	0.04	8.87E-10	Y
10	18448045	rs11014267	G	A	0.34	8	HTN	-0.11	0.02	1.46E-07	-0.07	0.01	1.71E-29	-0.05	0.01	7.14E-11	-0.09	0.08	2.47E-01	-0.06	0.00	1.39E-43	Y
11	16327586	rs7127937	C	A	0.21	9	SBP	1.04	0.19	7.93E-08	0.49	0.06	5.00E-17	0.29	0.06	3.27E-07	1.21	0.82	1.40E-01	0.41	0.04	1.69E-25	Y
11	16331652	NA	TA	T	0.19	9	DBP	0.70	0.12	1.64E-09	0.28	0.03	5.67E-16	0.25	0.04	7.76E-09	0.98	0.50	4.99E-02	0.29	0.03	1.13E-28	Y
12	20025130	rs4762917	C	T	0.77	10	DBP	0.60	0.11	3.74E-08	0.33	0.03	1.91E-25	0.12	0.04	1.44E-03	-0.15	0.45	7.41E-01	0.26	0.02	5.11E-28	Y
12	50167576	rs73106145	G	C	0.25	11	HTN	-0.12	0.02	6.95E-08	-0.04	0.01	2.61E-09	-0.03	0.01	8.47E-05	-0.03	0.09	7.60E-01	-0.04	0.01	4.44E-16	Y

12	89619312	rs2681492	T	C	0.17	12	SBP	-1.10	0.21	2.30E-07	-1.06	0.06	1.28E-62	-0.48	0.06	3.46E-17	-3.16	0.90	4.64E-04	-0.76	0.04	1.73E-74	Y
12	111591487	rs7953810	T	C	0.79	13	DBP	0.57	0.11	3.74E-07	0.42	0.03	1.82E-37	NA	NA	NA	-0.43	0.47	3.60E-01	0.43	0.03	3.43E-42	Y
12	114914926	rs2384550	G	A	0.36	14	DBP	-0.55	0.10	1.18E-08	-0.14	0.03	3.59E-07	-0.08	0.03	1.73E-02	-0.39	0.39	3.16E-01	-0.14	0.02	4.40E-11	Y
13	29563691	rs7338758	T	C	0.76	15	DBP	-0.53	0.11	8.93E-07	-0.20	0.03	1.00E-09	-0.14	0.04	1.06E-04	-0.18	0.46	6.95E-01	-0.19	0.02	6.66E-16	Y
17	64286156	rs8072421	G	A	0.79	16	HTN	0.13	0.02	3.37E-07	0.02	0.01	0.00802	0.03	0.01	2.61E-02	0.22	0.11	3.75E-02	0.03	0.01	3.80E-06	N

AAF, alternative allele frequency; Alt, alternative allele; Chr, chromosome; DBP, diastolic blood pressure (BP); HTN, hypertension; MVP, Million Veteran Program; NA, not available; Pheno, phenotype; Ref, reference allele; SBP, systolic BP; TOPMed, Trans-Omics for Precision Medicine; UKBB, UK Biobank.

Table S6. Novel lead variants achieving $P < 1E-06$ in single marker analyses of participants of Hispanic ancestry.

Chr	Position (B38)	rsID	Ref	Alt	AAF	Locus (1MB)	Pheno	TOPMed			MVP			Meta-analysis			Identified in Multi-ancestry Analyses
								Beta	SE	P	Beta	SE	P	Beta	SE	P	
<i>Novel Loci</i>																	
1	171349448	rs12121703	C	A	0.005	1	HTN	-2.02	0.39	2.12E-07	0.27	0.24	2.58E-01	-0.36	0.20	8.02E-02	N
2	233398463	rs142982073	T	A	0.003	2	SBP	23.22	4.18	2.74E-08	NA	NA	NA	NA	NA	NA	N
3	1251324	rs73002355	C	A	0.27	3	HTN	0.29	0.06	9.91E-07	0.00	0.03	9.66E-01	0.07	0.03	1.75E-02	N
3	108837985	rs1374819	G	A	0.99	4	HTN	1.16	0.22	8.32E-08	0.11	0.39	7.74E-01	0.91	0.19	1.51E-06	N
4	139434324	NA	TTTG	T	0.005	5	DBP	-10.25	1.91	8.03E-08	NA	NA	NA	NA	NA	NA	N
4	141555930	rs150742805	G	C	0.009	6	SBP	12.96	2.64	8.91E-07	2.18	0.96	2.24E-02	3.44	0.90	1.32E-04	N
5	85131700	rs13161070	A	G	0.27	7	HTN	-0.29	0.06	9.30E-07	0.01	0.03	6.88E-01	-0.06	0.03	4.75E-02	N
7	82718668	rs114415195	A	G	0.004	8	DBP	11.09	2.26	9.55E-07	1.43	1.39	3.04E-01	4.07	1.18	5.87E-04	N
9	7789671	rs73640528	T	G	0.01	9	SBP	-11.99	2.41	6.39E-07	NA	NA	NA	NA	NA	NA	N
9	101019274	rs1829803343	CT	C	0.004	10	SBP	19.84	3.89	3.43E-07	NA	NA	NA	NA	NA	NA	Y
10	52552315	rs140873521	C	T	0.002	11	SBP	-26.39	5.11	2.43E-07	1.95	2.10	3.54E-01	-2.15	1.94	2.69E-01	N
10	65663386	rs150860430	T	C	0.005	12	DBP	10.52	1.99	1.29E-07	-1.05	1.07	3.28E-01	1.54	0.94	1.02E-01	N
11	84308504	rs7130515	C	T	0.03	13	DBP	-4.17	0.81	2.32E-07	-0.12	0.46	8.03E-01	-1.12	0.40	5.20E-03	N
13	104854218	rs116125587	C	G	0.007	14	DBP	7.83	1.60	9.55E-07	NA	NA	NA	NA	NA	NA	N
17	50585349	rs73340234	G	A	0.10	15	DBP	2.51	0.47	9.62E-08	NA	NA	NA	NA	NA	NA	N
17	54148586	rs141053160	A	T	0.009	16	DBP	7.08	1.42	6.69E-07	-0.71	0.90	4.30E-01	1.52	0.76	4.61E-02	N
20	53813083	rs140277791	G	A	0.008	17	SBP	-13.10	2.61	5.38E-07	2.04	2.04	3.16E-01	-3.67	1.61	2.21E-02	N
22	17419355	rs5992045	A	G	0.04	18	SBP	-6.16	1.26	9.58E-07	-0.78	0.50	1.22E-01	-1.52	0.47	1.12E-03	N
<i>Novel Variants at Previously Reported Loci</i>																	
1	152720669	rs146580854	C	T	0.004	1	SBP	-21.44	4.04	1.09E-07	-0.18	1.82	9.23E-01	-3.76	1.66	2.33E-02	N
2	187635130	rs114208581	G	T	0.007	2	SBP	15.18	2.91	1.80E-07	-0.95	0.89	2.83E-01	0.42	0.85	6.20E-01	N
4	53651248	rs6819831	T	C	0.05	3	SBP	6.01	1.17	2.62E-07	-0.72	0.46	1.17E-01	0.18	0.43	6.74E-01	N
5	64432600	rs114242941	T	G	0.02	4	DBP	5.56	0.99	2.13E-08	-0.10	0.60	8.66E-01	1.41	0.51	5.96E-03	N
6	71349009	rs137992085	G	A	0.008	5	SBP	14.35	2.77	2.22E-07	0.32	1.08	7.71E-01	2.17	1.01	3.11E-02	N
6	169345812	rs6907101	A	C	0.04	6	HTN	-0.69	0.14	5.19E-07	0.04	0.13	7.71E-01	-0.30	0.09	1.46E-03	Y
7	42471062	rs28813987	A	G	0.11	7	SBP	3.95	0.77	3.16E-07	0.32	0.21	1.27E-01	0.56	0.20	5.06E-03	N
8	37850706	NA	GGAG	C	0.03	8	SBP	-7.55	1.45	1.97E-07	1.01	0.61	9.98E-02	-0.28	0.56	6.15E-01	N
9	21623989	rs111769602	T	A	0.007	9	SBP	15.06	2.92	2.49E-07	NA	NA	NA	NA	NA	NA	N
10	89557596	rs577309319	A	G	0.002	10	HTN	-3.79	0.74	3.37E-07	NA	NA	NA	NA	NA	NA	N

10	132528625	rs74569766	T	C	0.03	11	DBP	3.88	0.79	8.35E-07	0.24	0.45	6.05E-01	1.15	0.39	3.58E-03	N
11	111061016	rs185000995	C	A	0.002	12	SBP	28.84	5.67	3.62E-07	NA	NA	NA	NA	NA	NA	N
12	24684920	rs60519245	G	A	0.008	13	SBP	-13.27	2.67	6.75E-07	0.68	1.45	6.40E-01	-2.51	1.28	4.95E-02	N
13	50789167	rs17069393	T	C	0.17	14	SBP	-3.31	0.65	2.89E-07	-0.11	0.18	5.36E-01	-0.36	0.18	4.50E-02	N
14	51118919	rs10149439	A	G	0.39	15	DBP	-1.42	0.28	2.59E-07	0.04	0.11	7.35E-01	-0.16	0.10	1.13E-01	N
17	42149720	rs78680046	G	A	0.01	16	DBP	5.97	1.21	7.78E-07	NA	NA	NA	NA	NA	NA	N
20	17111142	rs76363605	T	C	0.008	17	SBP	14.10	2.74	2.63E-07	0.79	1.36	5.61E-01	3.41	1.22	5.02E-03	N
21	46020594	rs141563513	G	A	0.007	18	DBP	-7.77	1.52	3.45E-07	NA	NA	NA	NA	NA	NA	N
22	39571716	rs9623018	A	T	0.004	19	DBP	10.17	2.06	7.61E-07	-0.93	1.15	4.18E-01	1.73	1.01	8.62E-02	N
Previously Reported Loci																	
10	132539576	rs34282942	G	GT	0.27098	1	DBP	1.70	0.31	3.69E-08	-0.04	0.13	7.29E-01	0.21	0.12	7.13E-02	N

AAF, alternative allele frequency; Alt, alternative allele; Chr, chromosome; DBP, diastolic blood pressure (BP); HTN, hypertension; MVP, Million Veteran Program; NA, not available; Pheno, phenotype; Ref, reference allele; SBP, systolic BP; TOPMed, Trans-Omics for Precision Medicine; UKBB, UK Biobank.

Table S7. Novel variants achieving $P < 1E-06$ in single marker analyses of participants of Samoan ancestry.

Chr	Position (B38)	rsID	Ref	Alt	AAF	Locus (1MB)	Pheno	TOPMed			Identified in Multi-ancestry Analyses
								Beta	SE	P	
<i>Novel Loci</i>											
1	160906765	rs889484496	C	T	0.008	1	HTN	2.91	0.54	5.83E-08	Y
1	188546014	rs1586059	C	T	0.35	2	HTN	0.49	0.10	6.28E-07	N
7	21277699	rs141639223	C	T	0.08	3	SBP	-6.97	1.42	9.74E-07	N
20	56748383	rs375606398	G	A	0.05	4	HTN	1.03	0.21	8.73E-07	Y
<i>Novel Loci from Previously Reported Loci</i>											
18	50631599	rs8091238	G	C	0.94	1	HTN	-1.06	0.2	2.11E-07	N

AAF, alternative allele frequency; Alt, alternative allele; Chr, chromosome; DBP, diastolic blood pressure (BP); HTN, hypertension; MVP, Million Veteran Program; NA, not available; Pheno, phenotype; Ref, reference allele; SBP, systolic

Table S8. Genes and chromosomal regions with SMMAT-E $P < 1E-4$ in aggregate rare variant analyses of the multi-ancestry sample.

Aggregate Unit	Phe	TOPMed			UK Biobank WES Data			Meta-analysis P-value
		Rare Variant Sites (N)	Rare Alleles (N)	SMMAT-E P-value	Rare Variant Sites (N)	Rare Alleles (N)	SMMAT-E P-value	
<i>Gene-based analysis (high confidence loss of function variants only)</i>								
NAPEPLD (Chr7:103099576-103149560)	HTN	1	5	4.31E-05	0	0	NA	NA
GABRB3 (Chr15:26543546-26773763)	SBP	3	26	2.67E-06	1	2	1.29E-01	5.42E-06
<i>Gene-based analysis (Loss-of-function variants, missense variants, and protein altering indels)</i>								
DNAJB13 (Chr11:73950321-73970287)	DBP	16	451	2.91E-05	8	1,033	2.58E-02	1.13E-05
<i>Gene-based analysis (Enhancer, promoter, and exonic variants with predicted functional relevance)</i>								
RP13-514E23.1 (Chr4:86012296-86013874)	HTN	4	114	8.97E-05	8	145	2.97E-01	3.07E-04
SYT7 (Chr11:61513714-61588404)	SBP	92	3282	8.86E-05	35	1,485	1.82E-01	1.94E-04
DNAJB13 (Chr11:73950321-73970287)	DBP	30	874	7.14E-05	15	1,474	6.01E-02	5.29E-05
RASAL1 (Chr12:113096515-113136248)	SBP	98	1541	4.73E-05	58	3,204	1.43E-01	8.74E-05
SMARCD1 (Chr12:50085236-50100707)	HTN	65	1738	4.95E-05	20	2,024	5.10E-01	2.92E-04
RP11-297M9.1 (Chr16:9666885-9676843)	DBP	1	15	4.83E-05	0	0	NA	NA
ZNF431 (Chr19:21142009-21196053)	SBP	31	2073	8.40E-05	0	0	NA	NA
<i>Sliding window analysis</i>								
Chr1:227060001-227080000	DBP	17	178	4.93E-05	NA	NA	NA	NA
Chr2:196990001-197010000	DBP	34	923	8.12E-05	NA	NA	NA	NA
Chr2:211720001-211740000	HTN	5	122	8.15E-06	NA	NA	NA	NA

Chr2:137760001-137780000	SBP	7	609	4.98E-05	NA	NA	NA	NA
Chr2:137770001-137790000	SBP	3	291	2.75E-05	NA	NA	NA	NA
Chr3:60900001-60920000	DBP	17	539	4.14E-05	NA	NA	NA	NA
Chr3:60910001-60930000	DBP	20	562	8.32E-05	NA	NA	NA	NA
Chr3:130510001-130530000	DBP	10	1322	3.69E-05	NA	NA	NA	NA
Chr3:130520001-130540000	DBP	8	1315	3.37E-05	NA	NA	NA	NA
Chr3:179510001-179530000	DBP	6	455	6.44E-05	NA	NA	NA	NA
Chr3:100320001-100340000	HTN	29	429	4.32E-06	NA	NA	NA	NA
Chr3:121910001-121930000	HTN	26	417	2.33E-05	NA	NA	NA	NA
Chr4:44130001-44150000	DBP	13	749	1.47E-05	NA	NA	NA	NA
Chr4:44140001-44160000	DBP	13	833	1.50E-05	NA	NA	NA	NA
Chr4:124730001-124750000	DBP	2	464	2.62E-05	NA	NA	NA	NA
Chr4:124740001-124760000	DBP	3	467	1.77E-05	NA	NA	NA	NA
Chr4:154050001-154070000	DBP	2	8	6.22E-05	NA	NA	NA	NA
Chr4:75300001-75320000	HTN	1	3	1.60E-05	NA	NA	NA	NA
Chr4:98480001-98500000	HTN	4	18	3.55E-05	NA	NA	NA	NA
Chr4:38240001-38260000	SBP	2	34	6.97E-05	NA	NA	NA	NA
Chr4:47020001-47040000	SBP	15	577	2.28E-05	NA	NA	NA	NA
Chr4:47030001-47050000	SBP	16	581	4.43E-05	NA	NA	NA	NA
Chr5:57890001-57910000	DBP	5	16	1.93E-06	NA	NA	NA	NA
Chr5:67070001-67090000	DBP	23	2953	2.70E-05	NA	NA	NA	NA
Chr5:72090001-72110000	DBP	21	638	3.81E-05	NA	NA	NA	NA
Chr5:88000001-88020000	DBP	30	2259	8.81E-05	NA	NA	NA	NA
Chr5:57890001-57910000	SBP	5	16	5.45E-06	NA	NA	NA	NA
Chr6:137830001-137850000	DBP	1	3	5.34E-05	NA	NA	NA	NA
Chr7:90860001-90880000	DBP	10	154	8.07E-05	NA	NA	NA	NA
Chr7:98130001-98150000	HTN	1	4	5.88E-05	NA	NA	NA	NA
Chr8:137320001-137340000	DBP	3	539	1.46E-05	NA	NA	NA	NA
Chr8:137330001-137350000	DBP	2	535	1.06E-05	NA	NA	NA	NA
Chr8:122390001-122410000	SBP	2	17	3.94E-05	NA	NA	NA	NA
Chr9:23130001-23150000	HTN	41	1380	2.98E-05	NA	NA	NA	NA
Chr9:23140001-23160000	HTN	45	1577	3.31E-05	NA	NA	NA	NA
Chr9:29800001-29820000	HTN	2	15	9.43E-05	NA	NA	NA	NA
Chr10:37070001-37090000	HTN	1	112	8.38E-05	NA	NA	NA	NA

Chr10:65280001-65300000	HTN	3	937	3.91E-05	NA	NA	NA	NA
Chr10:13080001-13100000	SBP	1	9	1.42E-05	NA	NA	NA	NA
Chr10:13090001-13110000	SBP	3	12	4.21E-05	NA	NA	NA	NA
Chr10:32950001-32970000	SBP	1	3	5.92E-05	NA	NA	NA	NA
Chr11:44770001-44790000	DBP	7	232	7.72E-05	NA	NA	NA	NA
Chr11:61730001-61750000	DBP	40	440	7.56E-05	NA	NA	NA	NA
Chr11:73950001-73970000	DBP	21	639	3.18E-05	NA	NA	NA	NA
Chr12:50070001-50090000	HTN	50	1588	2.82E-05	NA	NA	NA	NA
Chr12:50080001-50100000	HTN	48	1515	9.66E-05	NA	NA	NA	NA
Chr12:113490001-113510000	HTN	23	491	8.71E-05	NA	NA	NA	NA
Chr12:31150001-31170000	SBP	1	14	8.83E-05	NA	NA	NA	NA
Chr12:113090001-113110000	SBP	59	931	6.93E-06	NA	NA	NA	NA
Chr13:50510001-50530000	DBP	8	70	5.23E-05	NA	NA	NA	NA
Chr14:18320001-18340000	HTN	2	6	2.59E-05	NA	NA	NA	NA
Chr15:24890001-24910000	DBP	30	549	4.80E-05	NA	NA	NA	NA
Chr15:24900001-24920000	DBP	36	659	5.43E-05	NA	NA	NA	NA
Chr15:38380001-38400000	DBP	5	94	8.63E-05	NA	NA	NA	NA
Chr15:47480001-47500000	DBP	14	133	9.55E-05	NA	NA	NA	NA
Chr15:41570001-41590000	HTN	31	325	4.89E-05	NA	NA	NA	NA
Chr15:48270001-48290000	HTN	15	132	3.86E-05	NA	NA	NA	NA
Chr17:70430001-70450000	SBP	14	235	2.92E-05	NA	NA	NA	NA
Chr18:76450001-76470000	HTN	3	349	5.74E-05	NA	NA	NA	NA
Chr19:21150001-21170000	SBP	18	1199	2.80E-05	NA	NA	NA	NA
Chr22:34420001-34440000	DBP	5	58	9.84E-05	NA	NA	NA	NA

DBP, diastolic blood pressure (BP); HTN, hypertension; Min-P, minimum P-value; SBP, systolic BP; SMMAT-E, variant set mixed model association test - Efficient hybrid

Table S9. Genes and chromosomal regions with SMMAT-E $P < 1E-4$ in aggregate rare variant analyses of the African ancestry sample.

Aggregate Unit	Associated Trait	Rare Variant Sites (N)	Rare Alleles (N)	SMMAT-E value	P.
<i>Gene-based analysis (high confidence loss of function variants only)</i>					
AGTRAP (Chr1:11736085-11750771)	SBP	3	46	9.70E-05	
G6PC3 (Chr17:44070700-44076344)	HTN	2	6	1.15E-05	
<i>Gene-based analysis (Loss-of-function variants, missense variants, and protein altering indels)</i>					
ERBB4 (Chr2:211375717-212538802)	HTN	24	190	6.50E-05	
PLAT (Chr8:42174718-42207565)	DBP	12	203	4.11E-05	
BLNK (Chr10:96189171-96271576)	HTN	2	26	9.49E-05	
GOLT1B (Chr12:21501176-21518408)	DBP	2	18	3.15E-05	
<i>Gene-based analysis (Enhancer, promoter, and exonic variants with predicted functional relevance)</i>					
LEXM (Chr1:54806063-54842264)	DBP	19	361	2.82E-05	
MCIDAS (Chr5:55218791-55227315)	DBP	7	451	1.89E-05	
WDR87 (Chr19:37884577-37906617)	SBP	5	48	7.67E-05	
WDR87 (Chr19:37884577-37906617)	DBP	5	48	3.84E-05	
GTPBP1 (Chr22:38704561-38738265)	SBP	26	623	8.79E-05	
<i>Sliding window analysis</i>					
Chr1:54800001-54820000	DBP	22	412	2.04E-05	
Chr1:54810001-54830000	DBP	11	265	2.04E-05	
Chr2:67990001-68010000	DBP	9	322	2.23E-05	
Chr2:49510001-49530000	HTN	15	338	8.68E-06	
Chr2:183010001-183030000	HTN	4	21	6.29E-05	
Chr2:211710001-211730000	HTN	4	112	3.04E-05	
Chr2:211720001-211740000	HTN	2	101	1.25E-05	
Chr2:67990001-68010000	SBP	9	322	6.29E-05	
Chr2:137760001-137780000	SBP	4	329	9.05E-05	
Chr2:137770001-137790000	SBP	2	266	7.97E-05	
Chr3:88430001-88450000	DBP	11	250	7.04E-05	
Chr3:88440001-88460000	DBP	8	242	6.66E-05	
Chr3:19030001-19050000	HTN	4	61	1.46E-05	
Chr3:59310001-59330000	SBP	25	780	9.30E-05	
Chr4:22930001-22950000	DBP	9	269	2.80E-06	
Chr4:22940001-22960000	DBP	15	352	1.52E-05	
Chr4:171450001-171470000	SBP	1	5	4.03E-07	

Chr5:55220001-55240000	DBP	13	545	3.48E-05
Chr5:178790001-178810000	DBP	4	175	4.11E-05
Chr5:1420001-1440000	HTN	1	4	5.29E-05
Chr5:117320001-117340000	SBP	4	121	7.04E-05
Chr5:139350001-139370000	SBP	9	48	3.87E-05
Chr6:43880001-43900000	DBP	10	116	6.77E-05
Chr6:43870001-43890000	SBP	11	134	2.64E-05
Chr6:43710001-43730000	SBP	9	324	8.64E-05
Chr6:43880001-43900000	SBP	10	116	5.54E-05
Chr7:156150001-156170000	HTN	4	32	4.04E-06
Chr7:33750001-33770000	SBP	8	177	5.02E-05
Chr8:63740001-63760000	HTN	11	299	5.57E-05
Chr8:63750001-63770000	HTN	10	294	4.82E-05
Chr8:40410001-40430000	SBP	1	5	9.89E-05
Chr8:79850001-79870000	SBP	8	35	4.52E-05
Chr8:122390001-122410000	SBP	1	6	7.61E-06
Chr9:68530001-68550000	SBP	7	52	2.96E-05
Chr10:79080001-79100000	DBP	9	316	9.48E-05
Chr10:83230001-83250000	DBP	1	258	9.29E-05
Chr10:125420001-125440000	HTN	3	61	2.72E-07
Chr10:79090001-79110000	SBP	6	179	6.43E-05
Chr10:121190001-121210000	SBP	3	22	3.82E-05
Chr12:67060001-67080000	HTN	2	13	6.85E-05
Chr12:113490001-113510000	HTN	11	289	1.69E-05
Chr13:50510001-50530000	DBP	5	46	2.45E-05
Chr13:52160001-52180000	DBP	1	48	4.04E-05
Chr13:65880001-65900000	SBP	12	178	5.57E-05
Chr13:65890001-65910000	SBP	10	163	8.76E-05
Chr14:65870001-65890000	SBP	4	20	7.06E-05
Chr16:86900001-86920000	HTN	24	598	4.17E-05
Chr16:86910001-86930000	HTN	27	726	1.54E-05
Chr16:7200001-7220000	SBP	22	490	7.65E-05
Chr19:3630001-3650000	DBP	12	175	5.30E-05
Chr19:18770001-18790000	SBP	25	281	9.68E-05
Chr20:10390001-10410000	DBP	7	137	4.18E-05
Chr21:29560001-29580000	SBP	5	164	7.55E-05

DBP, diastolic blood pressure (BP); HTN, hypertension; Min-P, minimum P-value; SBP, systolic BP; SMMAT-E, variant set mixed model association test - Efficient hybrid.

Table S10. Genes and chromosomal regions with SMMAT-E $P < 1E-4$ in aggregate rare variant analyses of the Asian ancestry sample.

Aggregate Unit	Phe	TOPMed			UK Biobank WES Data			Meta-analysis P-value
		Rare Variant Sites (N)	Rare Alleles (N)	SMMAT-E P-value	Rare Variant Sites (N)	Rare Alleles (N)	SMMAT-E P-value	
<i>Gene-based analysis (high confidence loss of function variants only)</i>								
PLA2G2D (Chr1:20111939-20119566)	SBP	1	17	5.27E-05	1	17	3.58E-01	2.24E-04
PLA2G2D (Chr1:20111939-20119566)	DBP	1	17	3.09E-06	1	17	6.78E-01	2.94E-05
ARMC3 (Chr10:22928024-23038527)	DBP	1	10	3.21E-05	0	0	NA	NA
GABRB3 (Chr15:26543546-26773763)	SBP	1	15	4.96E-07	0	0	NA	NA
ZSCAN10 (Chr16:3088890-3099294)	SBP	1	17	3.76E-05	1	8	6.43E-01	2.82E-04
PROCR (Chr20:35172072-35215989)	SBP	1	6	3.31E-05	0	0	NA	NA
<i>Gene-based analysis (Loss-of-function variants, missense variants, and protein altering indels)</i>								
PAPPA2 (Chr1:176463159-176845601)	SBP	1	10	1.87E-05	0	0	NA	NA
ZFYVE9 (Chr1:52142001-52348664)	SBP	5	29	2.27E-05	0	0	NA	NA
PDLIM5 (Chr4:94451857-94668227)	DBP	4	15	2.87E-05	1	48	1.52E-01	5.82E-05
PACS1 (Chr11:66070272-66244744)	DBP	3	12	6.86E-05	0	0	NA	NA
KIF3B (Chr20:32277651-32335011)	SBP	5	20	8.81E-07	0	0	NA	NA
<i>Gene-based analysis (Enhancer, promoter, and exonic variants with predicted functional relevance)</i>								
PLA2G2D (Chr1:20111939-20119566)	DBP	2	43	1.04E-05	1	17	6.78E-01	9.06E-05

ORC4 (Chr2:147930396-148021604)	DBP	12	121	3.37E-05	0	0	NA	NA
CFL1P5 (Chr5:69312818-69313953)	SBP	1	6	2.26E-05	0	0	NA	NA
GCDH (Chr19:12891129-12915345)	DBP	10	82	7.20E-05	1	4	1.21E-01	1.10E-04
SYCE2 (Chr19:12898229-12919674)	DBP	9	78	8.63E-05	1	4	1.21E-01	1.30E-04
KIF3B (Chr20:32277651-32335011)	SBP	9	38	1.41E-07	0	0	NA	NA

Sliding window analysis

Chr1:20100001-20120000	DBP	2	43	1.04E-05	NA	NA	NA	NA
Chr1:91330001-91350000	HTN	3	12	2.09E-06	NA	NA	NA	NA
Chr1:91340001-91360000	HTN	4	16	3.37E-06	NA	NA	NA	NA
Chr1:172090001-172110000	HTN	5	49	5.23E-05	NA	NA	NA	NA
Chr1:172100001-172120000	HTN	1	11	5.25E-05	NA	NA	NA	NA
Chr1:110680001-110700000	SBP	4	90	9.45E-06	NA	NA	NA	NA
Chr1:176580001-176600000	SBP	1	10	1.87E-05	NA	NA	NA	NA
Chr1:223780001-223800000	SBP	3	10	9.12E-05	NA	NA	NA	NA
Chr2:155630001-155650000	DBP	11	89	8.04E-05	NA	NA	NA	NA
Chr2:67010001-67030000	SBP	1	3	2.36E-05	NA	NA	NA	NA
Chr3:12250001-12270000	DBP	4	18	9.76E-05	NA	NA	NA	NA
Chr3:156210001-156230000	HTN	1	3	3.30E-05	NA	NA	NA	NA
Chr4:111290001-111310000	DBP	1	14	5.06E-05	NA	NA	NA	NA
Chr4:58130001-58150000	HTN	2	42	8.63E-05	NA	NA	NA	NA
Chr4:61610001-61630000	HTN	1	3	3.07E-05	NA	NA	NA	NA
Chr4:133140001-133160000	SBP	8	38	5.12E-05	NA	NA	NA	NA
Chr5:38020001-38040000	HTN	1	3	7.26E-05	NA	NA	NA	NA
Chr5:69310001-69330000	SBP	3	12	1.19E-05	NA	NA	NA	NA
Chr6:110080001-110100000	HTN	2	6	7.07E-05	NA	NA	NA	NA
Chr6:129290001-129310000	SBP	2	7	7.44E-05	NA	NA	NA	NA
Chr7:41660001-41680000	DBP	3	12	4.76E-05	NA	NA	NA	NA
Chr7:36430001-36450000	HTN	3	9	6.85E-05	NA	NA	NA	NA

Chr7:18840001-18860000	SBP	7	78	6.08E-05	NA	NA	NA	NA
Chr7:36860001-36880000	SBP	1	3	2.36E-05	NA	NA	NA	NA
Chr7:41660001-41680000	SBP	3	12	2.84E-05	NA	NA	NA	NA
Chr8:65490001-65510000	DBP	3	20	4.91E-05	NA	NA	NA	NA
Chr8:116210001-116230000	DBP	2	7	7.43E-05	NA	NA	NA	NA
Chr8:116210001-116230000	HTN	2	7	9.00E-05	NA	NA	NA	NA
Chr8:116220001-116240000	HTN	3	10	3.97E-06	NA	NA	NA	NA
Chr8:96340001-96360000	SBP	5	21	4.86E-05	NA	NA	NA	NA
Chr8:133640001-133660000	SBP	1	4	3.22E-05	NA	NA	NA	NA
Chr9:29800001-29820000	HTN	1	10	6.44E-05	NA	NA	NA	NA
Chr10:31410001-31430000	DBP	1	4	4.50E-05	NA	NA	NA	NA
Chr10:13080001-13100000	SBP	1	9	1.20E-05	NA	NA	NA	NA
Chr10:31410001-31430000	SBP	1	4	6.95E-05	NA	NA	NA	NA
Chr11:95690001-95710000	HTN	3	20	2.01E-05	NA	NA	NA	NA
Chr11:134570001-134590000	SBP	1	3	6.06E-05	NA	NA	NA	NA
Chr12:45900001-45920000	DBP	7	87	8.43E-05	NA	NA	NA	NA
Chr12:63260001-63280000	SBP	1	4	5.13E-05	NA	NA	NA	NA
Chr12:102950001-102970000	SBP	15	134	5.45E-05	NA	NA	NA	NA
Chr13:80100001-80120000	SBP	6	58	3.87E-05	NA	NA	NA	NA
Chr13:80110001-80130000	SBP	5	34	8.11E-05	NA	NA	NA	NA
Chr13:83680001-83700000	SBP	3	22	2.55E-05	NA	NA	NA	NA
Chr13:83690001-83710000	SBP	4	25	1.94E-05	NA	NA	NA	NA
Chr14:39140001-39160000	HTN	2	8	3.88E-05	NA	NA	NA	NA
Chr14:97240001-97260000	HTN	2	7	8.20E-05	NA	NA	NA	NA
Chr15:38390001-38410000	DBP	3	61	9.58E-05	NA	NA	NA	NA
Chr15:68330001-68350000	HTN	3	14	2.42E-05	NA	NA	NA	NA
Chr15:35310001-35330000	SBP	1	3	2.36E-05	NA	NA	NA	NA
Chr17:15270001-15290000	SBP	1	6	6.02E-05	NA	NA	NA	NA
Chr17:55240001-55260000	SBP	1	4	9.38E-05	NA	NA	NA	NA
Chr17:64920001-64940000	SBP	3	41	5.71E-05	NA	NA	NA	NA
Chr18:60200001-60220000	HTN	1	3	6.02E-05	NA	NA	NA	NA
Chr19:39780001-39800000	SBP	4	28	6.19E-05	NA	NA	NA	NA
Chr20:32300001-32320000	SBP	5	25	3.23E-08	NA	NA	NA	NA
Chr20:32310001-32330000	SBP	4	17	5.51E-07	NA	NA	NA	NA

Chr21:17640001-17660000	DBP	1	32	3.24E-05	NA	NA	NA	NA
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DBP, diastolic blood pressure (BP); HTN, hypertension; Min-P, minimum P-value; SBP, systolic BP; SMMAT-E, variant set mixed model association test -

Table S11. Genes and chromosomal regions with SMMAT-E $P < 1E-4$ in aggregate rare variant analyses of the European ancestry sample.

Aggregate Unit	Phe	TOPMed			UK Biobank WES Data			Meta-analysis P-value
		Rare Variant Sites (N)	Rare Alleles (N)	SMMAT-E P-value	Rare Variant Sites (N)	Rare Alleles (N)	SMMAT-E P-value	
<i>Gene-based analysis (high confidence loss of function variants only)</i>								
GPR156 (Chr3:120165481-120285074)	DBP	4	19	5.51E-05	4	195	6.04E-01	3.76E-04
DAND5 (Chr19:12969618-12974753)	DBP	4	24	7.48E-05	2	42	4.30E-01	3.65E-04
BPI (Chr20:38304150-38337505)	HTN	4	23	8.45E-05	3	54	8.63E-01	7.68E-04
<i>Gene-based analysis (Loss-of-function variants, missense variants, and protein altering indels)</i>								
AMY2B (Chr1:103554644-103579534)	HTN	22	507	4.27E-05	16	2548	5.10E-01	2.55E-04
RBM45 (Chr2:178112409-178129656)	SBP	7	82	1.01E-05	7	340	6.40E-01	8.37E-05
MZT2B (Chr2:130182262-130190727)	DBP	1	3	3.11E-05	1	5	3.10E-02	1.43E-05
RNF175 (Chr4:153710125-153760983)	SBP	6	278	8.25E-05	5	1545	7.54E-01	6.65E-04
TDRD1 (Chr10:114174442-114232669)	HTN	5	115	4.57E-05	4	775	1.00E+00	5.02E-04
ERG (Chr21:38367261-38661783)	DBP	8	41	3.28E-05	5	258	6.78E-01	2.60E-04
TST (Chr22:37010859-37020183)	DBP	18	95	3.43E-05	16	418	7.72E-01	3.05E-04
<i>Gene-based analysis (Enhancer, promoter, and exonic variants with predicted functional relevance)</i>								
RN7SL273P (Chr6:37361185-37361483)	HTN	1	4	7.52E-05	0	0	NA	NA
OR9N1P (Chr7:141911402-141912022)	SBP	4	44	1.38E-05	0	0	NA	NA
GATS (Chr7:100187988-100272274)	DBP	23	297	4.35E-05	17	1357	8.85E-01	4.30E-04

STAG3L5P-PVRIG2P-PILRB (Chr7:100336065-100367831)	DBP	16	266	3.98E-05	1	4	4.80E-01	2.27E-04
PVRIG2P (Chr7:100352318-100353936)	DBP	9	194	1.89E-05	0	0	NA	NA
STAG3L5P (Chr7:100336079-100341328)	DBP	15	261	3.24E-05	0	0	NA	NA
PILRB (Chr7:100358003-100367831)	DBP	10	199	2.41E-05	1	4	4.80E-01	1.43E-04
NDRG2 (Chr14:21016763-21070872)	DBP	64	1007	6.08E-05	34	3909	1.07E-02	9.95E-06
TPPP2 (Chr14:21024262-21036352)	DBP	36	649	5.87E-05	26	3237	1.69E-02	1.47E-05
RP11-297M9.1 (Chr16:9666885-9676843)	DBP	1	15	4.98E-05	0	0	NA	NA
RP11-27G24.3 (Chr18:59459072-59465682)	DBP	1	4	9.97E-05	1	11	8.51E-01	8.80E-04

Sliding window analysis

Chr1:185910001-185930000	DBP	10	92	2.8E-05	NA	NA	NA	NA
Chr1:2450001-2470000	HTN	2	23	4.3E-05	NA	NA	NA	NA
Chr1:94540001-94560000	HTN	3	56363	9.7E-05	NA	NA	NA	NA
Chr1:94550001-94570000	HTN	1	56342	1.9E-05	NA	NA	NA	NA
Chr1:28460001-28480000	SBP	5	22	3.7E-05	NA	NA	NA	NA
Chr1:99220001-99240000	SBP	5	23	8.4E-05	NA	NA	NA	NA
Chr1:99230001-99250000	SBP	2	16	3.9E-05	NA	NA	NA	NA
Chr2:50370001-50390000	DBP	10	66	8.2E-05	NA	NA	NA	NA
Chr2:174360001-174380000	DBP	4	48	7.0E-05	NA	NA	NA	NA
Chr2:10750001-10770000	HTN	1	3	6.1E-05	NA	NA	NA	NA
Chr2:117210001-117230000	HTN	2	7	8.0E-05	NA	NA	NA	NA
Chr2:193750001-193770000	HTN	1	4	7.2E-06	NA	NA	NA	NA
Chr3:130510001-130530000	DBP	8	752	4.4E-05	NA	NA	NA	NA
Chr3:130520001-130540000	DBP	6	746	3.9E-05	NA	NA	NA	NA
Chr3:41020001-41040000	HTN	2	15	8.9E-05	NA	NA	NA	NA
Chr3:145600001-145620000	HTN	1	17	5.3E-05	NA	NA	NA	NA
Chr4:124730001-124750000	DBP	2	403	2.3E-05	NA	NA	NA	NA

Chr4:124740001-124760000	DBP	3	406	1.6E-05	NA	NA	NA	NA
Chr4:154050001-154070000	DBP	2	68	4.5E-05	NA	NA	NA	NA
Chr4:181230001-181250000	DBP	28	556	7.9E-05	NA	NA	NA	NA
Chr4:75300001-75320000	HTN	1	3	3.1E-05	NA	NA	NA	NA
Chr5:117760001-117780000	HTN	5	42	2.4E-05	NA	NA	NA	NA
Chr5:6140001-6160000	SBP	1	4	9.9E-05	NA	NA	NA	NA
Chr5:127520001-127540000	SBP	12	151	1.7E-05	NA	NA	NA	NA
Chr5:172040001-172060000	SBP	16	164	6.5E-05	NA	NA	NA	NA
Chr5:172050001-172070000	SBP	11	138	4.3E-05	NA	NA	NA	NA
Chr6:37350001-37370000	HTN	1	4	7.5E-05	NA	NA	NA	NA
Chr7:100260001-100280000	DBP	1	135	9.1E-06	NA	NA	NA	NA
Chr7:100340001-100360000	DBP	10	199	2.4E-05	NA	NA	NA	NA
Chr7:133790001-133810000	DBP	11	277	1.9E-05	NA	NA	NA	NA
Chr7:98130001-98150000	HTN	1	4	5.2E-05	NA	NA	NA	NA
Chr7:141900001-141920000	SBP	7	69	4.0E-05	NA	NA	NA	NA
Chr8:83600001-83620000	DBP	8	54	1.4E-05	NA	NA	NA	NA
Chr8:49730001-49750000	HTN	5	26	3.6E-05	NA	NA	NA	NA
Chr8:62060001-62080000	HTN	1	21	9.2E-05	NA	NA	NA	NA
Chr8:141190001-141210000	HTN	1	38	9.9E-05	NA	NA	NA	NA
Chr9:23130001-23150000	HTN	17	520	9.3E-05	NA	NA	NA	NA
Chr9:23140001-23160000	HTN	21	510	1.5E-05	NA	NA	NA	NA
Chr9:23140001-23160000	SBP	21	510	6.5E-05	NA	NA	NA	NA
Chr9:125950001-125970000	SBP	64	1510	8.1E-05	NA	NA	NA	NA
Chr10:16900001-16920000	DBP	18	587	1.1E-05	NA	NA	NA	NA
Chr10:16990001-17010000	DBP	5	18	9.7E-05	NA	NA	NA	NA
Chr10:85480001-85500000	DBP	6	26	5.7E-05	NA	NA	NA	NA
Chr10:98310001-98330000	DBP	8	65	3.2E-05	NA	NA	NA	NA
Chr10:36150001-36170000	HTN	1	10	6.7E-07	NA	NA	NA	NA
Chr10:32950001-32970000	SBP	1	3	6.0E-05	NA	NA	NA	NA
Chr11:7670001-7690000	DBP	9	401	9.3E-05	NA	NA	NA	NA
Chr11:31950001-31970000	SBP	15	126	6.7E-05	NA	NA	NA	NA
Chr11:31960001-31980000	SBP	16	130	7.1E-05	NA	NA	NA	NA
Chr12:103130001-103150000	HTN	7	419	6.9E-05	NA	NA	NA	NA
Chr12:103140001-103160000	HTN	9	428	6.9E-05	NA	NA	NA	NA

Chr12:31140001-31160000	SBP	1	7	8.2E-05	NA	NA	NA	NA
Chr13:39670001-39690000	DBP	9	39	9.1E-05	NA	NA	NA	NA
Chr13:85800001-85820000	DBP	2	28	9.0E-05	NA	NA	NA	NA
Chr13:106210001-106230000	DBP	13	406	2.4E-05	NA	NA	NA	NA
Chr13:85800001-85820000	HTN	2	28	3.4E-05	NA	NA	NA	NA
Chr13:85800001-85820000	SBP	2	28	3.3E-05	NA	NA	NA	NA
Chr14:21010001-21030000	DBP	38	747	7.7E-05	NA	NA	NA	NA
Chr14:21020001-21040000	DBP	32	610	6.7E-05	NA	NA	NA	NA
Chr14:90360001-90380000	DBP	7	457	9.7E-05	NA	NA	NA	NA
Chr15:45870001-45890000	HTN	6	33	6.7E-05	NA	NA	NA	NA
Chr15:67440001-67460000	HTN	10	198	2.1E-05	NA	NA	NA	NA
Chr15:67450001-67470000	HTN	17	280	3.4E-06	NA	NA	NA	NA
Chr15:73990001-74010000	HTN	3	24	4.6E-05	NA	NA	NA	NA
Chr15:67440001-67460000	SBP	10	198	6.6E-05	NA	NA	NA	NA
Chr15:67450001-67470000	SBP	17	280	1.4E-05	NA	NA	NA	NA
Chr16:9660001-9680000	DBP	5	32	7.3E-05	NA	NA	NA	NA
Chr16:9670001-9690000	DBP	3	22	8.6E-05	NA	NA	NA	NA
Chr18:26260001-26280000	HTN	1	3	1.6E-05	NA	NA	NA	NA
Chr19:35430001-35450000	SBP	5	29	8.5E-05	NA	NA	NA	NA
Chr20:8100001-8120000	HTN	1	4	7.6E-05	NA	NA	NA	NA
Chr22:37000001-37020000		20	105	4.1E-05	NA	NA	NA	NA

DBP, diastolic blood pressure (BP); HTN, hypertension; Min-P, minimum P-value; SBP, systolic BP; SMMAT-E, variant set mixed model association test - Efficient hybrid.

Table S12. Genes and chromosomal regions with SMMAT-E $P < 1E-4$ in aggregate rare variant analyses of the Hispanic ancestry sample.

Aggregate Unit	Associated Trait	Rare Variant Sites (N)	Rare Alleles (N)	SMMAT-E P-value
<i>Gene-based analysis (high confidence loss of function variants only)</i>				
ESAM (Chr11:124753126-124762290)	DBP	1	47	2.86E-05
KIR3DL2 (Chr19:54850320-54867209)	HTN	1	3	7.57E-05
<i>Gene-based analysis (Loss-of-function variants, missense variants, and protein altering indels)</i>				
CACNA2D3 (Chr3:54122552-55074557)	HTN	8	117	8.59E-05
MRPS18B (Chr6:30617320-30626393)	DBP	2	7	4.09E-05
OSGIN2 (Chr8:89901868-89935614)	SBP	1	67	2.77E-05
SMC2 (Chr9:104093760-104141419)	SBP	7	128	6.56E-05
RTRAF (Chr14:51989546-52010694)	SBP	1	4	5.40E-05
<i>Gene-based analysis (Enhancer, promoter, and exonic variants with predicted functional relevance)</i>				
LYSMD1 (Chr1:151148496-151165902)	SBP	11	145	1.44E-05
FLOT1 (Chr6:30727709-30742851)	DBP	3	16	9.36E-05
TUBB (Chr6:30720201-30725426)	DBP	2	8	1.86E-05
TUBB (Chr6:30720201-30725426)	SBP	2	8	3.95E-06
OSGIN2 (Chr8:89901868-89935614)	SBP	1	67	2.77E-05
MSC (Chr8:71841542-71844496)	SBP	5	107	6.19E-05
SMC2 (Chr9:104093760-104141419)	SBP	10	145	7.43E-05
SMC2-AS1 (Chr9:104080024-104092474)	SBP	3	63	3.20E-05
C14orf166 (Chr14:51989546-52010694)	SBP	1	4	5.40E-05
RAB15 (Chr14:64945816-64972336)	SBP	5	50	6.48E-05
DNAH9 (Chr17:11598470-11970168)	SBP	48	715	2.76E-05
AC005387.2 (Chr19:18532908-18536188)	HTN	1	4	4.26E-05
<i>Sliding window analysis</i>				
Chr1:25020001-25040000	DBP	8	146	9.29E-05
Chr1:86630001-86650000	DBP	9	138	4.42E-06
Chr1:86640001-86660000	DBP	4	87	1.78E-06
Chr1:25020001-25040000	HTN	8	142	4.40E-05

Chr2:117940001-117960000	DBP	1	3	6.00E-05
Chr2:146430001-146450000	HTN	12	119	2.65E-05
Chr2:197000001-197020000	HTN	2	64	1.67E-05
Chr2:197000001-197020000	SBP	2	65	1.91E-05
Chr3:20001-40000	SBP	8	104	8.29E-06
Chr3:9660001-9680000	SBP	1	5	8.17E-05
Chr4:34510001-34530000	DBP	4	85	6.03E-05
Chr4:122920001-122940000	SBP	4	13	4.58E-05
Chr5:61820001-61840000	DBP	3	85	3.76E-05
Chr5:61830001-61850000	DBP	4	92	1.92E-05
Chr5:74150001-74170000	SBP	3	82	4.83E-05
Chr5:127470001-127490000	SBP	2	38	8.34E-05
Chr6:30720001-30740000	DBP	3	11	5.47E-06
Chr6:139830001-139850000	DBP	12	111	3.53E-05
Chr6:139840001-139860000	DBP	10	102	2.39E-05
Chr6:30720001-30740000	SBP	3	11	6.66E-05
Chr7:18650001-18670000	DBP	10	76	4.58E-05
Chr7:116040001-116060000	SBP	2	35	5.80E-05
Chr8:71830001-71850000	SBP	5	107	6.19E-05
Chr8:89910001-89930000	SBP	1	67	2.77E-05
Chr9:17010001-17030000	SBP	11	113	3.47E-05
Chr9:81360001-81380000	SBP	10	230	1.38E-05
Chr9:81370001-81390000	SBP	17	269	3.45E-05
Chr9:104080001-104100000	SBP	4	106	2.21E-05
Chr9:104090001-104110000	SBP	3	90	7.68E-06
Chr10:1130001-1150000	DBP	7	63	6.55E-05
Chr11:84500001-84520000	DBP	2	13	5.11E-05
Chr11:37780001-37800000	SBP	1	8	5.15E-05
Chr11:124950001-124970000	SBP	2	58	3.30E-05
Chr13:96860001-96880000	HTN	4	88	2.33E-05
Chr14:64940001-64960000	SBP	4	45	6.15E-05
Chr16:6610001-6630000	HTN	5	87	5.60E-05
Chr16:22750001-22770000	SBP	7	92	4.21E-05
Chr17:54410001-54430000	DBP	1	14	2.62E-05
Chr17:70420001-70440000	SBP	3	73	9.98E-05
Chr17:70430001-70450000	SBP	1	56	3.18E-05
Chr18:38460001-38480000	SBP	11	277	4.32E-06
Chr20:7000001-7020000	DBP	7	60	2.63E-05
Chr20:12860001-12880000	DBP	1	57	4.04E-06
Chr20:12870001-12890000	DBP	2	97	1.34E-05
Chr20:12860001-12880000	SBP	1	57	3.88E-06
Chr20:12870001-12890000	SBP	2	97	1.59E-05

DBP, diastolic blood pressure (BP); HTN, hypertension; Min-P, minimum P-value; SBP, systolic BP; SMMAT-E, variant set mixed model association test - Efficient hybrid.

Table S13. Genes and chromosomal regions with SMMAT-E $P < 1E-4$ in aggregate rare variant analyses of the Samoan ancestry sample.

Aggregate Unit	Associated Trait	Rare Variant Sites (N)	Rare Alleles (N)	SMMAT-E P-value
<i>Gene-based analysis (Enhancer, promoter, and exonic variants with predicted functional relevance)</i>				
RASL10B (Chr17:35731639-35743521)	HTN	1	3	4.16E-05
TAF15 (Chr17:35809484-35847242)	HTN	6	23	5.43E-05
GAS2L2 (Chr17:35744511-35753239)	HTN	1	3	4.16E-05
<i>Sliding window analysis</i>				
Chr1:213420001-213440000	HTN	1	4	5.20E-06
Chr2:224750001-224770000	SBP	1	4	7.97E-05
Chr13:103160001-103180000	SBP	3	27	4.64E-05
Chr16:71100001-71120000	DBP	1	3	9.97E-05
Chr16:50960001-50980000	SBP	3	9	5.45E-05
Chr17:35700001-35720000	HTN	1	4	9.81E-07
Chr17:35730001-35750000	HTN	1	3	4.16E-05
Chr22:33370001-33390000	HTN	1	25	7.58E-05

DBP, diastolic blood pressure (BP); HTN, hypertension; Min-P, minimum P-value; SBP, systolic BP; SMMAT-E, variant set mixed model association test - Efficient hybrid.

Table S14. SNVs identified by leave-one-out analyses of aggregated rare variant units with SMMAT-E $P < 1E-04$ in multi-ancestry analyses.

Aggregate Unit	Associated Trait	SMMAT-E P-value	Marker	rsID	Alleles (Alt/Ref)	AAF	LOO P-value	SVA P-value	Stage-2 Sample Availability
<i>Gene-based Analyses</i>									
RP13-514E23.1 (Chr4:86012296-86013874) [†]	HTN	8.97E-05	Chr4:86016539	rs974993552	G/A	4.90E-05	1.05E-02	1.72E-03	NA
RP13-514E23.1 (Chr4:86012296-86013874) [†]	HTN	8.97E-05	Chr4:86017181	rs183689080	C/T	1.00E-03	1.53E-03	2.62E-02	NA
SYT7 (Chr11:61513714-61588404) [†]	SBP	8.86E-05	Chr11:61515348	rs115815714	G/C	8.09E-03	6.07E-02	3.15E-05	MVP
DNAJB13 (Chr11:73950319-73970287) [*]	DBP	2.91E-05	Chr11:73964917	rs139317756	G/T	1.55E-03	4.13E-03	4.13E-04	UKBB
DNAJB13 (Chr11:73950319-73970287) [†]	DBP	7.14E-05	Chr11:73964917	rs139317756	G/T	1.55E-03	2.45E-02	4.13E-04	UKBB
DNAJB13 (Chr11:73950319-73970287) [*]	DBP	2.91E-05	Chr11:73969282	rs140556652	A/G	1.44E-03	2.24E-03	2.32E-03	UKBB, MVP
DNAJB13 (Chr11:73950319-73970287) [†]	DBP	7.14E-05	Chr11:73969282	rs140556652	A/G	1.44E-03	2.42E-03	2.32E-03	UKBB, MVP
RASAL1 (Chr12:113096515-113136248) [†]	SBP	4.73E-05	Chr12:113095320	rs566085858	G/T	5.29E-04	9.31E-04	8.06E-04	UKBB, MVP
RASAL1 (Chr12:113096515-113136248) [†]	SBP	4.73E-05	Chr12:113105737	rs142556970	G/A	1.86E-03	6.96E-03	1.32E-03	UKBB, MVP
SMARCD1 (Chr12:50085236-50100707) [†]	HTN	4.95E-05	Chr12:50081692	rs140894777	G/A	7.59E-03	2.86E-03	4.65E-03	UKBB, MVP
SMARCD1 (Chr12:50085236-50100707) [†]	HTN	4.95E-05	Chr12:50086319	rs139120093	T/G	2.75E-03	8.14E-03	1.23E-03	UKBB, MVP
GABRB3 (Chr15:26543546-26773763) [‡]	SBP	2.67E-06	Chr15:26628999	rs990895163	T/C	1.47E-04	3.95E-01	9.46E-07	MVP

ZNF431 (Chr19:21142009-21196053) [†]	SBP	8.40E-05	Chr19:21151200	rs145645636	T/C	9.47E-03	4.95E-02	2.34E-04	UKBB, MVP
<i>Sliding Window Analyses</i>									
Chr1:227060001-227080000	DBP	4.93E-05	Chr1:227068762	rs754226051	T/TAATA	6.27E-04	4.01E-01	1.50E-05	NA
Chr2:196990001-197010000	DBP	8.12E-05	Chr2:196992672	rs933406987	T/G	2.12E-03	7.59E-04	2.34E-02	NA
Chr2:211720001-211740000	HTN	8.15E-06	Chr2:211725173	rs148992844	G/T	3.82E-04	3.45E-01	5.39E-06	MVP
Chr2:137760001-137780000	SBP	4.98E-05	Chr2:137770284	rs189500544	G/A	1.32E-03	1.16E-01	1.04E-05	UKBB, MVP
Chr2:137770001-137790000	SBP	2.75E-05	Chr2:137770284	rs189500544	G/A	1.32E-03	3.95E-01	1.04E-05	UKBB, MVP
Chr3:60900001-60920000	DBP	4.14E-05	Chr3:60914975	rs191538623	A/T	1.02E-03	1.35E-03	3.02E-03	UKBB
Chr3:60900001-60920000	DBP	4.14E-05	Chr3:60916708	rs551024841	T/C	6.46E-04	2.03E-03	9.07E-04	UKBB, MVP
Chr3:60910001-60930000	DBP	8.32E-05	Chr3:60914975	rs191538623	A/T	1.02E-03	2.44E-03	3.02E-03	UKBB
Chr3:60910001-60930000	DBP	8.32E-05	Chr3:60916708	rs551024841	T/C	6.46E-04	3.28E-03	9.07E-04	UKBB, MVP
Chr3:100320001-100340000	HTN	4.32E-06	Chr3:100339146	rs373731645	T/C	2.74E-04	1.18E-04	2.46E-03	UKBB
Chr3:100320001-100340000	HTN	4.32E-06	Chr3:100339149	rs200416332	A/G	8.63E-04	2.09E-04	2.53E-03	UKBB, MVP
Chr3:130510001-130530000	DBP	3.69E-05	Chr3:130523920	rs191631641	A/G	7.05E-04	6.82E-04	1.16E-02	UKBB, MVP
Chr3:130520001-130540000	DBP	3.37E-05	Chr3:130523920	rs191631641	A/G	7.05E-04	6.38E-04	1.16E-02	UKBB, MVP
Chr3:179510001-179530000	DBP	6.44E-05	Chr3:179512562	rs150627458	T/G	4.15E-03	1.05E-03	2.08E-02	NA
Chr3:179510001-179530000	DBP	6.44E-05	Chr3:179512636	rs1010846518	A/T	1.76E-04	1.91E-02	4.85E-04	NA
Chr4:38240001-38260000	SBP	3.55E-05	Chr4:38254212	rs1000667787	C/T	3.03E-04	1.00E-02	4.10E-04	UKBB, MVP
Chr4:44130001-44150000	DBP	1.47E-05	Chr4:44148142	rs142082332	A/T	1.07E-03	6.88E-01	8.44E-07	UKBB
Chr4:44140001-44160000	DBP	1.50E-05	Chr4:44148142	rs142082332	A/T	1.07E-03	4.42E-01	8.44E-07	UKBB
Chr4:47020001-47040000	SBP	2.28E-05	Chr4:47031478	rs944297641	C/G	3.72E-04	3.41E-03	4.77E-04	UKBB, MVP
Chr4:47030001-47050000	SBP	4.43E-05	Chr4:47031478	rs944297641	C/G	3.72E-04	5.60E-03	4.77E-04	UKBB, MVP
Chr4:47030001-47050001	SBP	4.43E-05	Chr4:47031545	rs80151988	T/C	4.89E-04	7.01E-04	1.85E-02	UKBB, MVP
Chr4:98480001-98500000	HTN	3.55E-05	Chr4:98482187	rs767187895	T/G	5.88E-05	4.09E-01	1.13E-05	NA
Chr4:124730001-124750000	DBP	2.62E-05	Chr4:124746752	rs1050104610	C/T	5.97E-04	5.90E-01	6.24E-06	UKBB
Chr4:124740001-124760000	DBP	1.77E-05	Chr4:124746752	rs1050104610	C/T	5.97E-04	4.74E-01	6.24E-06	UKBB
Chr4:154050001-154070000	DBP	6.22E-05	Chr4:154069962	rs938675698	C/A	3.92E-05	3.68E-01	2.01E-05	UKBB
Chr5:57890001-57910000	DBP	1.93E-06	Chr5:57902163	rs780345403	G/A	2.94E-05	2.35E-04	9.53E-04	UKBB
Chr5:57890001-57910000	SBP	5.45E-06	Chr5:57902163	rs780345403	G/A	2.94E-05	1.35E-02	3.29E-05	UKBB, MVP
Chr5:67070001-67090000	DBP	2.70E-05	Chr5:67086333	rs114440422	A/G	3.80E-03	1.52E-01	2.19E-05	UKBB, MVP
Chr5:72090001-72110000	DBP	3.81E-05	Chr5:72108931	rs868778481	T/G	2.64E-04	2.58E-03	6.93E-04	NA
Chr5:88000001-88020000	DBP	8.81E-05	Chr5:88001000	rs114144963	T/C	9.23E-03	1.53E-03	3.60E-03	UKBB, MVP
Chr7:90860001-90880000	DBP	8.07E-05	Chr7:90863943	rs371264131	T/G	5.58E-04	2.04E-03	3.02E-03	NA

Chr7:90860001-90880000	DBP	8.07E-05	Chr7:90864174	rs1030911105	A/T	2.94E-04	1.08E-02	3.40E-04	NA
Chr8:137320001-137340000	DBP	1.46E-05	Chr8:137337574	rs141392410	G/A	5.21E-03	6.33E-01	1.46E-06	MVP
Chr8:137330001-137350000	DBP	1.06E-05	Chr8:137337574	rs141392410	G/A	5.21E-03	3.84E-01	1.46E-06	MVP
Chr8:122390001-122410000	SBP	3.94E-05	Chr8:122408882	rs367736389	G/T	5.87E-05	9.05E-01	8.45E-06	MVP
Chr9:23130001-23150000	HTN	2.98E-05	Chr9:23142518	rs564818044	A/G	3.79E-03	2.97E-01	4.72E-06	UKBB
Chr9:23140001-23160000	HTN	3.31E-05	Chr9:23142518	rs564818044	A/G	3.79E-03	2.57E-01	4.72E-06	UKBB
Chr9:29800001-29820000	HTN	9.43E-05	Chr9:29801378	rs1371954572	G/T	9.80E-05	7.12E-01	2.21E-05	NA
Chr10:65280001-65300000	HTN	3.91E-05	Chr10:65299666	rs7093615	C/A	9.10E-03	5.58E-02	1.85E-04	UKBB, MVP
Chr10:13090001-13110000	SBP	4.21E-05	Chr10:13098598	rs550006396	C/T	8.81E-05	3.76E-01	1.42E-05	MVP
Chr11:44770001-44790000	DBP	7.72E-05	Chr11:44777625	rs189859777	T/G	1.82E-03	2.41E-02	4.74E-04	UKBB, MVP
Chr11:61730001-61750000	DBP	7.56E-05	Chr11:61746842	rs983334527	G/A	7.83E-04	1.04E-03	1.14E-02	UKBB
Chr11:61730001-61750000	DBP	7.56E-05	Chr11:61746887	rs746100983	C/CTA	7.15E-04	4.63E-03	2.89E-03	UKBB
Chr11:73950001-73970000	DBP	3.18E-05	Chr11:73964917	rs139317756	G/T	1.55E-03	7.31E-03	4.13E-04	UKBB
Chr11:73950001-73970000	DBP	3.18E-05	Chr11:73969282	rs140556652	A/G	1.44E-03	1.70E-03	2.32E-03	UKBB, MVP
Chr12:50070001-50090000	HTN	2.82E-05	Chr12:50081692	rs140894777	G/A	7.59E-03	1.68E-03	4.65E-03	UKBB, MVP
Chr12:50080001-50100000	HTN	9.66E-05	Chr12:50081692	rs140894777	G/A	7.59E-03	2.73E-03	4.65E-03	UKBB, MVP
Chr12:50070001-50090000	HTN	2.82E-05	Chr12:50086319	rs139120093	T/G	2.75E-03	2.96E-03	1.23E-03	UKBB, MVP
Chr12:50080001-50100000	HTN	9.66E-05	Chr12:50086319	rs139120093	T/G	2.75E-03	8.22E-03	1.23E-03	UKBB, MVP
Chr12:113090001-113110000	SBP	6.93E-06	Chr12:113105737	rs142556970	G/A	1.86E-03	3.12E-04	1.32E-03	UKBB, MVP
			Chr12:113501009	rs755099793	A/G	1.96E-04		9.53E-04	UKBB
Chr12:113490001-113510000	HTN	8.71E-05	Chr12:113501133	rs1469796200	T/G	1.96E-04	8.04E-03	9.53E-04	NA
			Chr12:113505779	rs147740157	T/C	2.25E-04		7.72E-03	UKBB
Chr13:50510001-50530000	DBP	5.23E-05	Chr13:50522634	rs562185001	A/T	3.13E-04	5.82E-02	8.23E-05	MVP
Chr14:18320001-18340000	HTN	2.59E-05	Chr14:18333823	rs564618809	T/G	2.94E-05	9.92E-01	5.61E-06	NA
Chr15:38380001-38400000	DBP	8.63E-05	Chr15:38398323	rs755289280	T/C	9.79E-05	1.48E-03	6.96E-03	NA
Chr15:38380001-38400000	DBP	8.63E-05	Chr15:38398386	rs145063865	A/G	4.70E-04	1.53E-03	4.03E-03	UKBB
Chr15:47480001-47500000	DBP	9.55E-05	Chr15:47494978	rs564740962	T/G	1.08E-04	3.35E-03	1.49E-04	UKBB
Chr15:47480001-47500000	DBP	9.55E-05	Chr15:47496058	rs181561558	G/C	6.17E-04	1.12E-03	9.57E-04	MVP
Chr15:41570001-41590000	HTN	4.89E-05	Chr15:41570322	rs146237670	A/G	6.18E-04	6.72E-03	1.66E-03	UKBB
Chr15:48270001-48290000	HTN	3.86E-05	Chr15:48279516	rs896510696	C/A	2.55E-04	1.02E-02	1.36E-04	NA
Chr17:70430001-70450000	SBP	2.92E-05	Chr17:70438250	rs182046693	A/G	6.36E-04	8.46E-01	3.49E-06	UKBB, MVP
Chr18:76450001-76470000	HTN	5.74E-05	Chr18:76450108	rs566120109	G/T	7.84E-05	8.39E-03	1.45E-03	NA
Chr18:76450001-76470000	HTN	5.74E-05	Chr18:76451735	rs75564345	G/A	3.31E-03	5.34E-03	1.92E-03	NA
Chr19:21150001-21170000	SBP	2.80E-05	Chr19:21151200	rs145645636	T/C	9.47E-03	7.04E-03	2.34E-04	UKBB, MVP

Chr22:34420001-34440000 DBP 9.84E-05 Chr22:34433540 rs534864747 T/C 4.50E-04 4.81E-02 1.74E-04 UKBB

AAF, alternative allele frequency; DBP, diastolic blood pressure (BP); HTN, hypertension; LOO, leave-One-Out; MVP, Million Veteran Program; SBP, systolic BP; SMMAT-E, variant set mixed model association test - Efficient hybrid.; SVA, single variant analysis; UKBB, UK Biobank.

* Identified in gene-based analyses of exonic loss-of-function, missense, and protein altering insertion-deletion variants. † Identified in gene-based analyses of regulatory regions and exonic variants with predicted functional relevance. ‡ Identified in gene-based analyses of high confidence loss-of-function variants.

Table S15. SNVs identified by leave-one-out analyses of aggregate rare variant units with SMMAT-E $P < 1E-04$ in participants of African ancestry.

Aggregate Unit	Associated Trait	SMMAT-E P-value	Marker	rsID	Alleles (Alt/Ref)	AAF	LOO P-value	SVA P-value	Stage-2 Sample Availability
<i>Gene-based Analyses</i>									
AGTRAP (Chr1:11736085-11750771)*	SBP	9.70E-05	Chr1:11750140	rs17875960	T/C	1.35E-03	5.21E-02	4.74E-04	MVP
LEXM (Chr1:54806063-54842264) [†]	DBP	3.20E-05	Chr1:54810479	rs187674266	T/C	2.88E-03	6.77E-01	6.57E-06	MVP, REGARDS
			Chr1:54810596	rs377560726	G/C	2.95E-03		3.83E-06	NA
ERBB4 (Chr2:211375717-212538802) [‡]	HTN	6.50E-05	Chr2:211725173	rs148992844	G/T	1.28E-03	6.91E-01	4.08E-06	MVP, REGARDS
MCIDAS (Chr5:55218791-55227315) [†]	DBP	1.89E-05	Chr5:55220484	rs561481156	A/G	1.24E-03	7.35E-04	3.04E-03	MVP, REGARDS
MCIDAS (Chr5:55218791-55227315) [†]	DBP	1.89E-05	Chr5:55227016	rs186341559	T/C	1.20E-03	3.48E-04	8.43E-03	MVP
PLAT (Chr8:42174718-42207565) [‡]	DBP	4.11E-05	Chr8:42178946	rs61755432	G/C	4.01E-04	6.06E-04	1.54E-02	MVP
PLAT (Chr8:42174718-42207565) [‡]	DBP	4.11E-05	Chr8:42180509	rs140012141	T/C	2.19E-04	2.42E-03	2.35E-04	MVP
BLNK (Chr10:96189171-96271576) [‡]	HTN	9.49E-05	Chr10:96230820	rs148249957	T/C	8.42E-04	1.88E-02	4.14E-04	NA
GOLT1B (Chr12:21501176-21518408) [‡]	DBP	3.15E-05	Chr12:21512311	rs34378602	A/G	4.74E-04	8.32E-03	1.27E-04	MVP
G6PC3 (Chr17:44070700-44076344)*	HTN	1.15E-05	Chr17:44075766	rs763408993	A/G	1.10E-04	9.77E-01	9.77E-01	NA
WDR87 (Chr19:37884577-37906617) [†]	SBP	7.67E-05	Chr19:37906500	rs982829890	C/T	2.92E-04	2.86E-02	2.64E-04	MVP
			Chr19:37906499	rs934092610	A/C	2.92E-04		2.64E-04	NA
WDR87 (Chr19:37884577-37906617) [†]	DBP	3.84E-05	Chr19:37906500	rs982829890	C/T	2.92E-04	5.51E-03	2.09E-04	MVP
			Chr19:37906499	rs934092610	A/C	2.92E-04		2.09E-04	NA

GTPBP1 (Chr22:38704561-38738265) [†]	SBP	8.79E-05	Chr22:38730743	rs201889482	G/C	2.63E-03	7.06E-03	6.04E-04	REGARDS
<i>Sliding Windows Analyses</i>									
Chr1:54800001-54820000	DBP	2.04E-05	Chr1:54810479	rs187674266	T/C	2.88E-03	4.66E-01	6.57E-06	MVP, REGARDS
			Chr1:54810596	rs377560726	G/C	2.95E-03		3.83E-06	NA
Chr1:54810001-54830000	DBP	2.04E-05	Chr1:54810479	rs187674266	T/C	2.88E-03	4.84E-01	6.57E-06	MVP, REGARDS
			Chr1:54810596	rs377560726	G/C	2.95E-03		3.83E-06	NA
Chr2:67990001-68010000	DBP	2.23E-05	Chr2:67991717	rs186944582	C/T	6.20E-04	5.12E-03	4.68E-04	MVP
Chr2:49510001-49530000	HTN	8.68E-06	Chr2:49514339	rs185293219	A/T	8.79E-04	1.06E-04	2.00E-02	NA
Chr2:49510001-49530000	HTN	8.68E-06	Chr2:49516603	rs951053055	C/A	9.89E-04	3.25E-04	5.52E-03	NA
Chr2:183010001-183030000	HTN	6.29E-05	Chr2:18302497	rs560702795	A/G	1.83E-04	1.27E-01	1.74E-05	NA
Chr2:211710001-211730000	HTN	3.04E-05	Chr2:211725173	rs148992844	G/T	1.28E-03	5.18E-01	4.08E-06	MVP, REGARDS
Chr2:211720001-211740000	HTN	1.25E-05	Chr2:211725173	rs148992844	G/T	1.28E-03	3.56E-01	4.08E-06	MVP, REGARDS
Chr2:67990001-68010000	SBP	6.29E-05	Chr2:67991717	rs186944582	C/T	6.20E-04	1.51E-03	5.05E-03	MVP
Chr2:67990001-68010000	SBP	6.29E-05	Chr2:67997967	rs62143849	T/G	9.92E-03	3.23E-03	2.02E-03	MVP, REGARDS
Chr2:137760001-137780000	SBP	9.05E-05	Chr2:137770284	rs189500544	G/A	4.52E-03	5.73E-01	2.51E-05	MVP, REGARDS
Chr2:137770001-137790000	SBP	7.97E-05	Chr2:137770284	rs189500544	G/A	4.52E-03	3.79E-01	2.51E-05	MVP, REGARDS
Chr3:88430001-88450000	DBP	7.04E-05	Chr3:88441450	rs73140398	C/T	6.49E-03	2.10E-01	1.65E-05	MVP, REGARDS
Chr3:88440001-88460000	DBP	6.66E-05	Chr3:88441450	rs73140398	C/T	6.49E-03	1.86E-01	1.65E-05	MVP, REGARDS
Chr3:19030001-19050000	HTN	1.46E-05	Chr3:19043301	rs114748767	T/C	6.96E-04	1.42E-02	2.44E-01	NA
Chr3:59310001-59330000	SBP	9.30E-05	Chr3:59314770	rs147047791	G/A	9.85E-03	7.24E-02	1.55E-04	MVP, REGARDS
Chr4:22930001-22950000	DBP	2.80E-06	Chr4:22946729	rs538084432	C/A	3.25E-03	1.17E-02	3.52E-05	MVP, REGARDS
Chr4:22940001-22960000	DBP	1.52E-05	Chr4:22946729	rs538084432	C/A	3.25E-03	5.06E-02	3.52E-05	MVP, REGARDS
Chr5:55220001-55240000	DBP	3.48E-05	Chr5:55220484	rs561481156	A/G	0.00124	9.56E-04	3.04E-03	MVP, REGARDS
Chr5:178790001-178810000	DBP	4.11E-05	Chr5:178797566	rs56393219	C/T	5.36E-03	1.47E-01	6.82E-05	MVP, REGARDS
Chr5:117320001-117340000	SBP	7.04E-05	Chr5:117321344	rs1011005843	C/A	3.65E-04	4.00E-02	2.73E-04	MVP
Chr5:139350001-139370000	SBP	3.87E-05	Chr5:139369019	rs992889791	G/A	3.65E-04	3.07E-01	5.99E-06	MVP
Chr6:43880001-43900000	DBP	6.77E-05	Chr6:43886163	rs575546272	A/G	1.50E-03	1.00E-01	7.31E-05	MVP, REGARDS

Chr6:43710001-43730000	SBP	8.64E-05	Chr6:43716303	rs927672578	T/C	1.82E-04	1.24E-03	5.46E-02	NA
Chr6:43880001-43900000	SBP	5.54E-05	Chr6:43888614	rs187143472	A/G	1.46E-04	9.71E-02	3.44E-01	NA
Chr7:156150001-156170000	HTN	4.04E-06	Chr7:156151808	rs370654804	A/G	1.83E-04	2.44E-02	3.96E-06	NA
Chr7:156150001-156170000	HTN	4.04E-06	Chr7:156151872	rs951619037	G/T	1.46E-04	3.68E-04	1.84E-03	NA
Chr7:33750001-33770000	SBP	5.02E-05	Chr7:33768785	rs145533052	T/A	0.001677	1.75E-02	4.16E-04	NA
			Chr7:33768926	rs140330896	G/A	0.001677		4.16E-04	NA
Chr8:63740001-63760000	HTN	5.57E-05	Chr8:63750032	rs117550253	G/A	3.70E-03	1.00E-03	5.77E-03	REGARDS
Chr8:79850001-79870000	SBP	4.52E-05	Chr8:79864885	rs1361009224	T/C	2.19E-04	1.53E-02	1.28E-04	MVP
Chr9:68530001-68550000	SBP	2.96E-05	Chr9:68540871	rs967141166	C/G	3.65E-04	1.13E-03	1.76E-03	MVP
Chr10:79080001-79100000	DBP	9.48E-05	Chr10:79093901	rs376054383	A/G	2.59E-03	3.41E-03	1.60E-03	MVP, REGARDS
Chr10:125420001-125440000	HTN	2.72E-07	Chr10:125430074	.	T/TTATAACAATTAGA		1.18E-01	1.95E-10	NA
Chr10:79090001-79110000	SBP	6.43E-05	Chr10:79093901	rs376054383	A/G	2.59E-03	3.24E-03	2.25E-03	MVP, REGARDS
Chr10:79090001-79110000	SBP	6.43E-05	Chr10:79093991	rs181444929	A/C	2.63E-03	1.14E-03	4.55E-03	MVP, REGARDS
Chr12:67060001-67080000	HTN	6.85E-05	Chr12:67069886	rs940692929	T/G	1.46E-04	3.19E-03	1.09E-03	NA
Chr12:67060001-67080000	HTN	6.85E-05	Chr12:67078940	rs910612640	G/A	3.30E-04	1.09E-03	3.19E-03	NA
			Chr12:113501009	rs755099793	A/G	0.000696		7.83E-04	NA
Chr12:113490001-113510000	HTN	1.69E-05	Chr12:113501133	rs1469796200	T/G	0.000696	3.02E-03	7.84E-04	NA
			Chr12:113505779	rs147740157	T/C	0.000696		7.84E-04	NA
Chr13:50510001-50530000	DBP	2.45E-05	Chr13:50522634	rs562185001	A/T	1.09E-03	6.68E-02	5.46E-05	MVP
Chr13:65880001-65900000	SBP	5.57E-05	Chr13:65893301	rs190642412	G/A	9.85E-04	5.40E-03	1.98E-03	MVP, REGARDS
Chr13:65890001-65910000	SBP	8.76E-05	Chr13:65893301	rs190642412	G/A	9.85E-04	9.05E-03	1.98E-03	MVP, REGARDS
Chr14:65870001-65890000	SBP	7.06E-05	Chr14:65881012	rs966803342	G/A	1.46E-04	1.17E-02	6.55E-04	MVP
Chr14:65870001-65890000	SBP	7.06E-05	Chr14:65881049	rs1290317159	T/C	1.09E-04	8.53E-03	4.89E-04	MVP
Chr16:86900001-86920000	HTN	4.17E-05	Chr16:86910821	rs139148897	G/A	7.14E-03	6.48E-04	1.25E-02	REGARDS
Chr16:86900001-86920000	HTN	4.17E-05	Chr16:86919817	rs566276270	T/G	3.48E-03	1.48E-02	2.12E-04	REGARDS
Chr16:86910001-86930000	HTN	1.54E-05	Chr16:86910821	rs139148897	G/A	7.14E-03	2.75E-04	1.25E-02	REGARDS
Chr16:86910001-86930000	HTN	1.54E-05	Chr16:86919817	rs566276270	T/G	3.48E-03	5.81E-03	2.12E-04	REGARDS
Chr16:7200001-7220000	SBP	7.65E-05	Chr16:7206559	rs554538972	G/C	6.53E-03	1.94E-01	3.46E-05	MVP, REGARDS
Chr19:3630001-3650000	DBP	5.30E-05	Chr19:3641786	rs148921132	C/T	4.01E-04	1.16E-03	7.34E-03	MVP
Chr19:18770001-18790000	SBP	9.68E-05	Chr19:18789554	rs868041658	A/G	1.93E-03	1.12E-01	7.79E-05	MVP, REGARDS
Chr20:10390001-10410000	DBP	4.18E-05	Chr20:10405335	rs372944937	C/A	4.38E-04	3.11E-02	3.11E-07	MVP
Chr21:29560001-29580000	SBP	7.55E-05	Chr21:29579574	rs528525042	G/A	7.66E-04	4.77E-01	1.93E-05	MVP

AAF, alternative allele frequency; DBP, diastolic blood pressure (BP); HTN, hypertension; LOO, leave-One-Out; MVP, Million Veteran Program; SBP, systolic BP; SMMAT-E, variant set mixed model association test - Efficient hybrid.; SVA, single variant analysis; UKBB, UK Biobank.

* Identified in gene-based analyses of high confidence loss-of-function variants. † Identified in gene-based analyses of regulatory regions and exonic variants with predicted functional relevance. ‡ Identified in gene-based analyses of exonic loss-of-function, missense, and protein altering insertion-deletion variants.

Table S16. SNVs identified by leave-one-out analyses of aggregate rare variant units with SMMAT-E $P < 1E-04$ in participants of Asian ancestry.

Aggregate Unit	Associated Trait	SMMAT-E P-value	Marker	rsID	Alleles (Alt/Ref)	AAF	LOO P-value	SVA P-value	Stage-2 Sample Availability
<i>Gene-based Analyses</i>									
PLA2G2D (Chr1:20111939-20119566)*	DBP	1.04E-05	Chr1:20119457	rs200435430	C/A	2.25E-03	4.50E-01	5.27E-05	NA
ZFYVE9 (Chr1:52142001-52348664) [†]	SBP	2.27E-05	Chr1:52237880	rs759041526	A/C	9.25E-04	1.35E-03	2.46E-03	NA
ZFYVE9 (Chr1:52142001-52348664) [†]	SBP	2.27E-05	Chr1:52278519	rs751858399	G/A	1.32E-03	2.18E-03	1.56E-03	NA
ORC4 (Chr2:147930396-148021604)*	DBP	3.37E-05	Chr2:147958805	rs138317624	C/T	6.61E-03	3.00E-03	6.66E-04	NA
PDLIM5 (Chr4:94451857-94668227) [†]	DBP	2.87E-05	Chr4:94455353	rs75841704	G/A	3.97E-04	4.43E-04	1.40E-02	NA
PDLIM5 (Chr4:94451857-94668227) [†]	DBP	2.87E-05	Chr4:94523782	rs749144218	A/G	5.29E-04	4.52E-04	1.42E-02	NA
PDLIM5 (Chr4:94451857-94668227) [†]	DBP	2.87E-05	Chr4:94587018	rs746639901	A/C	6.61E-04	1.53E-03	3.38E-03	NA
PACS1 (Chr11:66070272-66244744) [†]	DBP	6.86E-05	Chr11:66216143	rs773415096	T/G	3.97E-04	1.81E-01	4.08E-05	NA
GCDH (Chr19:12891129-12915345)*	DBP	7.20E-05	Chr19:12894791	rs1199960037	C/G	2.91E-03	2.38E-01	1.80E-05	NA
SYCE2 (Chr19:12898229-12919674)*	DBP	8.63E-05	Chr19:12894791	rs1199960037	C/G	2.91E-03	2.57E-01	1.80E-05	NA
KIF3B (Chr20:32277651-32335011)*	SBP	1.41E-07	Chr20:32309709	rs1393521306	G/C	1.06E-03	1.90E-06	3.61E-03	NA
KIF3B (Chr20:32277651-32335011)*	SBP	1.41E-07	Chr20:32311097	rs758426820	A/G	9.25E-04	7.79E-03	6.25E-07	NA
KIF3B (Chr20:32277651-32335011) [†]	SBP	8.81E-07	Chr20:32311097	rs758426820	A/G	9.25E-04	6.41E-02	6.25E-07	NA

Sliding Windows Analyses

Chr1:20100001-20120000	DBP	1.04E-05	Chr1:20119457	rs200435430	C/A	2.25E-03	4.50E-01	3.09E-06	NA
Chr1:91330001-91350000	HTN	2.09E-06	Chr1:91343440	rs759737721	T/G	5.29E-04	1.61E-03	2.40E-05	NA
Chr1:91340001-91360000	HTN	3.37E-06	Chr1:91343440	rs759737721	T/G	5.29E-04	5.57E-03	2.40E-05	NA
Chr1:91330001-91350000	HTN	2.09E-06	Chr1:91347482	rs576342909	A/T	6.61E-04	8.23E-05	5.42E-04	NA
Chr1:91340001-91360000	HTN	3.37E-06	Chr1:91347482	rs576342909	A/T	6.61E-04	2.76E-04	5.42E-04	NA
Chr1:110680001-110700000	SBP	9.45E-06	Chr1:110688867	rs1198157802	A/G	1.45E-03	1.63E-04	1.33E-02	NA
Chr1:110680001-110700000	SBP	9.45E-06	Chr1:110697306	rs375447719	G/A	2.25E-03	2.20E-02	8.67E-05	NA
Chr1:172090001-172110000	HTN	5.23E-05	Chr1:172109590	rs1435289259	G/T	1.45E-03	7.68E-02	5.25E-05	NA
Chr1:223780001-223800000	SBP	9.12E-05	Chr1:223799909	rs756133979	T/C	5.29E-04	7.67E-02	3.55E-05	NA
Chr2:155630001-155650000	DBP	8.04E-05	Chr2:155643289	rs1206485253	T/G	1.32E-03	3.82E-01	3.73E-07	NA
Chr3:12250001-12270000	DBP	9.76E-05	Chr3:12264248	rs945462322	T/G	6.61E-04	2.43E-02	6.67E-04	NA
Chr3:12250001-12270000	DBP	9.76E-05	Chr3:12267974	rs1211914898	T/G	3.97E-04	2.56E-03	3.58E-03	NA
Chr4:58130001-58150000	HTN	8.63E-05	Chr4:58136852	rs142264842	T/G	5.02E-03	5.86E-01	1.75E-05	NA
Chr4:133140001-133160000	SBP	5.12E-05	Chr4:133153900	rs1468781808	C/T	3.97E-04	8.12E-04	4.21E-03	NA
Chr5:69310001-69330000	SBP	1.19E-05	Chr5:69313828	rs1295351182	A/G	7.93E-04	4.94E-02	2.26E-05	NA
Chr6:110080001-110100000	HTN	7.07E-05	Chr6:110099957	rs910798455	C/T	3.97E-04	2.69E-01	2.47E-05	NA
Chr6:129290001-129310000	SBP	7.44E-05	Chr6:129293066	rs1391821039	A/G	3.97E-04	3.04E-01	2.36E-05	NA
Chr7:18840001-18860000	SBP	6.08E-05	Chr7:18842339	rs1374997232	G/A	1.19E-03	6.15E-03	1.83E-03	NA
Chr7:18840001-18860000	SBP	6.08E-05	Chr7:18859501	rs1396276058	T/C	5.29E-04	1.23E-03	6.23E-03	NA
Chr7:36430001-36450000	HTN	6.85E-05	Chr7:36443846	rs1432523754	T/A	3.97E-04	9.61E-02	9.56E-05	NA
Chr7:41660001-41680000	SBP	2.84E-05	Chr7:41668653	rs536958510	G/C	7.93E-04	4.69E-04	2.20E-03	NA
Chr7:41660001-41680000	SBP	2.84E-05	Chr7:41669933	rs148140557	T/C	3.97E-04	7.34E-03	1.20E-04	NA
Chr7:41660001-41680000	DBP	4.76E-05	Chr7:41669933	rs148140557	T/C	3.97E-04	8.58E-03	1.18E-04	NA
Chr8:65490001-65510000	DBP	4.91E-05	Chr8:65490278	rs190587924	G/C	1.19E-03	5.98E-04	1.87E-02	NA
Chr8:65490001-65510000	DBP	4.91E-05	Chr8:65509625	rs1265424902	C/T	9.25E-04	5.57E-03	1.24E-03	NA
Chr8:96340001-96360000	SBP	4.86E-05	Chr8:96359351	rs570616203	T/G	5.29E-04	5.15E-04	2.11E-02	NA
Chr8:96340001-96360000	SBP	4.86E-05	Chr8:96359680	.	C/CTTAA	5.29E-04	9.98E-03	2.04E-04	NA
Chr8:116210001-116230000	HTN	9.00E-05	Chr8:116224549	.	C/CAA	5.29E-04	3.61E-02	1.19E-04	NA
Chr8:116220001-116240000	HTN	3.97E-06	Chr8:116224549	.	C/CAA	5.29E-04	6.09E-03	1.19E-04	NA
Chr8:116210001-116230000	DBP	7.43E-05	Chr8:116229791	rs1310952515	G/A	3.97E-04	2.36E-02	1.43E-04	NA
Chr8:116220001-116240000	HTN	3.97E-06	Chr8:116232111	rs1317238220	T/A	3.97E-04	9.00E-05	8.79E-03	NA
Chr11:95690001-95710000	HTN	2.01E-05	Chr11:95705633	rs927733621	C/T	1.06E-03	4.45E-01	3.97E-06	NA
Chr12:45900001-45920000	DBP	8.43E-05	Chr12:45905513	rs75082213	A/G	6.87E-03	8.38E-02	6.74E-05	NA

Chr12:102950001-102970000	SBP	5.45E-05	Chr12:102958346	rs756714075	G/GGCCGAG	2.91E-03	2.57E-03	8.99E-04	NA
Chr13:80100001-80120000	SBP	3.87E-05	Chr13:80118780	.	T/C	5.29E-04	3.91E-04	1.17E-04	NA
Chr13:80110001-80130000	SBP	8.11E-05	Chr13:80118780	.	T/C	5.29E-04	4.32E-02	1.17E-04	NA
Chr13:83680001-83700000	SBP	2.55E-05	Chr13:83696204	rs926387159	T/G	1.59E-03	7.52E-01	2.95E-06	NA
Chr13:83690001-83710000	SBP	1.94E-05	Chr13:83696204	rs926387159	T/G	1.59E-03	7.55E-01	2.95E-06	NA
Chr14:39140001-39160000	HTN	3.88E-05	Chr14:39157757	rs985705479	C/A	5.29E-04	9.90E-04	1.04E-03	NA
Chr14:39140001-39160000	HTN	3.88E-05	Chr14:39157760	rs1166238367	A/G	5.29E-04	1.04E-03	9.90E-04	NA
Chr14:97240001-97260000	HTN	8.20E-05	Chr14:97247305	rs1267061427	A/C	3.97E-04	2.05E-01	3.30E-05	NA
Chr15:38390001-38410000	DBP	9.58E-05	Chr15:38398323	rs755289280	T/C	1.32E-03	2.84E-03	6.91E-03	NA
Chr15:38390001-38410000	DBP	9.58E-05	Chr15:38398386	rs145063865	A/G	6.34E-03	3.13E-03	2.86E-03	NA
Chr15:68330001-68350000	HTN	2.42E-05	Chr15:68331038	rs745366518	C/T	6.61E-04	2.56E-01	1.49E-05	NA
Chr17:64920001-64940000	SBP	5.71E-05	Chr17:64928536	rs1170505050	A/G	3.97E-04	2.04E-03	5.99E-03	NA
Chr17:64920001-64940000	SBP	5.71E-05	Chr17:64932751	rs973806913	G/A	4.63E-03	1.32E-03	2.35E-02	NA
Chr17:64920001-64940000	SBP	5.71E-05	Chr17:64936519	rs1182086796	T/C	3.97E-04	1.43E-03	8.80E-03	NA
Chr19:39780001-39800000	SBP	6.19E-05	Chr19:39793314	rs1327798939	A/G	1.98E-03	1.64E-01	4.21E-05	NA
Chr20:32300001-32320000	SBP	3.23E-08	Chr20:32309709	rs1393521306	G/C	1.06E-03	5.51E-07	3.61E-03	NA
Chr20:32300001-32320000	SBP	3.23E-08	Chr20:32311097	rs758426820	A/G	9.25E-04	1.76E-03	6.25E-07	NA
Chr20:32310001-32330000	SBP	5.51E-07	Chr20:32311097	rs758426820	A/G	9.25E-04	3.90E-02	6.25E-07	NA

AAF, alternative allele frequency; DBP, diastolic blood pressure (BP); HTN, hypertension; LOO, leave-One-Out; MVP, Million Veteran Program; SBP, systolic BP; SMMAT-E, variant set mixed model association test - Efficient hybrid.; SVA, single variant analysis; UKBB, UK Biobank.

* Identified in gene-based analyses of regulatory regions and exonic variants with predicted functional relevance. † Identified in gene-based analyses of exonic loss-of-function, missense, and protein altering insertion-deletion variants.

Table S17. SNVs identified by leave-one-out analyses of aggregate rare variant units with SMMAT-E $P < 1E-04$ in participants of European ancestry.

Aggregate Unit	Associated Trait	SMMAT-E P-value	Marker	rsID	Alleles (Alt/Ref)	AAF	LOO P-value	SVA P-value	Stage-2 Sample Availability
<i>Gene-based Analyses</i>									
AMY2B (Chr1:103554644-103579534) [‡]	HTN	4.27E-05	Chr1:103575270	rs140209167	C/T	2.71E-03	1.53E-02	3.97E-04	UKBB, MVP, REGARDS
RBM45 (Chr2:178112409-178129656) [‡]	SBP	1.01E-05	Chr2:178112560	rs371141654	A/G	3.19E-04	1.31E-04	9.16E-03	UKBB
RBM45 (Chr2:178112409-178129656) [‡]	SBP	1.01E-05	Chr2:178123596	rs199636679	G/C	3.36E-04	1.94E-02	3.59E-05	UKBB
GPR156 (Chr3:120165481-120285074) [†]	DBP	5.51E-05	Chr3:120167323	rs751263400	A/AG	1.59E-04	4.26E-01	1.87E-05	UKBB
RNF175 (Chr4:153710125-153760983) [‡]	SBP	8.25E-05	Chr4:153748694	rs116158953	A/G	3.47E-03	2.41E-01	4.17E-05	UKBB, MVP, REGARDS
GATS (Chr7:100187988-100272274) [*]	DBP	4.35E-05	Chr7:100271832	rs3735244	T/G	2.40E-03	1.46E-01	9.14E-06	UKBB, REGARDS
OR9N1P (Chr7:141911402-141912022) [‡]	SBP	1.38E-05	Chr7:141907810	rs148829987	C/A	3.54E-04	5.04E-02	3.78E-05	UKBB, MVP
OR9N1P (Chr7:141911402-141912022) [‡]	SBP	1.38E-05	Chr7:141911897	rs782787616	C/G	3.19E-04	2.33E-04	1.31E-02	UKBB
STAG3L5P-PVRIG2P-PILRB (Chr7:100336065-100367831) [*]	DBP	3.98E-05	Chr7:100350450	rs12668834	T/C	2.53E-03	5.28E-01	9.00E-06	UKBB, REGARDS
STAG3L5P (Chr7:100336079-100341328) [*]	DBP	3.24E-05	Chr7:100350450	rs12668834	T/C	2.53E-03	4.48E-01	9.00E-06	UKBB, REGARDS
PVRIG2P (Chr7:100352318-100353936) [*]	DBP	1.89E-05	Chr7:100350450	rs12668834	T/C	2.53E-03	1.72E-01	9.00E-06	UKBB, REGARDS
PILRB (Chr7:100358003-100367831) [*]	DBP	2.41E-05	Chr7:100350450	rs12668834	T/C	2.53E-03	2.63E-01	9.00E-06	UKBB, REGARDS
TDRD1 (Chr10:114174442-114232669) [‡]	HTN	4.57E-05	Chr10:114222689	rs373299815	A/G	1.06E-04	4.88E-04	6.60E-03	NA
NDRG2 (Chr14:21016763-21070872) [*]	DBP	6.08E-05	Chr14:21024215	rs147773754	T/C	4.27E-03	3.65E-01	2.37E-05	UKBB, MVP, REGARDS

TPPP2 (Chr14:21024262-21036352)* DAND5	DBP	4.70E-05	Chr14:21024215	rs147773754	T/C	4.27E-03	3.06E-01	2.37E-05	UKBB, MVP, REGARDS
(Chr19:12969618-12974753) [†] DAND5	DBP	7.48E-05	Chr19:12969623	rs749251252	G/GGACA	1.59E-04	5.61E-03	1.18E-03	UKBB
(Chr19:12969618-12974753) [†] BPI	DBP	7.48E-05	Chr19:12973453	rs768842269	CCT/C	5.31E-05	1.77E-03	3.09E-03	NA
(Chr20:38304150-38337505) [†] ERG	HTN	8.45E-05	Chr20:38304261	rs1304485169	C/CCCTGATG	5.31E-05	1.52E-02	1.05E-04	UKBB
(Chr21:38367261-38661783) [‡] ERG	DBP	3.28E-05	Chr21:38383633	rs201647507	C/G	1.06E-04	5.84E-04	9.77E-03	UKBB
(Chr21:38367261-38661783) [‡] ERG	DBP	3.28E-05	Chr21:38383852	rs1407239004	C/T	7.08E-05	2.36E-03	8.88E-04	NA
(Chr21:38367261-38661783) [‡] TST	DBP	3.28E-05	Chr21:38445536	rs993206522	A/G	5.31E-05	3.34E-04	1.21E-02	NA
(Chr22:37010859-37020183) [‡]	DBP	3.43E-05	Chr22:37018363	rs147266371	T/C	3.54E-04	6.02E-01	5.94E-06	UKBB, MVP
<i>Sliding Windows Analyses</i>									
Chr1:2450001-2470000	HTN	4.34E-05	Chr1:2456028	rs754544624	A/G	3.36E-04	8.83E-03	3.32E-04	UKBB
Chr1:28460001-28480000	SBP	3.68E-05	Chr1:28460181	rs1034026250	A/T	8.85E-05	5.97E-03	3.24E-04	UKBB
Chr1:28460001-28480000	SBP	3.68E-05	Chr1:28473767	rs202061695	A/C	7.08E-05	1.01E-03	2.27E-03	NA
Chr1:94540001-94560000	HTN	9.72E-05	Chr1:94552963	rs841698	C/T	9.97E-01	7.59E-01	1.94E-05	UKBB, REGARDS
Chr1:185910001-185930000	DBP	2.76E-05	Chr1:185928650	rs149707772	T/C	4.43E-04	2.98E-01	9.86E-06	UKBB, MVP
Chr1:99220001-99240000	SBP	8.42E-05	Chr1:99228032	rs918472343	T/C	7.08E-05	2.15E-05	8.31E-01	NA
			Chr1:99229826	rs947408596	T/A	7.09E-05		8.31E-01	NA
Chr1:99220001-99240000	SBP	8.42E-05	Chr1:99233610	rs1187632768	A/G	1.06E-04	3.36E-01	8.59E-06	UKBB
Chr1:99230001-99250000	SBP	3.87E-05	Chr1:99233610	rs1187632768	A/G	1.06E-04	9.31E-01	8.59E-06	UKBB
Chr2:50370001-50390000	DBP	8.15E-05	Chr2:50387686	rs1018246038	T/G	3.54E-04	1.38E-01	7.80E-05	NA
Chr2:10750001-10770000	HTN	6.06E-05	Chr2:10764334	rs1012427631	G/A	5.31E-05	4.77E-01	6.06E-05	UKBB
Chr2:174360001-174380000	DBP	7.02E-05	Chr2:174371708	rs777425878	C/T	5.13E-04	4.60E-02	1.11E-04	UKBB
Chr3:41020001-41040000	HTN	8.92E-05	Chr3:41035135	rs1018569216	G/A	7.08E-05	6.69E-01	1.77E-05	UKBB
Chr3:130510001-130530000	DBP	4.43E-05	Chr3:130527375	rs184717230	C/G	4.07E-04	7.94E-04	1.76E-03	UKBB, MVP
Chr3:130510001-130530000	DBP	4.43E-05	Chr3:130527376	rs147702642	G/A	2.92E-03	6.68E-04	7.17E-03	UKBB, REGARDS

Chr3:130520001-130540000	DBP	3.90E-05	Chr3:130527375	rs184717230	C/G	4.07E-04	7.26E-04	1.76E-03	UKBB, MVP
Chr3:130520001-130540000	DBP	3.90E-05	Chr3:130527376	rs147702642	G/A	2.92E-03	5.43E-04	7.17E-03	UKBB, REGARDS
Chr4:124730001-124750000	DBP	2.33E-05	Chr4:124746752	rs1050104610	C/T	1.06E-03	6.02E-01	5.62E-06	UKBB
Chr4:124740001-124760000	DBP	1.56E-05	Chr4:124746752	rs1050104610	C/T	1.06E-03	4.78E-01	5.62E-06	UKBB
Chr4:154050001-154070000	DBP	4.51E-05	Chr4:154069962	rs938675698	C/A	7.08E-05	2.27E-01	2.02E-05	UKBB
Chr4:181230001-181250000	DBP	7.92E-05	Chr4:181248738	rs759992627	A/T	2.41E-03	4.60E-03	1.25E-03	NA
Chr5:117760001-117780000	HTN	2.41E-05	Chr5:117778836	rs759302724	T/C	1.59E-04	1.12E-03	2.09E-03	UKBB
Chr5:117760001-117780000	HTN	2.41E-05	Chr5:117779028	.	T/TTCCCCAG	1.06E-04	3.87E-03	9.07E-05	UKBB
Chr5:127520001-127540000	SBP	1.75E-05	Chr5:127524529	rs1441444936	G/A	5.31E-05	2.46E-04	7.10E-03	UKBB
Chr5:127520001-127540000	SBP	1.75E-05	Chr5:127524870	rs143589506	A/G	1.01E-03	5.43E-04	4.35E-03	UKBB, MVP
Chr5:172040001-172060000	SBP	6.51E-05	Chr5:172054563	rs113551500	G/C	7.61E-04	2.57E-01	1.43E-05	REGARDS
Chr5:172050001-172070000	SBP	4.29E-05	Chr5:172054563	rs113551500	G/C	7.61E-04	2.57E-01	1.43E-05	REGARDS
Chr7:100340001-100360000	DBP	2.41E-05	Chr7:100350450	rs12668834	T/C	2.53E-03	2.63E-01	9.00E-06	UKBB, REGARDS
Chr7:133790001-133810000	DBP	1.93E-05	Chr7:133796902	rs1008392627	T/G	2.48E-04	1.92E-04	1.49E-03	NA
Chr7:133790001-133810000	DBP	1.93E-05	Chr7:133797239	rs530457484	G/C	3.19E-03	2.54E-04	1.35E-03	UKBB, MVP, REGARDS
Chr7:141900001-141920000	SBP	3.99E-05	Chr7:141907810	rs148829987	C/A	3.54E-04	8.17E-02	3.78E-05	UKBB, MVP
Chr7:141900001-141920000	SBP	3.99E-05	Chr7:141911897	rs782787616	C/G	3.19E-04	4.10E-04	1.31E-02	UKBB
Chr8:49730001-49750000	HTN	3.64E-05	Chr8:49740597	rs539490305	C/A	1.24E-04	1.52E-03	3.19E-03	UKBB
Chr8:49730001-49750000	HTN	3.64E-05	Chr8:49741293	rs767681164	T/A	5.31E-05	1.03E-03	3.69E-03	UKBB
Chr8:83600001-83620000	DBP	1.38E-05	Chr8:83616239	rs755777228	C/A	2.30E-04	7.34E-03	1.82E-04	UKBB
Chr8:83600001-83620000	DBP	1.38E-05	Chr8:83616240	rs779635706	G/C	1.06E-04	1.72E-04	9.00E-03	UKBB
Chr9:23130001-23150000	HTN	9.27E-05	Chr9:23142518	rs564818044	A/G	5.59E-03	2.54E-01	2.44E-05	UKBB, MVP, REGARDS
Chr9:23140001-23160000	HTN	1.54E-05	Chr9:23142518	rs564818044	A/G	5.59E-03	3.40E-02	2.44E-05	UKBB, MVP, REGARDS
Chr9:23140001-23160000	SBP	6.48E-05	Chr9:23142518	rs564818044	A/G	5.59E-03	5.77E-02	1.08E-04	UKBB, MVP, REGARDS
Chr9:125950001-125970000	SBP	8.11E-05	Chr9:125950190	rs180914843	T/C	1.36E-03	1.37E-03	2.72E-03	NA
Chr9:125950001-125970000	SBP	8.11E-05	Chr9:125964158	rs181459338	A/G	1.26E-03	2.24E-03	8.88E-04	NA
Chr10:16900001-16920000	DBP	1.10E-05	Chr10:16900636	rs141737312	A/G	1.22E-03	2.89E-04	7.34E-03	UKBB, MVP, REGARDS

Chr10:16900001-16920000	DBP	1.10E-05	Chr10:16919996	rs2271460	C/A	5.91E-03	1.02E-03	1.97E-03	UKBB, MVP, REGARDS
Chr10:16990001-17010000	DBP	9.69E-05	Chr10:16990468	rs771763775	T/C	5.31E-05	1.81E-03	8.90E-03	UKBB
Chr10:16990001-17010000	DBP	9.69E-05	Chr10:17006929	rs771728408	T/C	8.85E-05	2.33E-03	8.45E-03	UKBB
Chr10:85480001-85500000	DBP	5.65E-05	Chr10:85490510	rs191823543	C/T	1.06E-04	4.97E-03	1.88E-03	UKBB
Chr10:85480001-85500000	DBP	5.65E-05	Chr10:85490511	rs147538650	C/G	5.32E-05	9.48E-04	6.30E-03	UKBB
Chr10:98310001-98330000	DBP	3.18E-05	Chr10:98326572	rs574886265	G/A	2.83E-04	4.05E-02	1.59E-04	UKBB
Chr11:7670001-7690000	DBP	9.34E-05	Chr11:7675742	rs7130592	T/C	3.84E-03	6.76E-02	3.25E-05	UKBB, REGARDS
Chr11:31950001-31970000	SBP	6.71E-05	Chr11:31969443	rs886110723	C/T	8.32E-04	3.78E-01	1.70E-05	UKBB
Chr11:31960001-31980000	SBP	7.08E-05	Chr11:31969443	rs886110723	C/T	8.32E-04	4.28E-01	1.70E-05	UKBB
Chr12:103130001-103150000	HTN	6.90E-05	Chr12:103147959	rs192926117	C/A	3.97E-03	6.17E-02	3.37E-05	UKBB
Chr12:103140001-103160000	HTN	6.92E-05	Chr12:103147959	rs192926117	C/A	3.97E-03	5.53E-02	3.37E-05	UKBB
Chr13:39670001-39690000	DBP	9.13E-05	Chr13:39687612	rs34555836	T/C	7.08E-05	3.22E-02	3.01E-05	UKBB, MVP
Chr13:85800001-85820000	SBP	3.28E-05	Chr13:85800049	rs9602841	G/T	4.43E-04	4.46E-01	9.04E-06	UKBB
Chr13:85800001-85820000	DBP	9.00E-05	Chr13:85800049	rs9602841	G/T	4.43E-04	9.74E-02	9.04E-06	NA
Chr13:85800001-85820000	HTN	3.39E-05	Chr13:85800049	rs9602841	G/T	4.43E-04	1.94E-01	9.04E-06	NA
Chr13:106210001-106230000	DBP	2.40E-05	Chr13:106212621	rs181084228	C/T	3.63E-03	1.91E-03	1.63E-03	REGARDS
Chr13:106210001-106230000	DBP	2.40E-05	Chr13:106212932	rs190645521	A/C	2.16E-03	5.45E-03	3.60E-04	REGARDS
Chr14:21010001-21030000	DBP	7.67E-05	Chr14:21024215	rs147773754	T/C	4.27E-03	5.82E-01	2.37E-05	UKBB, MVP, REGARDS
Chr14:21020001-21040000	DBP	6.74E-05	Chr14:21024215	rs147773754	T/C	4.27E-03	3.26E-01	2.37E-05	UKBB, MVP, REGARDS
Chr14:90360001-90380000	DBP	9.73E-05	Chr14:90366809	rs182881580	T/G	7.21E-03	2.18E-03	4.24E-03	UKBB, MVP, REGARDS
Chr15:45870001-45890000	HTN	6.70E-05	Chr15:45884394	rs761729326	A/G	1.06E-04	7.34E-03	1.85E-03	UKBB
Chr15:45870001-45890000	HTN	6.70E-05	Chr15:45884567	rs992870969	A/T	5.31E-05	8.05E-04	1.38E-02	NA
Chr15:67440001-67460000	HTN	2.08E-05	Chr15:67457164	rs184474917	C/T	1.93E-03	5.62E-01	5.40E-06	UKBB, REGARDS
Chr15:67440001-67460000	SBP	6.64E-05	Chr15:67457164	rs184474917	C/T	1.93E-03	9.33E-01	1.50E-05	UKBB, REGARDS
Chr15:67450001-67470000	HTN	3.42E-06	Chr15:67457164	rs184474917	C/T	1.93E-03	4.29E-02	5.40E-06	UKBB, REGARDS

Chr15:67450001-67470000	SBP	1.41E-05	Chr15:67457164	rs184474917	C/T	1.93E-03	9.82E-02	1.50E-05	UKBB, REGARDS
Chr15:73990001-74010000	HTN	4.62E-05	Chr15:73992202	rs199911341	A/G	2.66E-04	7.16E-02	5.87E-05	UKBB
Chr16:9660001-9680000	DBP	7.34E-05	Chr16:9679372	rs1032414483	T/G	2.66E-04	5.78E-02	4.98E-05	UKBB
Chr16:9670001-9690000	DBP	8.62E-05	Chr16:9679372	rs1032414483	T/G	2.66E-04	2.21E-01	4.98E-05	UKBB
Chr19:35430001-35450000	SBP	8.48E-05	Chr19:35449824	rs369914056	A/G	1.24E-04	4.63E-01	3.05E-06	UKBB
Chr22:37000001-37020000	DBP	4.12E-05	Chr22:37018363	rs147266371	T/C	3.54E-04	6.68E-01	5.94E-06	UKBB, MVP

AAF, alternative allele frequency; DBP, diastolic blood pressure (BP); HTN, hypertension; LOO, leave-One-Out; MVP, Million Veteran Program; SBP, systolic BP; SMMAT-E, variant set mixed model association test - Efficient hybrid.; SVA, single variant analysis; UKBB, UK Biobank.

* Identified in gene-based analyses of exonic loss-of-function, missense, and protein altering insertion-deletion variants. † Identified in gene-based analyses of high confidence loss-of-function variants. ‡ Identified in gene-based analyses of regulatory regions and exonic variants with predicted functional relevance.

Table S18. SNVs identified by leave-one-out analyses of aggregate rare variant units with SMMAT-E $P < 1E-04$ in participants of Hispanic ancestry.

Aggregate Unit	Associated Trait	SMMAT-E P-value	Marker	rsID	Alleles (Alt/Ref)	AAF	LOO P-value	SVA P-value	Stage-2 Sample Availability
<i>Gene-based Analyses</i>									
LYSMD1 (Chr1:151148496-151165902)*	SBP	1.44E-05	Chr1:151170527	rs11800088	C/T	4.16E-03	2.94E-02	1.25E-05	NA
CACNA2D3 (Chr3:54122552-55074557) [†]	HTN	8.59E-05	Chr3:54891399	rs112362995	T/C	3.56E-03	3.02E-03	1.38E-03	MVP
CACNA2D3 (Chr3:54122552-55074557) [†]	HTN	8.59E-05	Chr3:55009388	rs142687394	T/G	3.19E-03	1.43E-02	2.09E-04	MVP
MRPS18B (Chr6:30617320-30626393) [†]	DBP	4.09E-05	Chr6:30625588	rs564504951	C/G	3.67E-04	6.03E-01	1.02E-05	NA
FLOT1 (Chr6:30727709-30742851)*	DBP	9.36E-05	Chr6:30724399	.	G/GC	6.12E-04	1.55E-01	8.36E-05	NA
TUBB (Chr6:30720201-30725426)*	DBP	3.95E-06	Chr6:30720412	rs113155531	A/C	3.67E-04	8.36E-05	1.72E-03	NA
TUBB (Chr6:30720201-30725426)*	SBP	1.86E-05	Chr6:30720412	rs113155531	A/C	3.67E-04	5.73E-04	1.05E-03	NA
TUBB (Chr6:30720201-30725426)*	DBP	3.95E-06	Chr6:30724399	.	G/GC	6.12E-04	1.72E-03	8.36E-05	NA
TUBB (Chr6:30720201-30725426)*	SBP	1.86E-05	Chr6:30724399	.	G/GC	6.12E-04	1.05E-03	5.73E-04	NA
MSC (Chr8:71841542-71844496)*	SBP	6.19E-05	Chr8:71843161	rs76011963	G/A	9.30E-03	5.85E-02	8.89E-05	MVP
SMC2 (Chr9:104093760-104141419)*	SBP	7.43E-05	Chr9:104095548	rs181793444	G/C	4.04E-03	2.81E-01	3.25E-06	MVP
SMC2 (Chr9:104093760-104141419) [†]	SBP	6.56E-05	Chr9:104095548	rs181793444	G/C	4.04E-03	2.53E-01	3.25E-06	MVP
SMC2-AS1 (Chr9:104080024-104092474)*	SBP	3.20E-05	Chr9:104095548	rs181793444	G/C	4.04E-03	9.21E-01	3.25E-06	MVP

RAB15 (Chr14:64945816-64972336)*	SBP	6.48E-05	Chr14:64942749		T/G		5.39E-02		NA
DNAH9 (Chr17:11598470-11970168)*	SBP	2.76E-05	Chr17:11894431	rs78870819	T/C	3.06E-03	3.19E-04	3.43E-03	MVP
<i>Sliding Windows Analyses</i>									
Chr1:25020001-25040000	HTN	4.40E-05	Chr1:25031885	rs183101733	G/T	3.67E-03	2.32E-02	4.89E-05	MVP
Chr1:25020001-25040000	DBP	9.29E-05	Chr1:25031885	rs183101733	G/T	3.67E-03	8.34E-02	8.82E-05	MVP
Chr1:86630001-86650000	DBP	4.42E-06	Chr1:86643872	rs138352629	A/G	1.22E-03	6.47E-05	3.39E-03	MVP
Chr1:86640001-86660000	DBP	1.78E-06	Chr1:86643872	rs138352629	A/G	1.22E-03	4.11E-05	3.39E-03	MVP
Chr1:86630001-86650000	DBP	4.42E-06	Chr1:86647783	rs115221669	A/G	4.53E-03	2.93E-02	2.73E-05	MVP
Chr1:86640001-86660000	DBP	1.78E-06	Chr1:86647783	rs115221669	A/G	4.53E-03	5.70E-03	2.73E-05	MVP
Chr2:146430001-146450000	HTN	2.65E-05	Chr2:146440972	rs116735556	G/A	3.44E-03	6.97E-04	4.29E-03	MVP
Chr2:197000001-197020000	SBP	1.91E-05	Chr2:197007954	rs368155784	T/A	4.89E-04	2.37E-03	4.03E-04	NA
Chr2:197000001-197020000	HTN	1.67E-05	Chr2:197015132	rs116000415	C/G	7.46E-03	1.72E-02	2.37E-03	MVP
Chr2:197000001-197020000	SBP	1.91E-05	Chr2:197015132	rs116000415	C/G	7.46E-03	4.03E-04	6.78E-05	MVP
Chr3:20001-40000	SBP	8.29E-06	Chr3:21615	rs557900814	G/C	3.59E-04	4.33E-04	1.57E-03	NA
Chr3:20001-40000	SBP	8.29E-06	Chr3:21683	rs192545714	C/G	7.34E-04	1.43E-04	4.40E-03	NA
Chr3:20001-40000	SBP	8.29E-06	Chr3:31808	rs565142363	G/A	3.59E-04	4.33E-04	1.57E-03	NA
Chr4:34510001-34530000	DBP	6.03E-05	Chr4:34529522	rs73130132	G/T	3.18E-03	1.33E-01	7.12E-05	MVP
Chr4:122920001-122940000	SBP	4.58E-05	Chr4:122922409	rs201814451	T/C	7.34E-04	1.18E-02	2.68E-04	NA
Chr4:122920001-122940000	SBP	4.58E-05	Chr4:122936160	rs752274594	C/CTCTT	3.67E-04	9.11E-04	4.43E-03	NA
Chr5:61820001-61840000	DBP	3.76E-05	Chr5:61832411	rs77933963	A/T	6.12E-03	3.74E-02	1.13E-04	MVP
Chr5:61830001-61850000	DBP	1.92E-05	Chr5:61832411	rs77933963	A/T	6.12E-03	1.34E-02	1.13E-04	MVP
Chr5:61820001-61840000	DBP	3.76E-05	Chr5:61833029	rs112075463	C/T	3.91E-03	6.88E-04	1.70E-02	MVP
Chr5:61830001-61850000	DBP	1.92E-05	Chr5:61833029	rs112075463	C/T	3.91E-03	2.26E-04	1.70E-02	MVP
Chr5:74150001-74170000	SBP	4.83E-05	Chr5:74164320	rs975948	G/A	4.28E-03	1.58E-03	1.29E-03	NA
Chr5:74150001-74170000	SBP	4.83E-05	Chr5:74169815	rs188297906	T/C	2.32E-03	5.78E-04	4.54E-03	NA
Chr5:127470001-127490000	SBP	8.34E-05	Chr5:127477345	rs182251332	A/G	7.34E-04	6.44E-01	2.03E-05	MVP
Chr6:30720001-30740000	DBP	5.47E-06	Chr6:30720412	rs113155531	A/C	3.67E-04	9.56E-05	1.72E-03	NA
Chr6:30720001-30740000	SBP	6.66E-05	Chr6:30720412	rs113155531	A/C	3.67E-04	1.77E-03	1.05E-03	NA
Chr6:30720001-30740000	DBP	5.47E-06	Chr6:30724399	.	G/GC	6.12E-04	1.48E-03	8.36E-05	NA
Chr6:30720001-30740000	SBP	6.66E-05	Chr6:30724399	.	G/GC	6.12E-04	2.85E-03	5.73E-04	NA
Chr6:139830001-139850000	DBP	3.53E-05	Chr6:139847207	rs192664048	A/G	3.91E-03	3.63E-02	6.16E-05	MVP
Chr6:139830001-139850000	DBP	3.53E-05	Chr6:139846741	rs537444215	G/A	1.47E-03	3.69E-04	1.05E-02	MVP

Chr6:139840001-139860000	DBP	2.39E-05	Chr6:139846741	rs537444215	G/A	1.47E-03	2.69E-04	1.05E-02	MVP
Chr6:139840001-139860000	DBP	2.39E-05	Chr6:139847207	rs192664048	A/G	3.91E-03	2.83E-02	6.16E-05	MVP
Chr6:139830001-139850000	DBP	3.53E-05	Chr6:139847287	rs538591715	A/C	1.47E-03	3.69E-04	1.05E-02	MVP
Chr6:139840001-139860000	DBP	2.39E-05	Chr6:139847287	rs538591715	A/C	1.47E-03	2.69E-04	1.05E-02	MVP
Chr7:18650001-18670000	DBP	4.58E-05	Chr7:18655840	rs568828254	G/A	6.12E-04	6.02E-04	9.94E-05	NA
Chr7:116040001-116060000	SBP	5.80E-05	Chr7:116043118	rs115804855	T/A	8.57E-04	2.58E-03	9.74E-04	MVP
Chr7:116040001-116060000	SBP	5.80E-05	Chr7:116043222	rs114105105	A/G	3.43E-03	9.74E-04	2.58E-03	MVP
Chr8:71830001-71850000	SBP	6.19E-05	Chr8:71843161	rs76011963	G/A	9.30E-03	5.85E-02	8.89E-05	MVP
Chr9:17010001-17030000	SBP	3.47E-05	Chr9:17012533	rs183551779	G/T	4.65E-03	6.45E-04	5.30E-03	NA
Chr9:17010001-17030000	SBP	3.47E-05	Chr9:17025317	rs573669946	G/T	2.45E-03	1.43E-03	3.31E-03	MVP
Chr9:81360001-81380000	SBP	1.38E-05	Chr9:81370921	rs569681992	A/G	1.71E-03	9.36E-04	3.02E-05	NA
Chr9:81370001-81390000	SBP	3.45E-05	Chr9:81370921	rs569681992	A/G	1.71E-03	1.03E-03	3.02E-05	NA
Chr9:81360001-81380000	SBP	1.38E-05	Chr9:81374995	rs140227099	C/T	1.00E-02	4.39E-03	3.93E-04	MVP
Chr9:81370001-81390000	SBP	3.45E-05	Chr9:81374995	rs140227099	C/T	1.00E-02	6.37E-03	3.93E-04	MVP
Chr9:104080001-104100000	SBP	2.21E-05	Chr9:104095548	rs181793444	G/C	4.04E-03	1.55E-01	3.25E-06	MVP
Chr9:104090001-104110000	SBP	7.68E-06	Chr9:104095548	rs181793444	G/C	4.04E-03	1.06E-01	3.25E-06	MVP
Chr10:1130001-1150000	DBP	6.55E-05	Chr10:1130075	rs140002716	C/T	3.79E-03	9.77E-02	9.08E-05	MVP
Chr11:84500001-84520000	DBP	5.11E-05	Chr11:84518735	rs536612181	T/A	8.56E-04	8.16E-01	1.21E-05	NA
Chr13:96860001-96880000	HTN	2.33E-05	Chr13:96863307	rs181061777	C/T	1.35E-03	3.36E-03	1.66E-03	NA
Chr13:96860001-96880000	HTN	2.33E-05	Chr13:96871582	rs114114288	C/A	8.22E-03	5.01E-04	2.45E-02	MVP
Chr14:64940001-64960000	SBP	6.15E-05	Chr14:64942749	rs180757175	T/G	1.59E-03	5.44E-02	1.88E-04	NA
Chr16:6610001-6630000	HTN	5.60E-05	Chr16:6625793	rs77893217	G/A	6.26E-03	6.02E-02	1.06E-04	MVP
Chr16:22750001-22770000	SBP	4.21E-05	Chr16:22753705	rs79024532	C/T	4.28E-03	2.33E-03	1.45E-03	MVP
Chr16:22750001-22770000	SBP	4.21E-05	Chr16:22764683	rs113577723	A/G	4.89E-04	5.70E-04	2.40E-05	NA
Chr17:70420001-70440000	SBP	9.98E-05	Chr17:70438250	rs182046693	A/G	6.85E-03	4.31E-01	3.18E-05	NA
Chr18:38460001-38480000	SBP	4.32E-06	Chr18:38474965	rs907054029	A/G	2.45E-03	9.51E-05	5.53E-03	NA
Chr18:38460001-38480000	SBP	4.32E-06	Chr18:38475076	rs144770061	C/CAGG	7.22E-03	1.02E-02	9.61E-05	MVP
Chr20:7000001-7020000	DBP	2.63E-05	Chr20:7016079	rs1009819453	A/C	1.47E-03	3.53E-03	1.63E-03	NA
Chr20:12870001-12890000	DBP	1.34E-05	Chr20:12876757	rs181517230	G/A	6.97E-03	4.31E-01	4.04E-06	MVP
Chr20:12870001-12890000	SBP	1.59E-05	Chr20:12876757	rs181517230	G/A	6.97E-03	6.65E-01	3.88E-06	MVP

AAF, alternative allele frequency; DBP, diastolic blood pressure (BP); HTN, hypertension; LOO, leave-One-Out; MVP, Million Veteran Program; SBP, systolic BP; SMMAT-E, variant set mixed model association test - Efficient hybrid.; SVA, single variant analysis; UKBB, UK Biobank.

* Identified in gene-based analyses of exonic loss-of-function, missense, and protein altering insertion-deletion variants. † Identified in gene-based analyses of regulatory regions and exonic variants with predicted functional relevance.

Table S19. SNVs identified by leave-one-out analyses of aggregate rare variant units with SMMAT-E $P < 1E-04$ in participants of Samoan ancestry.

Aggregate Unit	Associated Trait	SMMAT-E P-value	Marker	rsID	Alleles (Alt/Ref)	AAF	LOO P-value	SVA P-value	Stage-2 Sample
<i>Gene-based Analyses</i>									
RASL10B (Chr17:35731639-35743521)*	HTN	5.43E-05	Chr17:35719994	rs587619480	C/A	1.59E-03	7.13E-03	9.81E-07	NA
RASL10B (Chr17:35731639-35743521)*	HTN	5.43E-05	Chr17:35742070	rs587628312	A/G	1.20E-03	2.60E-04	4.16E-05	NA
<i>Sliding Windows Analyses</i>									
Chr13:103160001-103180000	SBP	4.64E-05	Chr13:103164302	rs72661412	G/A	2.79E-03	6.38E-04	9.40E-03	NA
Chr13:103160001-103180000	SBP	4.64E-05	Chr13:103179137	rs17357972	A/C	6.37E-03	2.33E-02	1.79E-04	NA
Chr16:50960001-50980000	SBP	5.45E-05	Chr16:50977026	rs949641194	A/G	1.19E-03	3.63E-01	1.06E-05	NA

AAF, alternative allele frequency; DBP, diastolic blood pressure (BP); HTN, hypertension; LOO, leave-One-Out; MVP, Million Veteran Program; SBP,

* Identified in gene-based analyses of exonic loss-of-function, missense, and protein altering insertion-deletion variants.

Table S20. Suggestive signals from meta-analyses of variants identified by single variant analyses ($5 \times 10^{-8} < P < 1 \times 10^{-6}$).

Chr	Position (GRCh38)	rsID	Trait	Ancestry	Locus*	Classification	Alleles (Ref/Alt)	Sample	AAC	Beta [‡]	SE	P
Novel Variants with MAF<1% from Novel Loci												
1	71055350	rs1396751049	SBP	Multi	<i>ZRANB2-AS1</i>	Intron	A/G	TOPMed/CCDG	24	-21.55	4.16	2.29E-07
								UK Biobank	7	-4.43	29.80	8.82E-01
								Meta-analysis		-21.22	4.12	2.67E-07
3	380679	rs932205533	DBP	Multi	<i>CHL1</i>	Intron	C/T	TOPMed/CCDG	12	17.01	3.38	4.89E-07
								UK Biobank	6	61.07	22.42	6.44E-03
								Meta-analysis		17.99	3.34	7.42E-08
4	154348736	rs892714163	HTN	White	<i>DCHS2</i>	Intron	T/C	TOPMed/CCDG	26	2.32	0.47	9.05E-07
								UK Biobank	27	1.04	0.75	1.66E-01
								Meta-analysis		1.95	0.40	9.86E-07
7	93871514	rs1166654114	HTN	Multi	<i>GNGT1</i>	Intron	T/C	TOPMed/CCDG	11	-3.63	0.72	4.32E-07
								UK Biobank	1	-31.22	22.47	1.65E-01
								Meta-analysis		-3.66	0.72	3.47E-07
7	120623195	rs959927014	DBP	Multi	<i>KCND2</i>	Intron	A/T	TOPMed/CCDG	14	14.12	2.86	7.96E-07
								UK Biobank	3	49.71	38.11	1.92E-01
								Meta-analysis		14.32	2.85	5.17E-07
7	120623195	rs959927014	DBP	White	<i>KCND2</i>	Intron	A/T	TOPMed/CCDG	14	14.11	2.86	8.20E-07
								UK Biobank	3	49.71	38.11	1.92E-01
								Meta-analysis		14.31	2.85	5.32E-07

12	83815309	rs561552220	SBP	White	<i>RP11-384P14.1</i>	Intergenic	ACTT/A	TOPMed/CCDG	17	-22.82	4.63	8.17E-07
								UK Biobank	7	-16.17	12.26	1.87E-01
								Meta-analysis		-21.99	4.33	3.79E-07
Novel variants with MAF<1% from Previously Reported Loci												
1	36845873	rs966779519	HTN	Multi	<i>GRIK3</i>	Intron	T/C	TOPMed/CCDG	26	-2.48	0.49	4.66E-07
								UK Biobank	2	-0.75	2.83	7.90E-01
								Meta-analysis		-2.43	0.48	5.42E-07
1	112064726	rs550856031	SBP	Multi	<i>KCND3</i>	Intergenic	G/C	TOPMed/CCDG	31	-20.48	3.94	2.00E-07
								UK Biobank	2	-32.57	75.69	6.67E-01
								Meta-analysis		-20.51	3.93	1.84E-07
1	150513095	rs12031974	SBP	Multi	<i>ECM1</i>	Intron	T/C	TOPMed/CCDG	76	12.46	2.37	1.44E-07
								REGARDS	73	4.68	3.31	1.58E-01
								Meta-analysis		9.82	1.93	3.40E-07
1	150513095	rs12031974	SBP	African	<i>ECM1</i>	Intron	T/C	TOPMed/CCDG	74	12.59	2.39	1.39E-07
								REGARDS	73	4.68	3.31	1.58E-01
								Meta-analysis		9.88	1.94	3.46E-07
7	73727423	rs530529907	DBP	Multi	<i>ABHD11-AS1</i>	Intergenic	C/A	TOPMed/CCDG	52	-8.76	1.73	4.04E-07
								UK Biobank	6	-8.53	6.73	2.05E-01
								Meta-analysis		-8.74	1.67	1.76E-07
11	30758017	rs759526273	SBP	Multi	<i>DCDC5</i>	Intergenic	G/A	TOPMed/CCDG	54	-12.80	2.56	5.95E-07
								UK Biobank	11	-9.19	6.62	1.65E-01
								Meta-analysis		-12.33	2.39	2.49E-07

11	30758017	rs759526273	SBP	White	<i>DCDC5</i>	Intergenic	G/A	TOPMed/CCDG	53	-13.33	2.60	2.80E-07
								UK Biobank	11	-9.19	6.62	1.65E-01
								Meta-analysis		-12.78	2.42	1.24E-07
16	59640176	rs999280636	HTN	Multi	<i>DUXAP11</i>	Intergenic	G/A	TOPMed/CCDG	14	-4.06	0.71	1.02E-08
								UK Biobank		-0.57	0.94	5.44E-01
								Meta-analysis		-2.79	0.57	7.82E-07

AAC, alternative allele count, corresponding to the specified ancestry group in TOPMed; Alt, alternative; Chr, chromosome; CCDG, Centers for Common Disease Genomics; DBP, diastolic blood pressure (BP); HTN, hypertension; MAF, minor allele frequency; Multi, multi-ancestry; Ref, reference; REGARDS, Reasons for Geographic and Racial Differences in Stroke; SBP, systolic BP; TOPMed, Trans-Omics for Precision Medicine.

*Gene (if genic) or nearest gene (if intergenic). †Because none of the listed variants were available for replication in MVP, the meta-analysis reflects the combined analysis of TOPMed/CCDG and UK Biobank or REGARDS results only. ‡Beta corresponds to the effect size in mmHg and natural logarithm of the odds ratio per coded allele for the continuous and discrete blood pressure phenotypes, respectively.

Table S21. Suggestive signals from meta-analyses of aggregate gene-based analyses ($P < 1 \times 10^{-4}$).

Gene Symbol	Chr	GRCh38 Position (start, end)	Trait	Ancestry	Sample	Rare variant sites (N)	Rare alleles (N)	SMMAT-E P-value
<i>Gene-based analysis (Loss-of-function variants, missense variants, and protein altering indels)</i>								
MZT2B	2	130182262, 130190727	DBP	White	TOPMed	1	3	3.11×10^{-5}
					UK Biobank	1	5	3.10×10^{-2}
					Meta-analysis			1.43×10^{-5}
DNAJB13	11	73950321, 73970287	DBP	Multi	TOPMed	16	451	2.91×10^{-5}
					UK Biobank	8	1,033	2.58×10^{-2}
					Meta-analysis			1.13×10^{-5}
<i>Gene-based analysis (Enhancer, promoter, and exonic variants with predicted functional relevance)</i>								
DNAJB13	11	73950321, 73970287	DBP	Multi	TOPMed	30	874	7.14×10^{-5}
					UK Biobank	15	1,474	6.01×10^{-2}
					Meta-analysis			5.29×10^{-5}
NDRGB	14	21016763, 21070872	DBP	White	TOPMed	64	1,007	6.08×10^{-5}
					UK Biobank	34	3,909	1.07×10^{-2}
					Meta-analysis			9.95×10^{-6}
TPPP2	14	21024262, 21036352	DBP	White	TOPMed	36	649	5.87×10^{-5}
					UK Biobank	26	3,237	1.69×10^{-2}
					Meta-analysis			1.47×10^{-5}

Chr, chromosome; DBP, diastolic blood pressure; TOPMed, Trans-omics for Precision Medicine program.

Table S22. Suggestive signals from meta-analyses of rare variants identified by leave-one-out analyses ($P < 1 \times 10^{-4}$).

Chr	Position (GRCh38)	rsID	Associated Trait	Ancestry	Gene	Classification(s)	Alleles (Ref/Alt)	Sample	AAC	Beta*	SE	P-value
Novel Loci												
1	54810596	rs377560726 ^{†,‡}	DBP	African	<i>LEXM</i> [§]	Intronic	C/G	TOPMed	81	-6.16	1.33	3.83E-06
								MVP	60	-1.97	1.31	1.32E-01
								REGARDS	64	-2.21	1.57	0.16
								Meta-analysis		-3.56	0.80	9.59E-06
2	211725173	rs148992844 [‡]	HTN	Multi	<i>ERBB4</i> [§]	Missense	T/G	TOPMed	39	-1.69	0.37	5.39E-06
								MVP	17	-0.62	0.46	0.17
								REGARDS	22	-0.38	0.49	0.44
								Meta-analysis		-1.04	0.25	2.91E-05
2	211725173	rs148992844 ^{‡,}	HTN	African	<i>ERBB4</i> [§]	Missense	T/G	TOPMed	35	-1.84	0.40	4.08E-06
								MVP	17	-0.62	0.46	0.17
								REGARDS	22	-0.38	0.49	0.44
								Meta-analysis		-1.06	0.26	3.55E-05
10	85490510	rs191823543 [‡]	DBP	White	<i>LINC01520</i> [§]	Intronic	T/C	TOPMed	6	-13.89	4.47	1.88E-03
								UKBB	11	-13.78	5.62	1.43E-02
								Meta-analysis		-13.85	3.50	7.57E-05
19	12969623	rs140618957	DBP	White	<i>DAND5</i> [§] , <i>PRRG2</i> [#]	hcLOF; 5'UTR	GGACA/G	TOPMed	9	-11.68	3.60	1.18E-03
								UKBB	45	-9.01	4.01	2.47E-02
								Meta-analysis		-10.49	2.68	9.06E-05

Novel Variants at Previously Reported Loci

11	31969443	rs886110723 [‡]	SBP	White	<i>LOC100506675</i> [§]	Intergenic	T/C	TOPMed	48	-11.90	2.77	1.70E-05
								UKBB	10	-14.67	7.02	3.66E-02
								Meta-analysis		-12.28	2.57	1.86E-06

AAF, alternative allele frequency, corresponding to the specified ancestry group in TOPMed; Alt, alternative; Chr, chromosome; DBP, diastolic blood pressure (BP); hcLOF, high-confidence loss-of-function variant; HTN, hypertension; MVP, Million Veteran Program; Ref, reference; REGARDS, Reasons for Geographic and Racial Differences in Stroke; SBP, systolic BP; TOPMed, Trans-Omics for Precision Medicine; UKBB, UK Biobank.

*Beta corresponds to the effect size in mmHg and natural logarithm of the odds ratio per coded allele for the continuous and discrete blood pressure phenotypes, respectively. [†]Derived from gene-based analyses of regulatory and exonic variants with predicted functional relevance. [‡]Derived from sliding window analyses. [§]Gene (if genic) or nearest gene (if intergenic).

^{||}Derived from gene-based analyses of loss-of-function, missense, or protein altering variants. [¶]Derived from gene-based analyses of high-confidence loss-of-function variants. [#]Identified in eQTL analyses.

Table S23. Results of conditional analyses at previously reported loci harboring potentially novel variants.

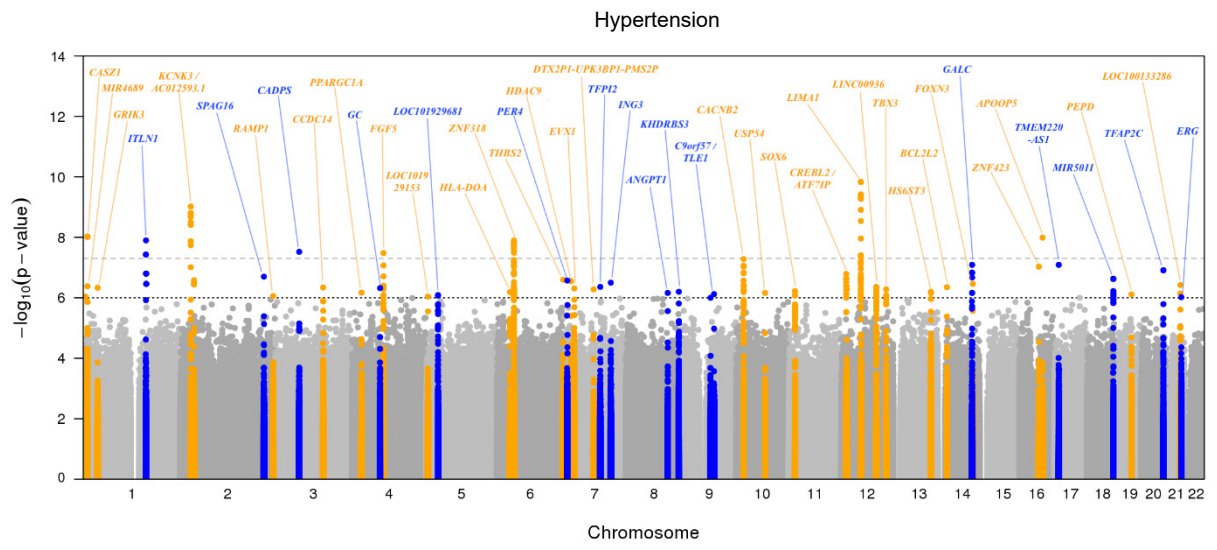
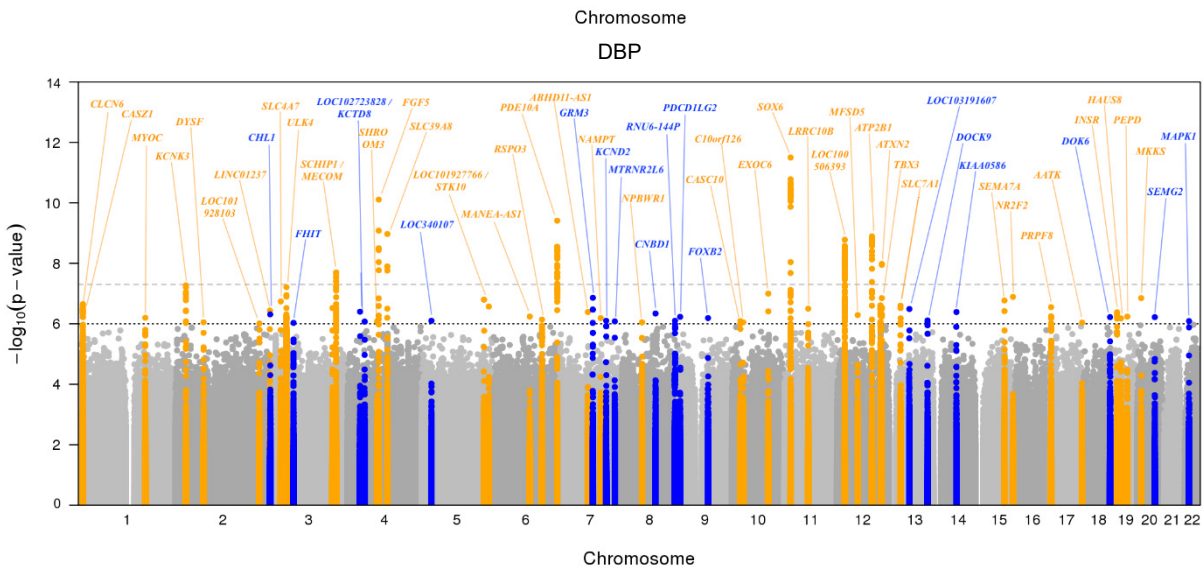
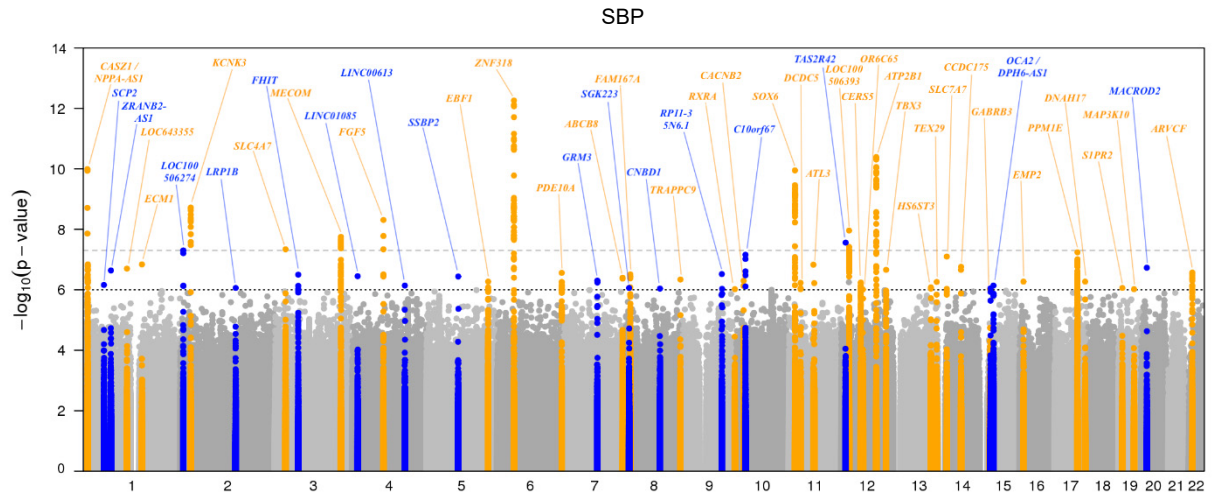
Chr	Pos (B38)	rsID	Associated Trait	Ancestry	Alleles (Ref/Alt)	AAF	Discovery stage analysis			Conditional analysis*		
							Beta	SE	P	Beta	SE	P
Newly identified rare variants from previously reported loci												
1	36845873	rs966779519	HTN	Multi	T/C	0.0003	-2.48	0.49	4.66E-07	-2.48	0.49	4.67E-07
1	112064726	rs550856031	SBP	Multi	G/C	0.0003	-20.48	3.94	2.00E-07	-20.45	3.94	2.05E-07
1	150513095	rs12031974	SBP	Multi	T/C	0.999	12.46	2.37	1.44E-07	12.47	2.37	1.41E-07
1	150513095	rs12031974	SBP	African	T/C	0.997	12.59	2.39	1.39E-07	12.63	2.39	1.28E-07
7	73727423	rs530529907	DBP	Multi	C/A	0.0005	-8.76	1.73	4.04E-07	-9.33	2.92	1.42E-03
11	30758017	rs759526273	SBP	Multi	G/A	0.0005	-12.80	2.56	5.95E-07	-12.91	2.57	4.89E-07
11	30758017	rs759526273†	SBP	European	G/A	0.001	-13.33	2.60	2.80E-07	-13.62	2.60	1.64E-07
11	31969443	rs886110723†	SBP	European	T/C	0.0008	-11.90	2.77	1.70E-05	-12.06	2.77	1.33E-05
16	59640176	rs999280636	HTN	Multi	G/A	0.0001	-4.06	0.71	1.02E-08	-19.83	5.43	2.60E-04
Newly identified common variants from previously reported loci												
19	7325055	rs36136513	DBP	Multi	A/G	0.45	-0.36	0.07	4.18E-07	-0.37	0.07	2.64E-07

AAF, alternative allele frequency; Alt, alternative allele; Chr, chromosome; DBP, diastolic blood pressure (BP); HTN, hypertension; MVP, Million Veteran Program; Multi, multi-ancestry; Pos, position; SBP, systolic BP.

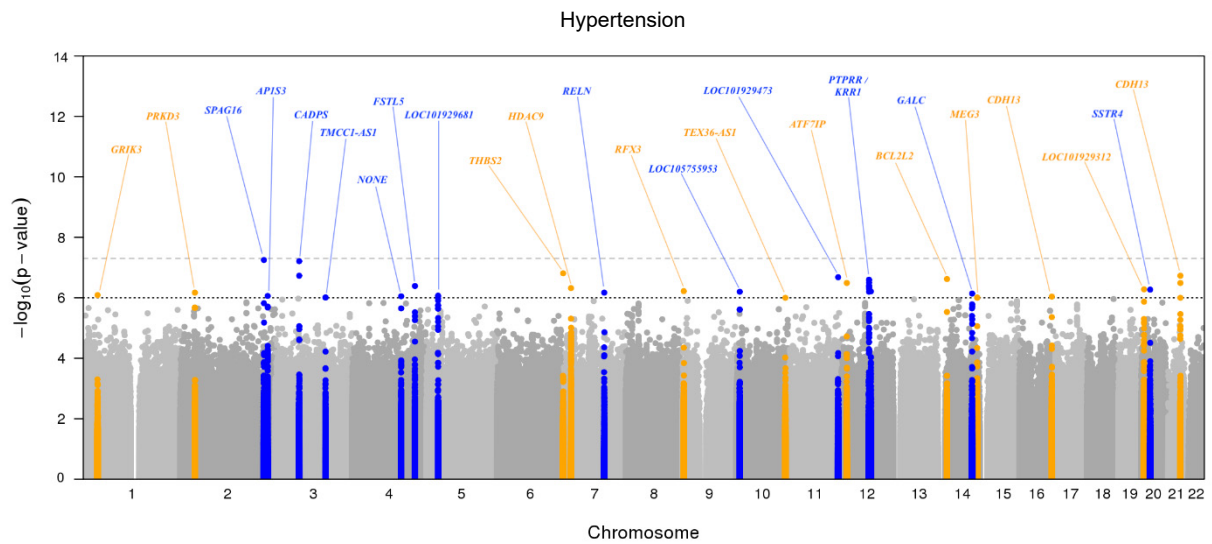
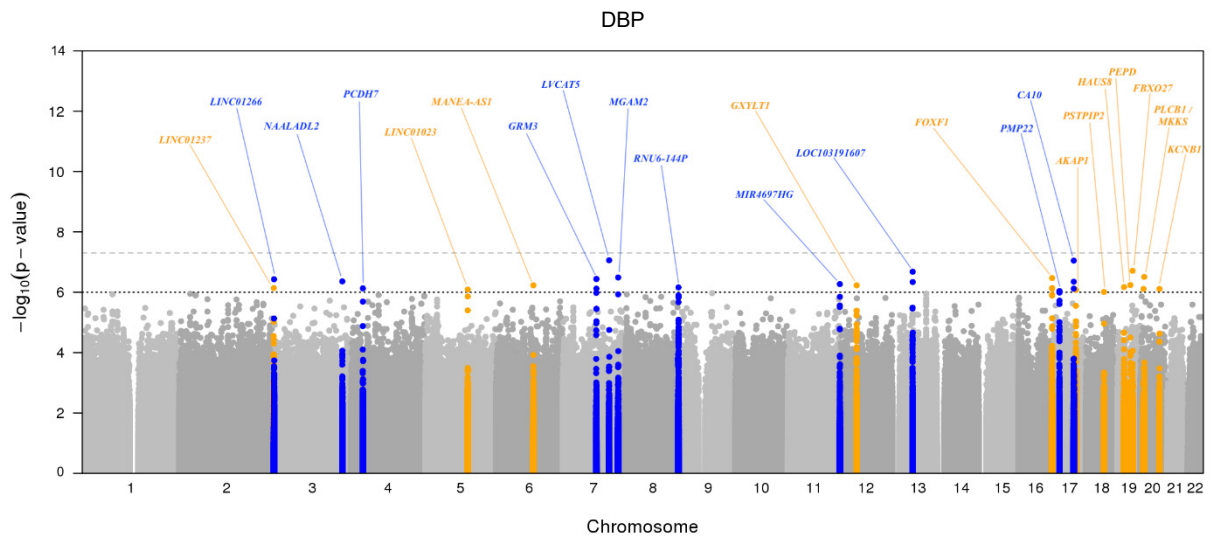
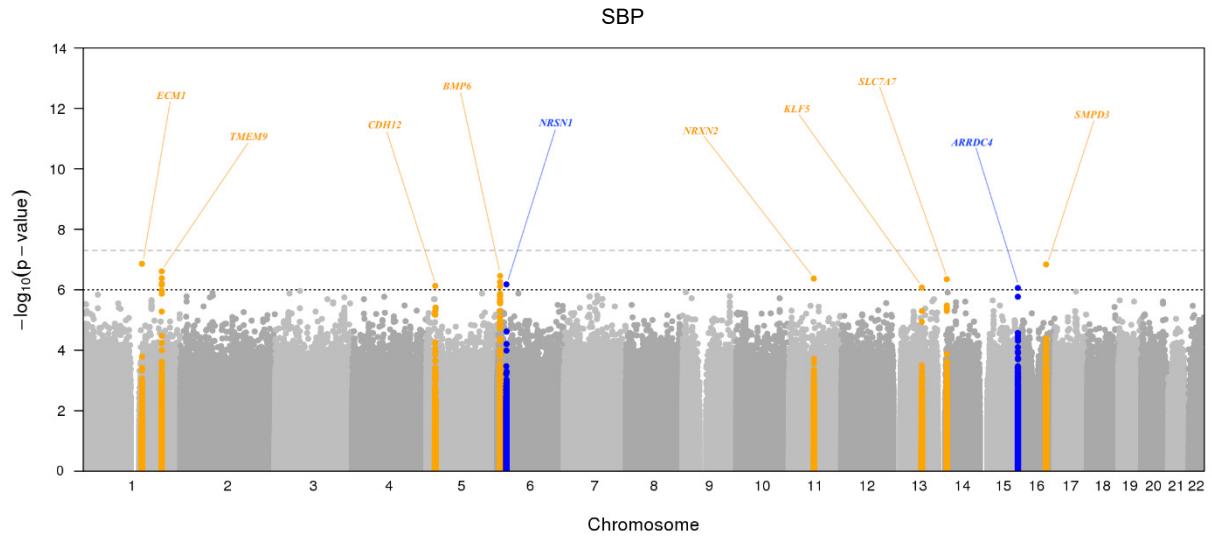
* Association of identified variant after conditioning on all previously reported variants in the 1 MB region simultaneously.

†rs759526273 and rs886110723 are in moderate LD, with both p-values attenuated when conditioning on the other (P=4.25E-03 and 0.83, respectively).

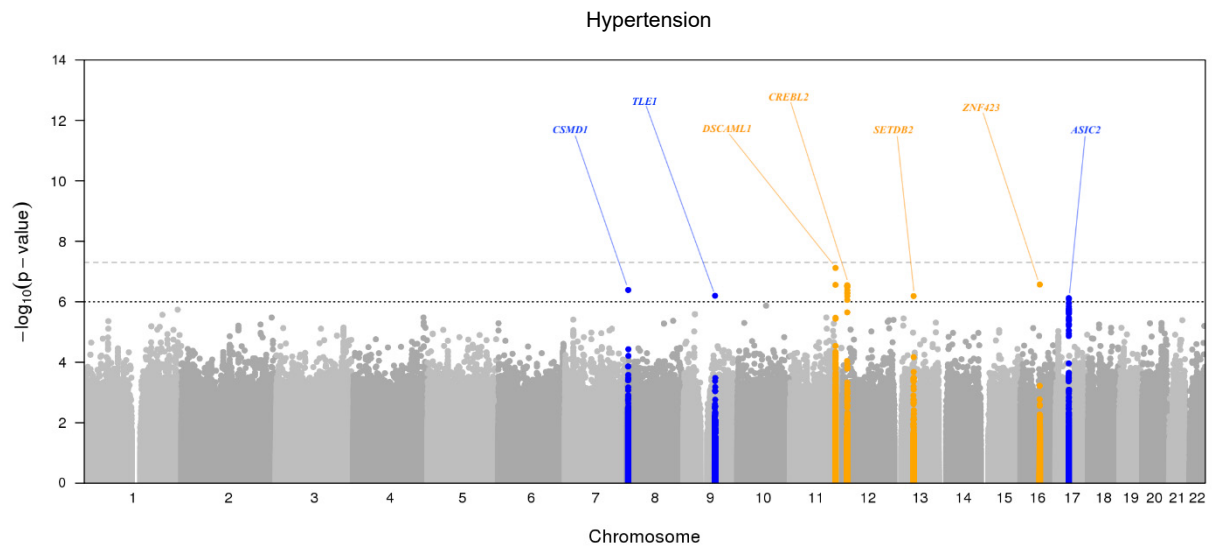
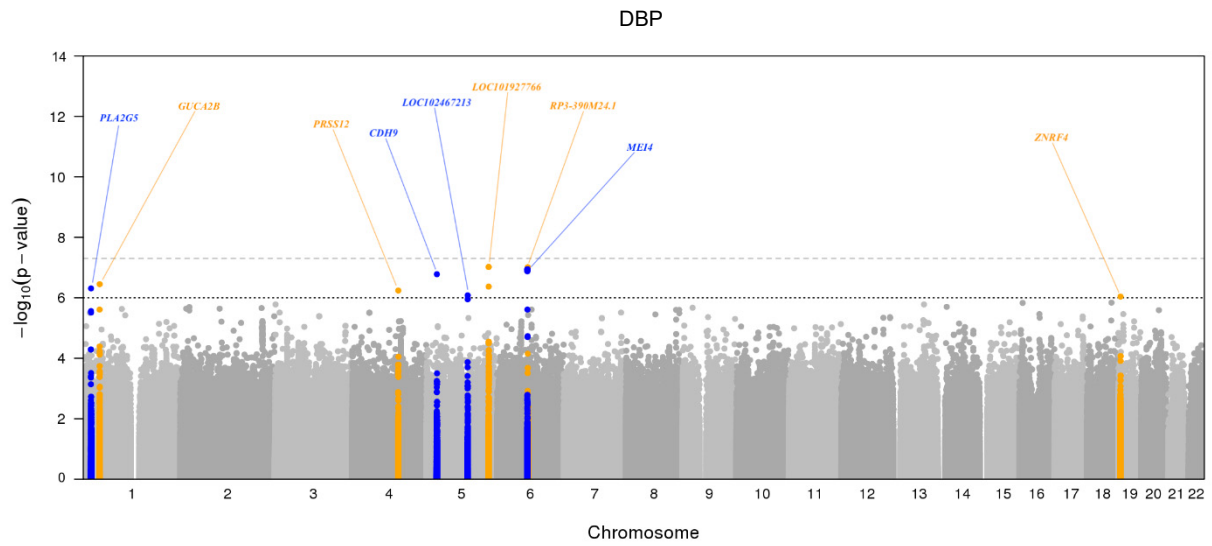
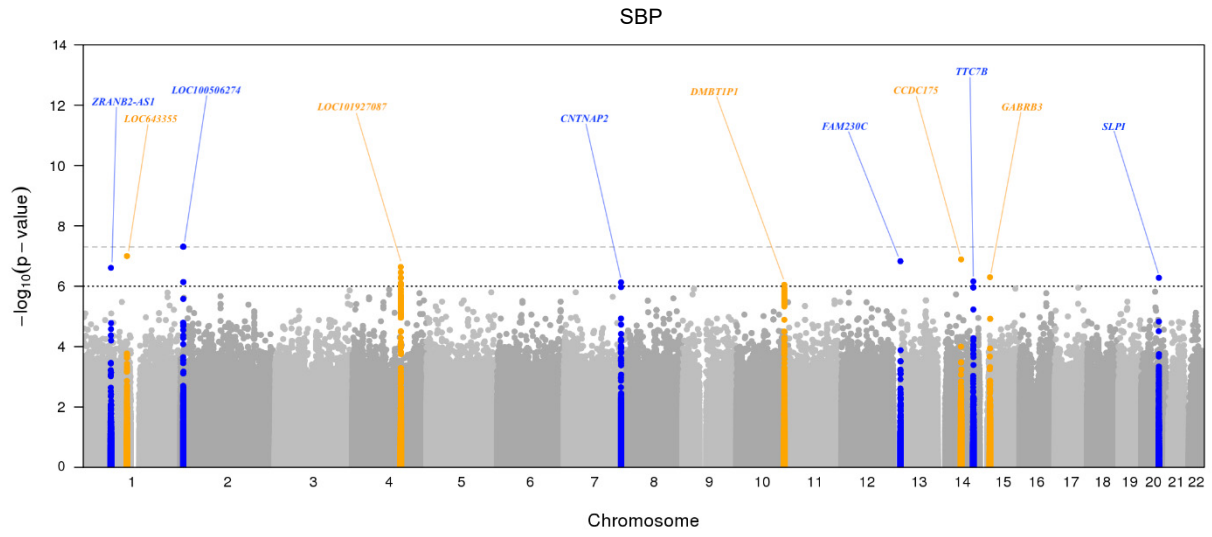
A.) Multi-ancestry sample (N=51,456)



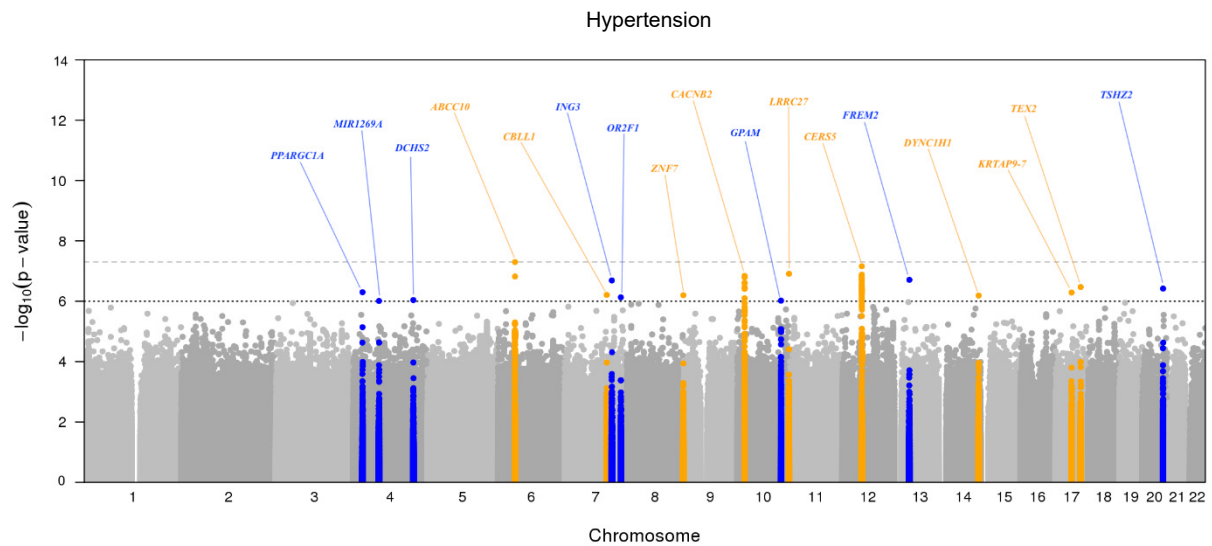
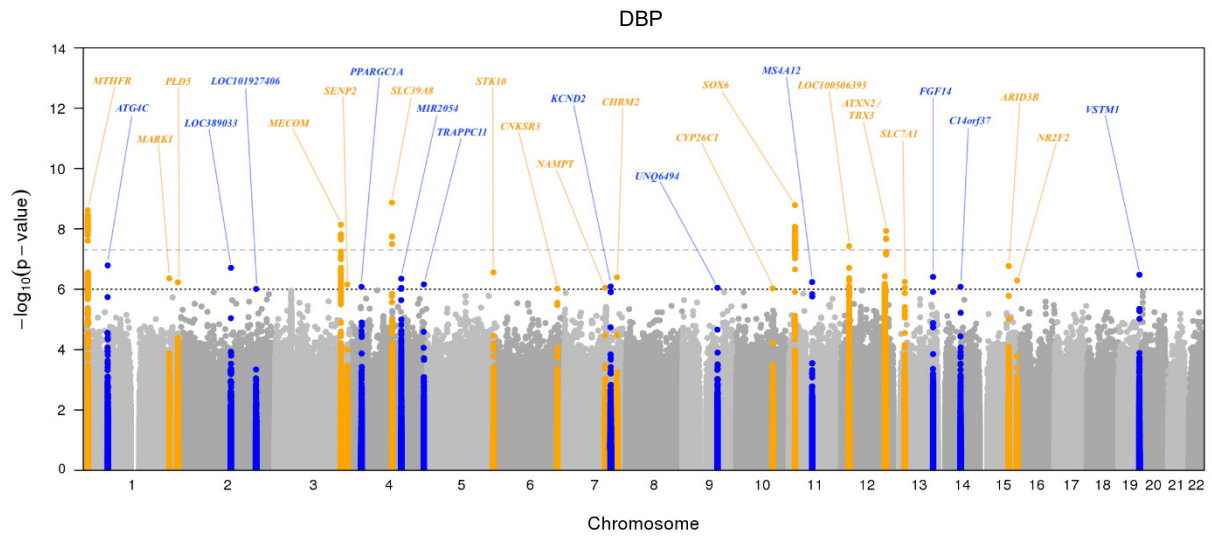
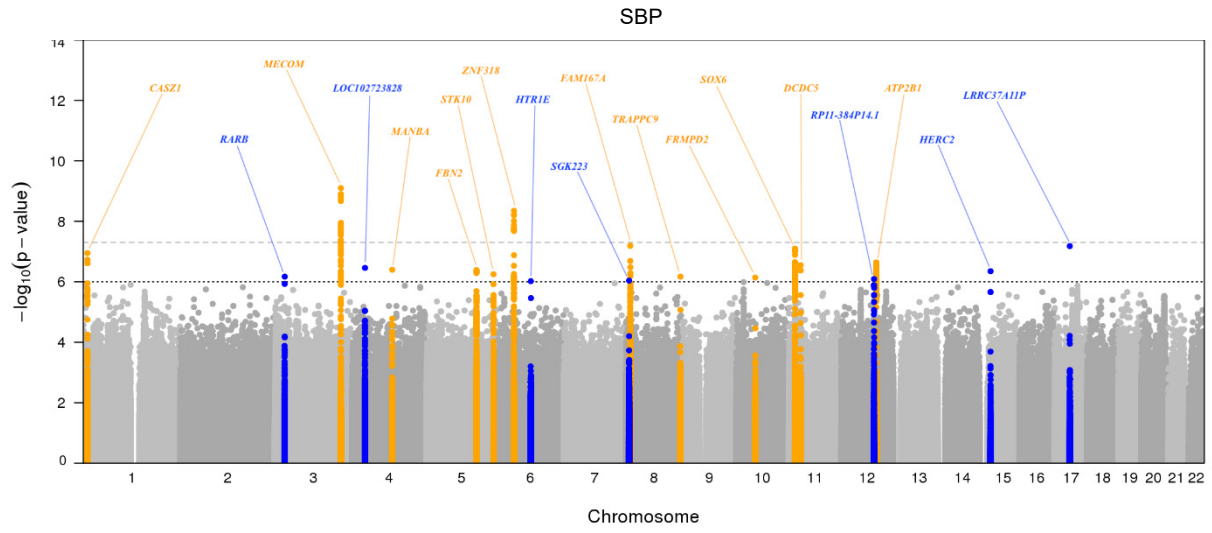
B.) African ancestry sample (N=13,836)



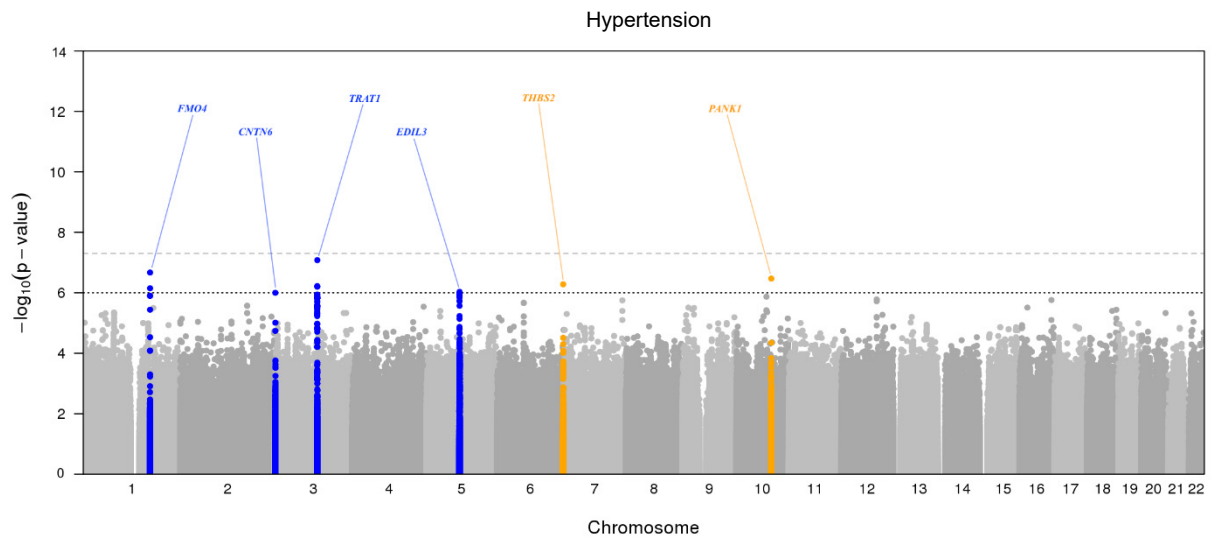
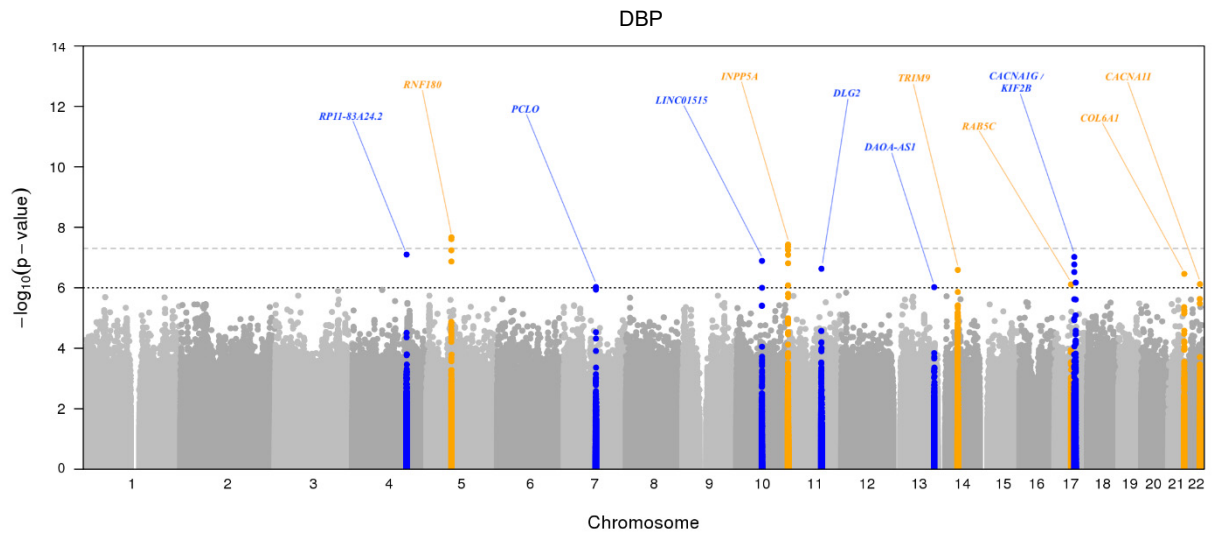
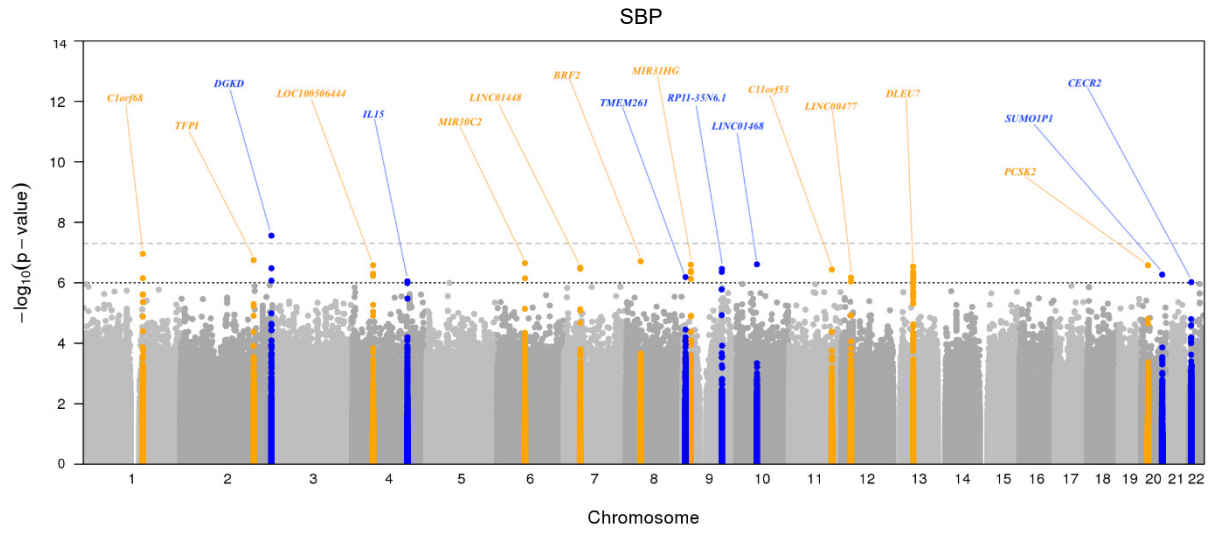
C.) Asian ancestry sample (N=3,796)



D.) European ancestry sample (N=28,390)



E.) Hispanic ancestry sample (N=4,173)



F.) Samoan ancestry sample (N=1,261)

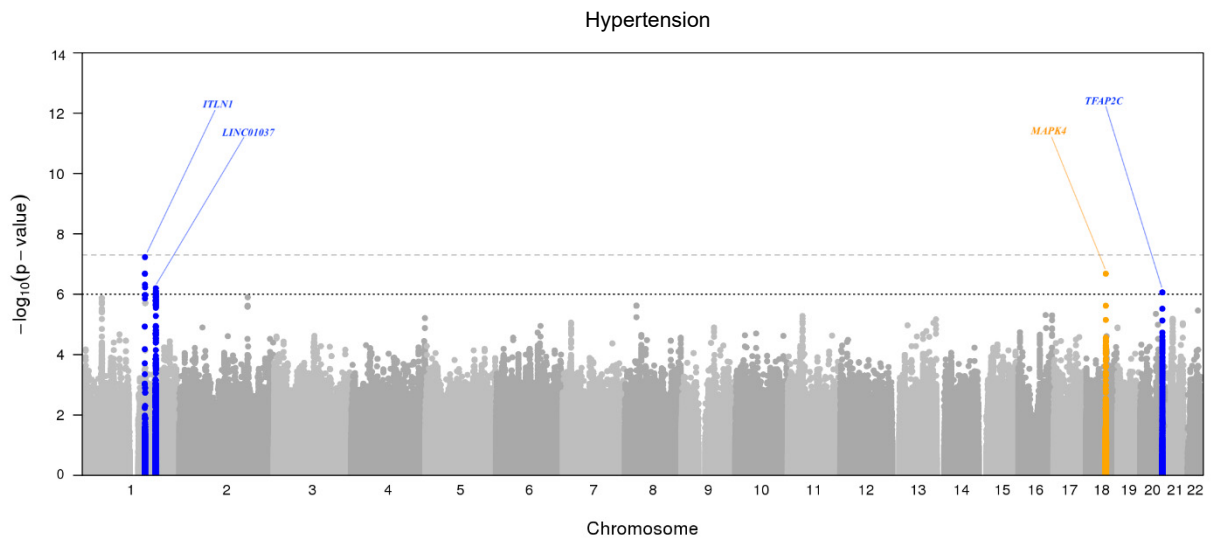
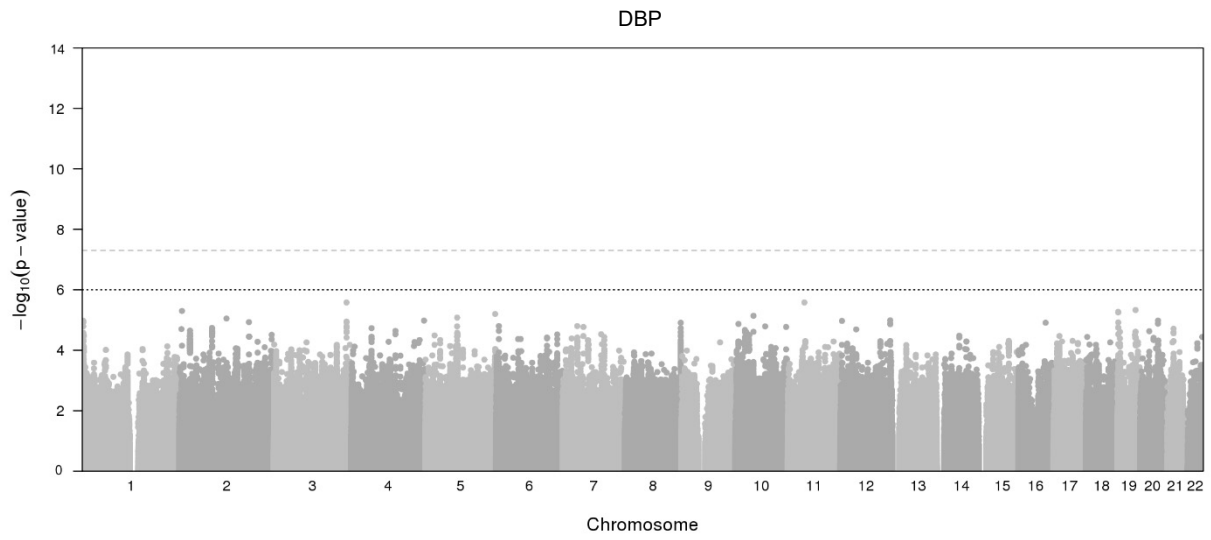
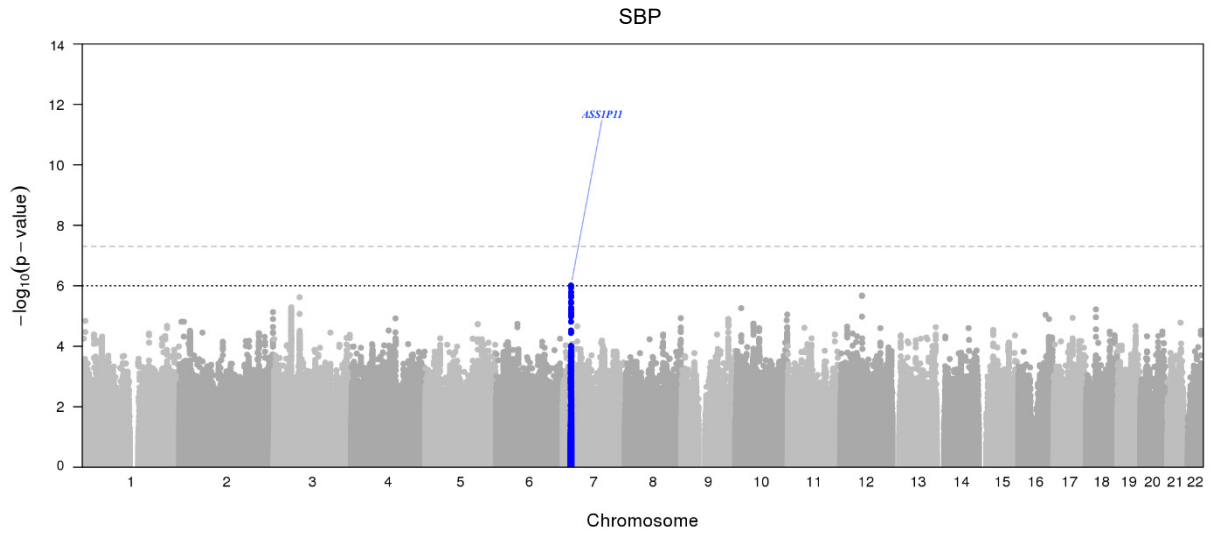
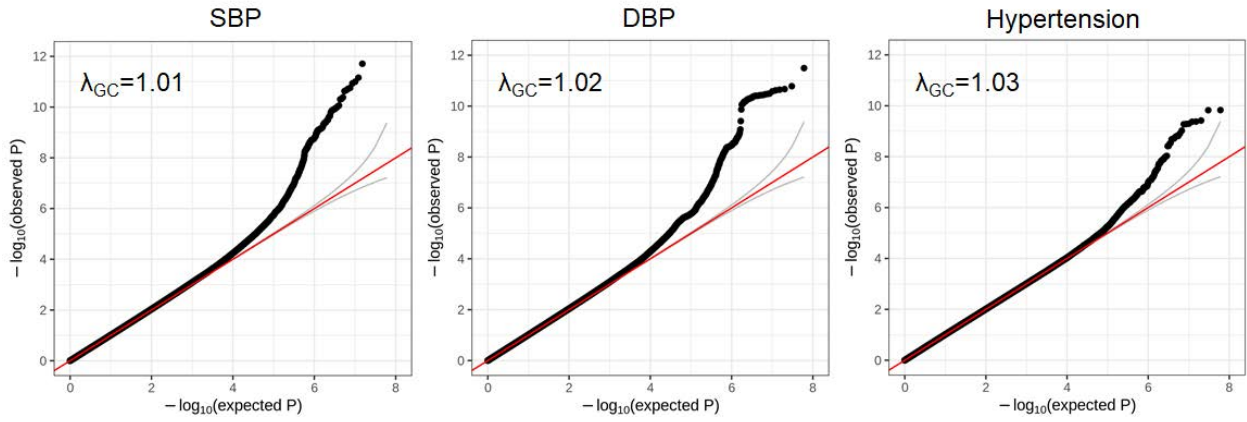
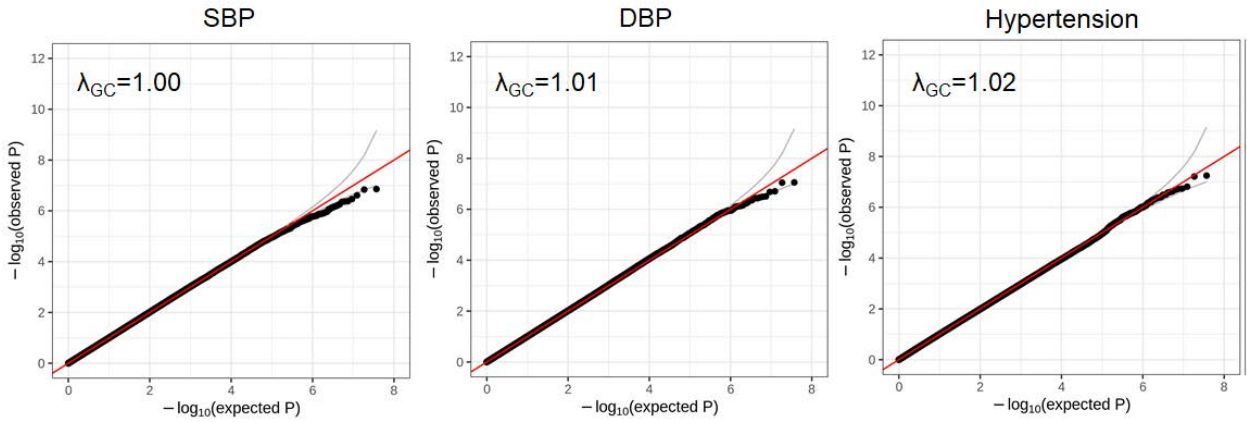


Figure S1. Manhattan plots from discovery stage (TOPMed/CCDG) single variant analyses of systolic blood pressure, diastolic blood pressure, and hypertension. Manhattan plots for SBP, DBP, and hypertension are displayed individually for the (A.) multi-ancestry, (B.) African ancestry, (C.) Asian ancestry, (D.) European ancestry, (E.) Hispanic ancestry, and (F.) Samoan ancestry samples. Novel loci are depicted in blue, and previously reported loci are depicted in yellow.

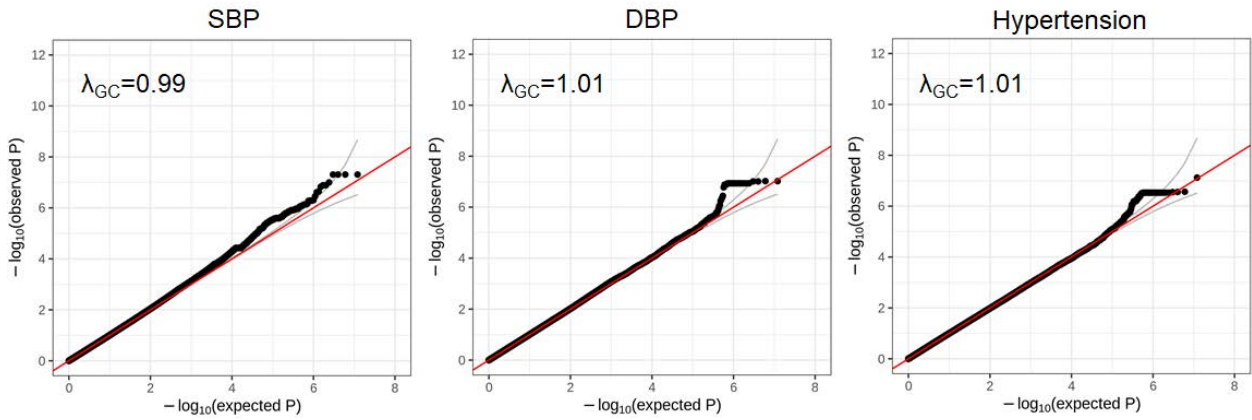
A.) Multi-ancestry sample (N=51,456)



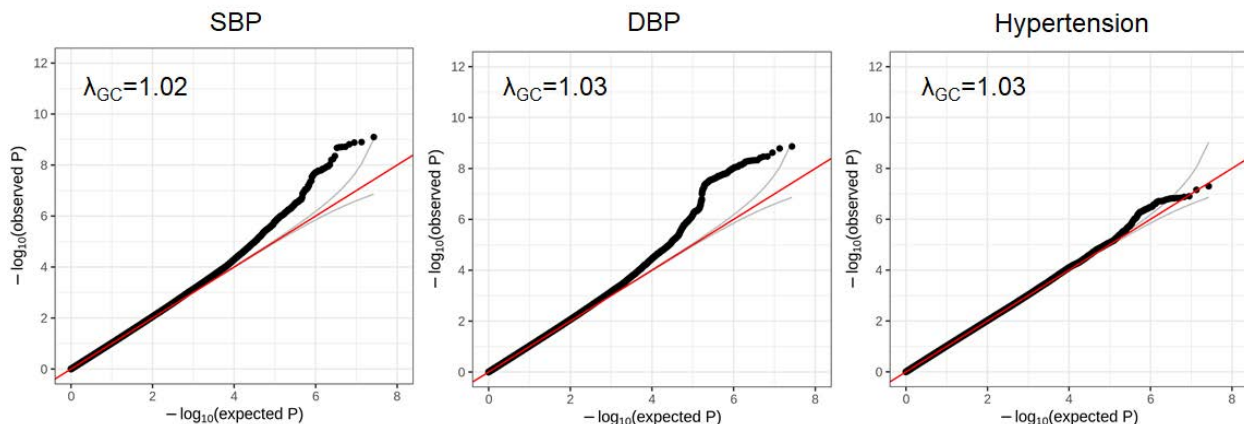
B.) African ancestry sample (N=13,836)



C.) Asian ancestry sample (N=3,796)



D.) European ancestry sample (N=28,390)



E.) Hispanic ancestry sample (N=4,173)

F.) Samoan ancestry sample (N=1,261)

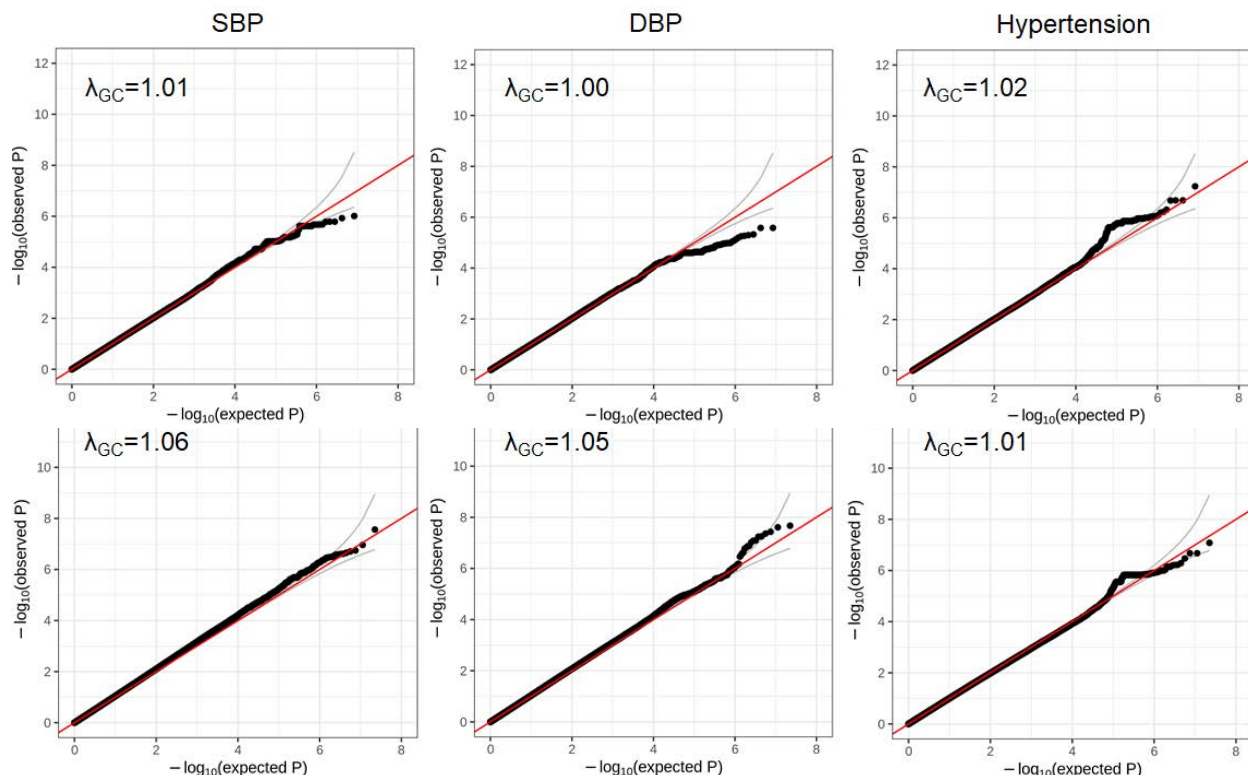


Figure S2. Quantile-quantile (QQ) plots from discovery stage (TOPMed/CCDG) single variant analyses of systolic blood pressure, diastolic blood pressure, and hypertension. QQ plots for SBP, DBP, and hypertension are displayed individually for the (A.) multi-ancestry, (B.) African ancestry, (C.) Asian ancestry, (D.) European ancestry, (E.) Hispanic ancestry, and (F.) Samoan ancestry samples.

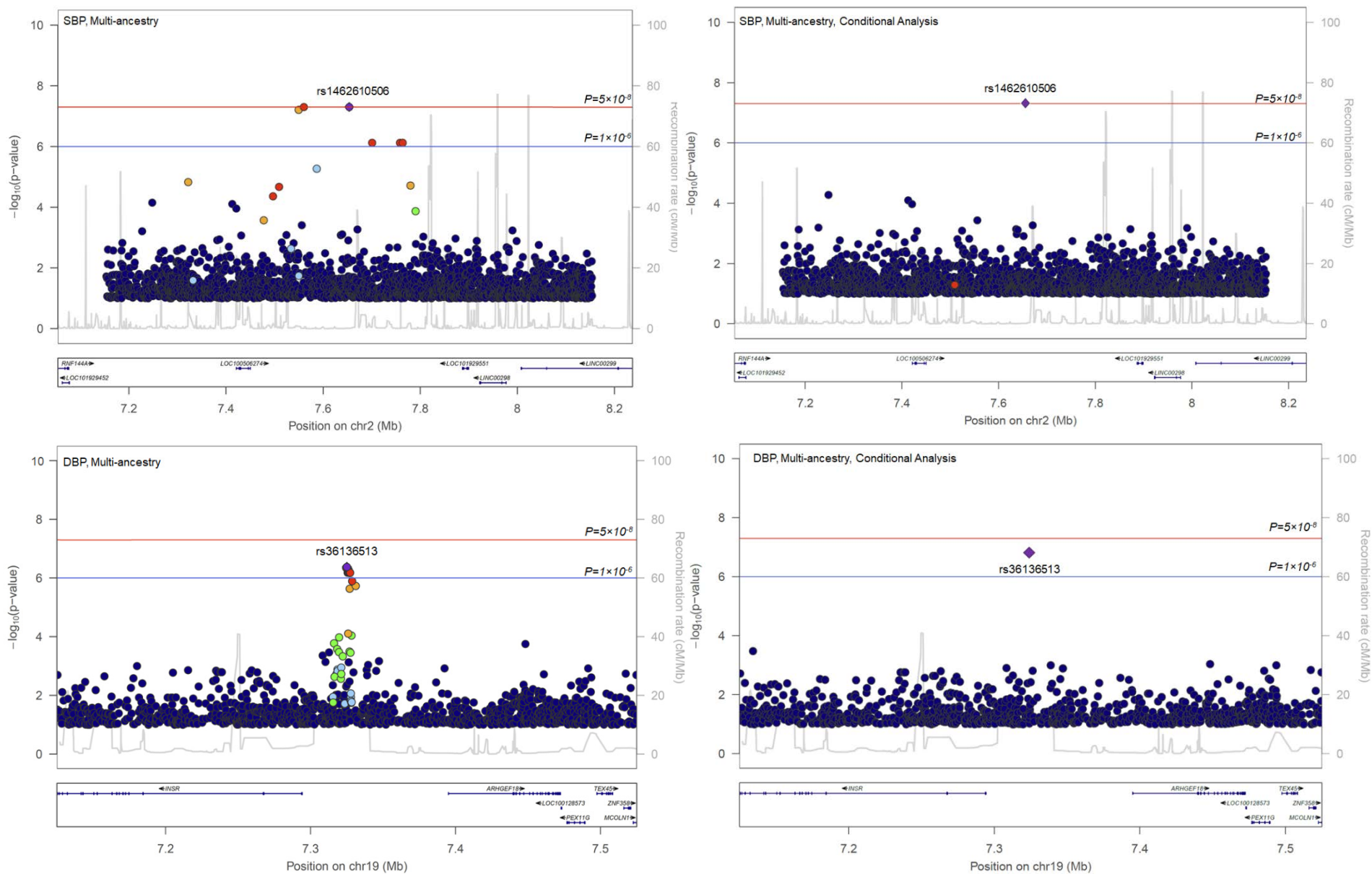


Figure S3. Conditional analyses. Results of the original analysis (left) and stepwise conditional analyses (right) for rs1462610506 (top) and rs36136513 (bottom).

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