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Methods

Our sample included 15 studies: Atherosclerosis Risk in Communities study (ARIC), British Genetics of Hypertension (BRIGHT), MGH Cardiology and Metabolic Patient cohort (CAMP), Cardiovascular Health Study (CHS), Erasmus Rucphen Family (ERF), Framingham Heart Study (FHS), INTER99, Kooperative Gesundheitsforschung in der Region Augsburg (KORA), Lifelines Cohort Study (LIFELINES), Multi-Ethnic Study of Atherosclerosis (MESA), Netherlands Epidemiology of Obesity study (NEO), Rotterdam Study (RS), Study of Health in Pomerania (SHIP), the Utrecht Health Project (UHP), and the Women's Health Initiative (WHI). Each study was reviewed and approved by the local or institutional IRB, and each participant provided consent. Study-specific details are provided in **Supplemental Material**, under "Description of participating studies" and in **Supplemental Table 1**.

Sample selection

Exclusion criteria were: AF or atrial flutter on the electrocardiogram (ECG), pacemakers or implantable cardioverter defibrillators, junctional or undetermined rhythms, complete heart block, medications that alter AV nodal conduction (beta blockers, dihydropyridine calcium channel blockers, digoxin, type I and III antiarrhythmic medications), or missing genotype or phenotype data.

PWD measurements

PWD was calculated as the sum of the positive (P) and the negative (P') phase of the PWD in each lead of a 12-lead ECG and reported in milliseconds. We tested associations between genetic variants and the maximum PWD across 12 leads in each study.

Study-specific analyses

Details of genotyping, variant calling, and genotype quality control are provided in **Supplemental Table 2**. We performed single variant score tests to evaluate the additive genetic effect of each variant on ethnicity-stratified PWD residuals using RAREMETALWORKER.[1] PWD residuals were obtained from linear regression models adjusted for age, sex, RR interval, and study-specific population structure covariates. We analyzed these PWD residuals along with the inverse normal transformed (quantile normalization) PWD residuals, and accounted for relatedness between samples using the kinship matrix or empirical kinship matrix estimated by RAREMETALWORKER. We display details on study-specific analyses in **Supplemental Table 2**.

Pooled common and rare variant (gene-based) analyses

Before aggregating results from individual studies, we removed genotyped variants with call rates <95% or deviations from Hardy-Weinberg proportions (*P*-value $<1\times10^{-5}$) from each study. We assigned monomorphic variants in individual studies a zero contribution for pooled allele frequencies. We used RAREMETAL 4.15.1[1] to perform meta-analysis of single variant and gene-level association tests.

We assessed single variant meta-analysis score statistics from each study with pooled minor allele frequencies (MAF) ≥5%. We included only variants where data were available in greater than or equaled to 60% of the maximum sample size, a cutoff imposed to avoid including cohort-specific variants. For multi-ethnic analyses, we set the significance threshold for single variant analysis at 1.9×10^{-6}, after Bonferroni correction (*P*-value/25996 [total number of tests]; **Supplemental Table 3**). When ≥2 variants exceeded our significance threshold, and were within ±500kb of the most significant variant, we reported only the top variant for that locus. We estimated genetic effect heterogeneity (I^2) among studies for the top exome-wide significant loci using the R package, metafor (version 1.9-9).[2] For inflated common variant results (lambda ≥1.10), we performed linkage disequilibrium (LD) score regression[3] restricted to variants in the GWAS backbone (LD score of HapMap3 variants provided by LD score package) to assess for polygenic architecture or confounding bias. To identify additional independent variants associated with PWD at the same locus, we performed conditional analyses in the multi-ethnic results using variance-covariance matrices after adjusting for the top exome-wide significant variants. If the remaining top variant exceeded the exome-wide significance threshold, we performed an additional round of conditional testing.

For rare and low-frequency variants with pooled MAF <5% or <1%, we performed a meta-analysis of the gene-based burden test and sequence kernel association test (SKAT) using the approach of Liu *et al*.[4] We included single nucleotide variants annotated as 1) missense, 2) splice acceptor, 3) splice donor, or 4) stop gained by Sequence Ontology in Variant Effect Predictor.[5] We tested genes with cumulative minor allele counts (cMAC) ≥10 and restricted variants with at least 60% of the maximum sample size. The significance threshold for gene-

based analyses in the multi-ethnic analysis was set at $P \leq 3.0\times10^{-6}$. Ethnic-specific *P*-value significance thresholds are presented in **Supplemental Table 3.** We additionally performed look-up of single variant tests among the significant genes. If any low-frequency variants exceed the single variant significant threshold in such ethnic group, we report them as top exome-wide significant variants in **Table 2**.

Relation between PWD, other ECG traits, and AF

To annotate the underlying biological functions of the top PWD loci, we examined whether top variants and proxies (LD: $r^2>0.8$; 1000 Genomes: phase 3 version 5, all individuals from LDlink[6]) were cis-eQTLs in heart tissues (right atrial appendage (RAA, n=264) and left ventricle (LV, n=272)) using GTEx version 7.[7] We defined significant cis-eQTLs using a false discovery rate (FDR) threshold of ≤0.05. When a significant cis-eQTL was observed in one heart tissue, we assessed the cis-eQTL association in the other heart tissue, then tested for a difference in association (regression effect beta) between the two heart tissues using Z-statistics, accounting for correlations in gene expression in the two tissues. The correlation was estimated using 179 individuals who had LV and RAA expression data. We used the Bonferroni correction to establish the *P*-value significance threshold for differences in association for the 10 significant cis-eQTLs (P<0.05/10 tests=0.005). We performed a search of our top loci in published genetic association analyses of AF[8] and other ECG traits.[9-12] Quantile-quantile (QQ) plots, Manhattan plots, and correlation plots were made using R version 3.3.0.[13]

Description of participating studies

ARIC

The Atherosclerosis Risk in Communities study (http://www.cscc.unc.edu/aric/) includes 15,792 men and women from four communities in the United States (Jackson, Mississippi; Forsyth County, North Carolina; Washington County, Maryland; suburbs of Minneapolis, Minnesota) enrolled in 1987–1989 and prospectively followed.[14] The study ECGs were recorded with MAC PC ECG machines (Marquette Electronics, Milwaukee, WI) in all clinical centers. ECGs were initially processed in a central laboratory at the EPICORE Center (University of Alberta, Edmonton, Alberta, Canada) and during later phases of the study at the EPICARE Center (Wake Forest University, Winston-Salem, NC). All ECGs were visually inspected for technical errors and inadequate quality. Initial ECG processing was done by the Dalhousie ECG program, and processing was later repeated with the 2001 version of the GE Marquette 12-SL program (GE Marquette, Milwaukee, WI). P-wave duration (maximum, mean, and in lead II) was measured in milliseconds as the first "onset" and last "offset" deflection from the baseline. P-wave area (maximum and mean) was measured in microvolt · milliseconds2 as the area under the P-wave in the 12 leads of the ECG. PR duration was measured in milliseconds as the mean P-wave duration plus the mean PR-segment duration in the 12-lead ECG.

BRIGHT

Cohort description: http://www.brightstudy.ac.uk/

Twelve-lead ECG recordings (Siemens-Sicard 440;http://www.brightstudy.ac.uk/info/sop04.html), which produces an automated

measurements of ECG parameters, were available for all subjects. All data were transferred from each recruitment center by electronic modem to electrophysiologists from the West of Scotland Primary Prevention Study (Professor Peter MacFarlane) for central reporting. P-wave duration was calculated as the maximum of the sum of the positive and negative P-wave durations in each lead. Then, we excluded any P-wave duration <40ms or P-wave duration>180ms.

CAMP

The MGH Cardiology and Metabolic Patient (CAMP MGH) cohort comprises 3857 subjects recruited between 2008 and 2012. Two thirds of the subjects were drawn from patients who had appointments with a physician in the MGH Heart Center, whereas one third were recruited independent of any hospital visit. All subjects had plasma and serum samples collected, as well as blood for genomic DNA. ECG was performed on subjects who did not have a tracing within the past 6 months. ECG information was obtained by GE Mac 5000 and processed by GE Marquette 5500.

CHS

The Cardiovascular Health Study (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.[15] 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 were enrolled for a total sample of

5,888. Study electrocardiograms were recorded using MAC PC ECG machines (Marquette Electronics, Milwaukee, Wisconsin) in all clinical centers. ECGs were initially processed in a central laboratory at the EPICORE Center (University of Alberta, Edmonton, Alberta, Canada) and during later phases of the study, at the EPICARE Center (Wake Forest University, Winston-Salem, North Carolina). All ECGs were visually inspected for technical errors and inadequate quality. All measurements are from the baseline ECG for eligible subjects. Initial ECG processing was done by the Dalhousie ECG program, and processing was later repeated with the 2001 version of the GE Marquette 12-SL program (GE Marquette, Milwaukee, Wisconsin).

Erasmus Rucphen Family Study (ERF)

Erasmus Rucphen Family study (ERF) is a family based study conducted in a genetically isolated population in the South-West of the Netherlands, studied as part of the Genetic Research in Isolated Population (GRIP) program.[16, 17] The aim of this study is to identify genetic risk factors of complex diseases and genetic associations to complex traits. Study population includes approximately 3,000 participants who are descendants of a limited number of founders living in the 19th century. All data were collected between 2002 and 2005. All participants gave written informed consent and the Medical Ethics Committee at Erasmus MC University Medical Center approved the study. Study participants from the ERF cohort (N = 1,527) were genotyped on the Illumina Infinium HumanExome BeadChip, version 1.1. Calling was performed with GenomeStudio and the ZCall variant calling tool (Broad Institute).[18] A 10s 12-lead ECG (on average, 8–10 beats) was recorded with an ACTA-ECG electrocardiograph (Esaote, Florence,

Italy) with a sampling frequency of 500 Hz. Digital measurements of the ECG parameters were made using the Modular ECG Analysis System (MEANS).[19, 20]

FHS

Study descriptions and methods are provided elsewhere.[21-23] ECGs from FHS were read independently by FHS and analyzed using GE 12-SL software; the PWD calculated using this software have been reported as having a repeatability of 100%. This study included 5878 participants from three generations (Original cohort exam 20, Offspring cohort exam 6, and third Gen exam 1), and the mean age was 48 years.

INTER99

The Inter99 study carried out in 1999-2001 included invitation of 12,934 persons aged 30-60 years drawn from an age- and sex-stratified random sample of the population. The baseline participation rate was 52.5%, and the study included 6,784 persons. The Inter99 study was a population-based randomized controlled trial (CT00289237, ClinicalTrials.gov) and investigated the effects of lifestyle intervention on CVD.[24] ECG information was obtained from the MUSE Cardiology Information System (GE Healthcare, Wauwatosa, Wisconsin) analyzed by the Marquette 12SL algorithm version 21.

KORA

Details on the KORA Study have been described elsewhere.[25, 26] In brief, the KORA Study (Cooperative Health Research in the Region of Augsburg, Germany) is a community-based

cohort study comprising several surveys. Between 1999 and 2001, the KORA Survey S4 enrolled 4261 participants between 25 and 75 years of age. In 2006 to 2008, the KORA Survey F4 was conducted as a 7-year follow-up examination of the Survey S4. The current data are based on KORA Survey F4. All participants received a detailed interview and assessment of their demographic and medical background. In addition, all participants provided a biosample for genetic analyses and all received an ECG. A 10 sec 12-lead ECG was recorded in a systematic fashion following 10 minutes rest in supine position using the Hannover ECG System (HES MWZ Version 3.22-11). For the present analysis, the duration of the P-wave was defined from the first positive or negative deflection of the P-wave in any of 12 leads until the last return of the P-wave to the isoelectric line in any of 12 leads, resulting in the maximum P-wave duration.

LifeLines

LifeLines is a multi-disciplinary prospective population-based cohort study examining in a unique three-generation design the health and health-related behaviors of 165,000 persons living in the North East region of The Netherlands. It employs a broad range of investigative procedures in assessing the biomedical, socio-demographic, behavioral, physical and psychological factors which contribute to the health and disease of the general population, with a special focus on multimorbidity and complex genetics. Details of the protocol have been described elsewhere (https://www.lifelines.nl/lifelines-research/news). Standard 12-lead electrocardiograms were recorded with CardioPerfect equipment (Cardio Control; currently

192 Welch Allyn, Delft, The Netherlands) and digital measurements of the P-wave duration were
193 extracted.[27]
194
195 ***UHP***
196 The Utrecht Health Project (UHP) is an ongoing dynamic population study initiated in a newly
197 developed large residential area in Leidsche Rijn, part of the city of Utrecht.[28] All new
198 inhabitants were invited by their general practitioner to participate in the UHP. Written
199 informed consent was obtained and an individual health profile (IHP) was made by dedicated
200 research nurses. The UHP study was approved by the Medical Ethical Committee of the
201 University Medical Center, Utrecht, The Netherlands. A large number of measures were taken,
202 including anthropomorphic and blood pressure measurements, and each participant filled out a
203 questionnaire. ECGs were recorded with CardioPerfect equipment (Welch Allyn, USA). The 12-
204 lead ECG, taken in the resting condition, was digitally stored and analyzed by the Modular ECG
205 Analysis System (MEANS).[29] P-wave duration was calculated automatically.
206
207 ***MESA***
208 The Multi-Ethnic Study of Atherosclerosis (MESA) is a study of the characteristics of subclinical
209 cardiovascular disease (disease detected non-invasively before it has produced clinical signs and
210 symptoms) and the risk factors that predict progression to clinically overt cardiovascular
211 disease or progression of the subclinical disease. The cohort is a diverse, population-based
212 sample of 6,814 asymptomatic men and women aged 45-84. Approximately 38% of the
213 recruited participants are European, 28% African-American, 22% Hispanic, and 12% Asian

(predominantly of Chinese descent). Participants were recruited during 2000-2002 from 6 field centers across the US (at Wake Forest University; Columbia University; Johns Hopkins University; the University of Minnesota; Northwestern University; and the University of California – Los Angeles). All underwent anthropomorphic measurement and extensive evaluation by questionnaires at baseline, followed by 4 subsequent examinations at intervals of approximately 2-4 years. Age and sex were self-reported.

ECGs were recorded in the supine position after a period of rest. MESA ECG data were collected using GE MAC 1200 electrocardiographs. Digitally collected ECGs were transferred via phone lines to the MESA ECG center (EPICARE). The ECGs were automatically processed by use of GE Marquette 12-SL software (2001 version), after visual inspection of the recordings for quality.

For genotyping, samples were processed on the HumanExome BeadChip v1.0 (Illumina, Inc., San Diego, CA; 247,870 variants). Raw genotyping data were jointly called by the Human Genetics Center of the University of Texas Health Science Center at Houston in 10 cohorts from the CHARGE Exome Chip working group (AGES, ARIC, CARDIA, CHS, FamHS, FHS, Health ABC, JHS, MESA, RS). Initial quality control procedures were applied to all samples in joint calling.

Further information can be found at: http://www.mesa-nhlbi.org and http://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/study.cgi?study_id=phs000209.v13.p3

NEO

Study descriptions and methods are provided elsewhere.[30] A 12-lead ECG was obtained using a Mortara Eli-350 electrocardiograph (Mortara Instrument Inc., Best, the Netherlands) after a

resting period of at least 10 minutes. ECGs were analysed using the automatic MATLAB-based (The MathWorks, Natick, MA) program BEATS and the semiautomatic program LEADS. P-wave duration was determined by ECG.

Rotterdam Study

Rotterdam Study is a prospective population-based cohort study.[31] The Rotterdam study started in 1989 with an initial cohort of 7,983 persons (out of 10,215 invitees; response rate 78%) 55 years of age or older living in the Ommoord district in the city of Rotterdam in the Netherlands. Approximately every 4-5 years follow-up examinations are conducted. Examinations consist of a home interview and an extensive set of tests at a research facility in the study district. By linking the general practitioners' and municipality records to the study database, participants are continuously monitored for major morbidity and mortality. Standard 12-lead resting ECGs were recorded with an ACTA electrocardiograph (ESAOTE, Florence, Italy) at a sampling frequency of 500 Hertz and stored digitally. All ECGs were processed by the Modular ECG Analysis System (MEANS) to obtain ECG measurements. The duration of the P-wave was measured from the start until the end of the P-wave. The amplitude of the P-wave was taken as the maximum (absolute) amplitude of the P-wave in all 12 leads.

SHIP

SHIP is a population-based project in West Pomerania, a region in the northeast of Germany, that consists of two independent prospectively collected cohorts (SHIP and SHIP-Trend) assessing the prevalence and incidence of common population-based diseases and their risk

factors.[32] The study design has been previously described in detail. Briefly, a sample from the population aged 20 to 79 years was drawn from population registries. First, the three cities of the region (with 17,076 to 65,977 inhabitants) and the 12 towns (with 1,516 to 3,044 inhabitants) were selected, and then 17 out of 97 smaller towns (with less than 1,500 inhabitants), were drawn at random. Second, from each of the selected communities, subjects were drawn at random, proportional to the population size of each community and stratified by age and gender. Only individuals with German citizenship and main residency in the study area were included. For SHIP, baseline examinations were carried out from 1997 until 2001, and the sample finally comprised 4,308 participants. Baseline examinations for SHIP-Trend were carried out between 2008 and 2012, finally comprising 4,420 participants. Participants underwent a standardized, digital 12-lead ECG at rest in the supine position as a component of the cohort examination. All P-wave indices were quantified using contemporary software algorithms from digitized tracings. Electrocardiograms were recorded using the Personal 120LD (Esaote, Genova, Italy) and analyzed with the Modular ECG Analysis System.[33]

WHI

The Women's Health Initiave (WHI) is a long-term national health study that has focused on strategies for preventing heart disease, breast and colorectal cancers, and osteoporotic fractures in postmenopausal women. Briefly, the WHI was designed as a set of randomized controlled clinical trials (CTs) and an observational study (OS). The CT (n= 68,132) included 3 overlapping components: the hormone therapy trials (n= 27,347), dietary modification trial (n= 48,835), and calcium and vitamin D trial (n= 36,282). Eligible women could be randomly

assigned into 1, 2, or all 3 of the CT components. Women who were ineligible or unwilling to join the CT were invited to join the OS (n= 93,676).

All subjects (N=68,132) in the WHI clinical trial received ECGs at baseline (1992-1998).[34, 35] A variety of WHI ancillary studies, focusing on different parts of the cohort and/or different phenotypes had subjects genotyped on the exome chip. The largest sub-groups among those women were a case-control study of colorectal cancer, subjects that enrolled in the Hormone Therapy clinical trial, and subjects who had bone mineral density measured. The overall study website is www.whi.org. The ECG measurement protocol is described in Volume 2, Chapter 13 of the WHI manual of operations (https://www.whi.org/researchers/studydoc/_layouts/15/WopiFrame.aspx?sourcedoc=/researchers/studydoc/WHI and ES1 Manual of Operations/1993-2005 WHI CT and OS/Vol 2, 13 - ECG Procedures.pdf). Briefly, 12 lead ECGs were recorded while subjects were, supine, at rest, using the MACPC ECG machines (Marquette Electronics, Milwaukee, WI). ECGs were analyzed by Epicare using standard Minnesota-code and Nova-code algorithms, which included determination of the P-wave.

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CHARGE

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ARIC

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BRIGHT

This work was supported by the National Institutes of Health Research (NIHR) Cardiovascular Biomedical Centre at Barts and The London, Queen Mary University of London, by the UCLH Biomedicine NIHR, Barts Heart Centre BRC. This research utilized Queen Mary's Apocrita HPC facility, supported by QMUL Research-IT. http://doi.org/10.5281/zenodo.438045.

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CAMP

The recruitment, collection of samples, and genotyping was supported by Pfizer. Analysis of data was a three-way collaboration between MGH, the Broad Institute, and Pfizer.

CHS

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ERF

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FHS

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KORA

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368

369 ***LifeLines***

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378

379 ***Multi-Ethnic Study of Atherosclerosis (MESA)***

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384 75N92020D00003, N01-HC-95162, 75N92020D00006, N01-HC-95163, 75N92020D00004, N01-
385 HC-95164, 75N92020D00007, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168,
386 N01-HC-95169, UL1-TR-000040, UL1-TR-001079, UL1-TR-001420, UL1-TR-001881, and
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388 Genotyping was performed at Affymetrix (Santa Clara, California, USA) and the Broad Institute

of Harvard and MIT (Boston, Massachusetts, USA) using the Affymetrix Genome-Wide Human SNP Array 6.0.

NEO

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RS

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425 Website http://www.epib.nl/research/ergo.htm
426
427 ***SHIP-0 and SHIP-Trend***
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WHI

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Supplemental Tables

Supplemental Table 1: Study participant characteristics

Study acronym	Study Full Name	Study design	Ethnicity and origin	Total sample size (genotype + phenotype)	Participants in analysis, N
ARIC	The Atherosclerosis Risk in Communities study	Population based	Americans with European and African Ancestry	11478 4266	8861 2922
BRIGHT	British Genetics of Hypertension	Hypertensive cases	White Europeans from United Kingdom	1361	195
CAMP	MGH Cardiology and Metabolic Patient cohort	Population based	MGH Heart Center subjects	2336	1887
CHS	Cardiovascular Health Study	Cohort	European American African American	2648 445	2648 445
ERF	Erasmus Rucphen Family Study	Family-based study	Genetically isolated population in the South-West of the Netherlands	1527 (1515 after QC)	514
FHS	Framingham Heart Study	Community-based	European American	7837	5677
INTER99	INTER99	Population based	Europeans from the Denmark	5887	5872
KORA	Kooperative Gesundheitsforschung in der Region Augsburg	Population based	Europeans from Germany	2883	2435
LIFELINES	The Lifelines Cohort Study	Population based	Europeans from the Netherlands	1949	1914
UHP	Utrecht Health Project	Population based	Dutch citizens of European Ancestry	1657	1657
MESA	Multi-Ethnic Study of Atherosclerosis	Population based	Thirty-eight percent of the recruited participants are white, 28 percent African-American, 22 percent Hispanic, and 12 percent Asian, predominantly of Chinese descent.	6814	2083 1131 1186 630
NEO	The Netherlands Epidemiology of Obesity study	Population based	Europeans from the Netherlands	6052	5119
RS	Rotterdam Study	Population based	Europeans from the Netherlands	2750	1740
SHIP-0 SHIP-Trend	Study of Health in Pomerania	Population based	Europeans from Germany	3368 3906	5575
WHI	Women's Health Initiative	Clinical Trial	Self-Identified European American and African American. Residing in the United States at time of recruitment (1992-1998).	21866 3519	10766 1183

Supplemental Table 2: Study genome-wide genotyping characteristics

Study	Exome Chip version	Genotype calling software	Short description on QC	Related individuals (yes/no)?	Familial adjustment method	Population stratification assessment and adjustment	Software version	Covariates
ARIC	Illumina HumanExome Beadchip 1.0	centrally at CHARGE	centrally at CHARGE	No	N/A	10 PCs	v4.13.8	age, sex, RR, PC1-PC10, center
BRIGHT	Illumina Human Exome BeadChip v1.0	GenCall and zCall	(Sample CallRate <95%; Sample het: separately <1%, >1% MAF, excl ±3 SD; sex discordance; SNP call rate <99%; HWE-p $<10^{-4}$; cluster separation score < 0.4)	No	N/A	Ethnicity (outlier in plink IBD test when compared to HapMap set), remaining ancestry outliers excluded by PCA, then adjustment using 10 PCs as covariates	v4.13.5	age, sex, RR, PC1-PC10
CAMP	Illumina Human Core Exome Array v1.1	GeneCall + Zcall	QC of SNPs were as follows: MAF ≥0%, Call-rate >98%, HWE-Pvalue> 10^{-6}, Samples were excluded based on Call-rate <95%.	Yes	Empirical kinship matrix in raremetalworker	10 PCs	v4.15.1	age, sex, RR, PC1-PC10
CHS	Illumina HumanExome BeadChip v1.0	Illumina GenomeStudio v2011.1	called centrally at CHARGE	No	Empirical kinship	10 PCs	v4.13.6	age, male, RR, PC1- PC10
ERF	Illumina Infinium HumanExome BeadChip v1.1	GenomeStudio and zCall	QC of SNPs were as follows: MAF>=0%, Call-rate >=95%, Samples were excluded based on Call-rate <95%, heterozygous haploid genotypes set to missing.	Yes	Empirical kinship in RAREMETAL WORKER.	NA (family)	4.13.8	age, sex, RR
FHS	Illumina HumanExome BeadChip v1.0	GenomeStudio v.2011.1 and zCall	Called centrally at CHARGE	Yes	Kinship matrix	PCA	v4.13	age, sex, RR, cohort, PC1-PC10
INTER99	Illumina HumanExome Beadchip V1.0	GenCall + zCall	Exome-chip QC SOP v5	No	Kinship matrix in raremetalworker	Mds. Adjust PC1-10 AND kinship matrix	v4.13.5	age, sex, AvgRRInterval, C1-C10
KORA	Illumina HumanExome Beadchip v1.0	genomestudio	Exome-chip QC SOP v5.pdf	No	Exclusion of samples with	MDS	v4.13.8	age, sex, RR

Study	Exome Chip version	Genotype calling software	Short description on QC	Related individuals (yes/no)?	Familial adjustment method	Population stratification assessment and adjustment	Software version	Covariates
					PI_HAT>0.1875			
LIFELINES	Illumina HumanExome Beadchip v1.1	GeneCall + Zcall	QC of SNPs were as follows: MAF≥0%, Call-rate >=95%, HWE-Pvalue> 10^{-6}, Samples were excluded based on Call-rate <95%, identified as an outlier in the first 5 PCA's, mean IBS and sex-mismatches.	No	No	exclusion based on PCA and mean IBS + PCA's as covariates	v4.13.5	age, sex, RR, PCA1-PCA5
UHP	Illumina HumanExome BeadChip 1.1	GenomeStudio and zCall	Plink v1.07 was used for quality control. All samples with a missing SNP rate > 5% and with discordant sex were excluded. Using only independent high quality SNPs (missingness < 1%, minor allele frequency > 5%, Hardy-Weinberg P < 0.001, LD-pruned leaving no pairs with r^2 > 0.2), we removed samples based on heterozygosity (keeping samples within four standard deviations from the mean), related samples (randomly removing one sample until there were no samples with IBD > 0.2), and samples from non-European descent (based on manual inspection of PCA results that were calculated with Eigensoft). SNPs with missing rates > 5% or Hardy-Weinberg equilibrium P < 0.001 were removed.	No	N/A	PCA	v4.13.8	age, sex, height, BMI, PC1-PC10, RR
MESA	Illumina HumanExome Beadchip v1.0	Illumina GenomeStudio2011.1	CHARGE QC	No	N/A	YES, adjusted for first two PCs	v4.13.5	age, sex, RR, pc1-pc10, site4, site5, site6, site7, site8
NEO	Illumina HumanCoreExome24_v1	GenomeStudio	Exome-chip QC SOP v5.pdf	No	N/A	Correction for 10 PCs generated by MDS in Plink	v4.13.5	age, sex, RR, PC1-PC10

Study	Exome Chip version	Genotype calling software	Short description on QC	Related individuals (yes/no)?	Familial adjustment method	Population stratification assessment and adjustment	Software version	Covariates
RS	Illumina Human Exome BeadChip v1.0	Gencall	Removed duplicates, monomorphics, 5% missing genotypes MIND >0.05 and 916 SNPS failed the missingness testCalled centrally at CHARGE	No	Corrected for first 10 PCs	N/A	v4.14.1	age, sex, RR, PC1-PC10
SHIP-0 & SHIP-Trend	Illumina HumanExome Beadchip v1.0	GenCall	Genotype calling was performed in the Illumina GenomeStudio using the cluster file provided by the CHARGE consortium (CHARGE_ExomeChip_v1.0_Cluster_File.egt) and the HumanExome-12v1_B manifest file. Contaminated samples, samples with a call rate <90%, extreme heterozygosity (>5 SD of the mean for MAF >1% or MAF <1%), extensive estimated IBD sharing with a large number of samples (>10 first degree relatives), outliers based on an ancestry information markers related PCA (>10 SD of the mean for the first 10 PCs), or mismatch between reported and genotyped gender were excluded. In both cohorts together, 8230 individuals were successfully genotyped in SHIP and SHIP-Trend together.	No	N/A	PC1-10	v4.13.8	age, PC1- PC10, cohort, RR
WHI	Illumina Human Exome BeadChip v1.0	GenomeStudio v2010.3		No		PC Adjustment	v4.13.5	age, RR, EV1-EV10

N/A: Not applicable

Supplemental Table 3: Significant P-value threshold

Study group	Test	Allele frequency cutoff	Number of variants/genes	Significant p-value threshold
Multi-ancestry	Single variant	0.05	25996	1.9×10^{-6}
European ancestry	Single variant	0.05	25172	2.0×10^{-6}
African ancestry	Single variant	0.05	27262	1.8×10^{-6}
Multi-ancestry	Gene-based	0.05	16949	3.0×10^{-6}
Multi-ancestry	Gene-based	0.01	16842	3.0×10^{-6}
European ancestry	Gene-based	0.05	16319	3.1×10^{-6}
European ancestry	Gene-based	0.01	16160	3.1×10^{-6}
African ancestry	Gene-based	0.05	14251	3.5×10^{-6}
African ancestry	Gene-based	0.01	13528	3.7×10^{-6}

Supplemental Table 4: Top exome-wide significant loci from single variant meta-analysis

Supplemental Table 4a: Multi-ethnic analysis

									Multi-ethnic					
									Residuals			Inverse normal transformed residuals		
Locus	Closest gene	Location	rsID	Ethnicity	OA	EA	N	EAF	Beta	SE	P	Beta	SE	P
Novel loci														
1	*PKP1*	1q32.1	rs1626370	Multi-ethnic	G	A	64431	0.21	0.39	0.08	2×10^{-6}	0.03	0.01	2×10^{-6}
2	*TTN*	2q31.2	rs2042995	Multi-ethnic	T	C	64410	0.26	0.41	0.08	4×10^{-7}	0.03	0.01	5×10^{-7}
3	*DLEC1**	3p22.2	rs116202356	Multi-ethnic, European	A	G	64331	0.98	1.72	0.27	2×10^{-10}	0.14	0.02	2×10^{-10}
4	*PITX2*	4q25	rs17042171	Multi-ethnic, European	A	C	64399	0.86	0.64	0.10	8×10^{-11}	0.06	0.01	2×10^{-11}
5	*ARHGAP10*	4q31.23	rs6845865	Multi-ethnic, European	T	C	64437	0.19	0.54	0.09	2×10^{-10}	0.05	0.01	9×10^{-11}
6	*TCF21*	6q23.2	rs2327429	Multi-ethnic	T	C	64434	0.28	0.39	0.07	2×10^{-7}	0.03	0.01	1×10^{-7}
7	*JAZF1*	7p15.1	rs864745	Multi-ethnic	T	C	64388	0.47	-	-	-	0.03	0.01	1×10^{-6}
8	*CDK6*	7q21.2	rs2282978	Multi-ethnic, European	T	C	64424	0.36	0.39	0.07	2×10^{-8}	0.03	0.01	5×10^{-8}
9	*SYNPO2L*	10q22.2	rs3812629	Multi-ethnic, European	G	A	64423	0.15	0.47	0.09	4×10^{-7}	0.04	0.01	7×10^{-7}
10	*SOX5*	12p12.1	rs17287293	Multi-ethnic, European	G	A	64429	0.86	0.49	0.10	3×10^{-7}	0.04	0.01	3×10^{-7}
11	*HMGA2*	12q14.3	rs8756	Multi-ethnic	A	C	64418	0.48	0.33	0.07	7×10^{-7}	0.03	0.01	5×10^{-7}
12	*RPL3L**	16p13.3	rs113956264	Multi-ethnic	T	C	64403	0.97	0.99	0.20	1×10^{-6}	-	-	-
13	*GOSR2*	17q21.32	rs17608766	Multi-ethnic, European	T	C	64435	0.12	0.80	0.10	9×10^{-15}	0.07	0.01	1×10^{-15}
14	*MC4R*	18q21.32	rs12970134	Multi-ethnic	G	A	64430	0.25	0.38	0.08	1×10^{-6}	-	-	-
Previously reported loci														
15	*CAND2*	3p25.2	rs11718898	Multi-ethnic	C	T	52472	0.33	0.39	0.08	9×10^{-7}	-	-	-
	CAND2	3p25.2	rs3732675	Multi-ethnic, European	C	T	64395	0.39	-	-	-	0.03	0.01	3×10^{-7}
16	*SCN10A*	3p22.2	rs6800541	Multi-ethnic, European	T	C	64423	0.37	1.18	0.07	4×10^{-63}	0.10	0.01	2×10^{-65}
	SCN5A	3p22.2	rs3922844	African	T	C	-	-	-	-	-	-	-	-
17	*HCN1*	5p12	rs6892594	Multi-ethnic, European	C	T	64427	0.45	0.43	0.07	2×10^{-10}	0.04	0.01	3×10^{-10}
18	*CAV1*	7q31.2	rs3807989	Multi-ethnic, European	G	A	64430	0.43	0.47	0.07	2×10^{-12}	0.04	0.01	8×10^{-13}
19	*FADS1*	11q12.2	rs174546	Multi-ethnic	T	C	64430	0.68	0.50	0.07	2×10^{-11}	0.04	0.01	6×10^{-12}
	FADS2	11q12.2	rs1535	European	G	A	-	-	-	-	-	-	-	-
20	*TBX5*	12q24.21	rs883079	Multi-ethnic, European	T	C	64435	0.29	0.80	0.07	9×10^{-28}	0.07	0.01	6×10^{-29}
21	*MYH6*	14q11.2	rs452036	Multi-ethnic, European	G	A	64422	0.38	0.68	0.07	8×10^{-23}	0.06	0.01	1×10^{-23}

OA: other allele, EA: effect allele, N: sample size, EAF: effect allele frequency, Beta: the changes of (inverse normal transformed) P-wave duration residuals per 1 effect allele increment, SE: standard error. * Locus with minor allele frequency <5% identified from gene-based analysis

Supplemental Table 4b: European ancestry analysis

										European Residuals		Inverse normal transformed residuals		
Locus	Closest gene	Location	rsID	Ethnicity	OA	EA	N	EAF	Beta	SE	P	Beta	SE	P
Novel loci														
1	*PKP1*	1q32.1	rs1626370	Multi-ethnic	G	A	-	-	-	-	-	-	-	-
2	*TTN*	2q31.2	rs2042995	Multi-ethnic	T	C	-	-	-	-	-	-	-	-
3	*DLEC1**	3p22.2	rs116202356	Multi-ethnic, European	A	G	56895	0.98	1.71	0.27	5×10^{-10}	0.14	0.02	6×10^{-10}
4	*PITX2*	4q25	rs17042171	Multi-ethnic, European	A	C	56910	0.88	0.67	0.11	1×10^{-9}	0.06	0.01	3×10^{-10}
5	*ARHGAP10*	4q31.23	rs6845865	Multi-ethnic, European	T	C	56940	0.16	0.51	0.10	7×10^{-8}	0.04	0.01	3×10^{-8}
6	*TCF21/TARID*	6q23.2	rs2327429	Multi-ethnic	T	C	-	-	-	-	-	-	-	-
7	*JAZF1*	7p15.1	rs864745	Multi-ethnic	T	C	-	-	-	-	-	-	-	-
8	*CDK6*	7q21.2	rs2282978	Multi-ethnic, European	T	C	56928	0.35	0.39	0.07	2×10^{-7}	0.03	0.01	4×10^{-7}
9	*SYNPO2L*	10q22.2	rs3812629	Multi-ethnic, European	G	A	56929	0.15	0.50	0.10	8×10^{-7}	0.04	0.01	1×10^{-6}
10	*SOX5*	12p12.1	rs17287293	Multi-ethnic, European	G	A	56932	0.85	0.50	0.10	4×10^{-7}	0.04	0.01	4×10^{-7}
11	*HMGA2*	12q14.3	rs8756	Multi-ethnic	A	C	-	-	-	-	-	-	-	-
12	*RPL3L**	16p13.3	rs113956264	Multi-ethnic	T	C	-	-	-	-	-	-	-	-
13	*GOSR2*	17q21.32	rs17608766	Multi-ethnic, European	T	C	56938	0.13	0.79	0.11	7×10^{-14}	0.07	0.01	8×10^{-15}
14	*MC4R*	18q21.32	rs12970134	Multi-ethnic	G	A	-	-	-	-	-	-	-	-
Previously reported loci														
15	*CAND2*	3p25.2	rs11718898	Multi-ethnic	C	T	-	-	-	-	-	-	-	-
	CAND2	3p25.2	rs3732675	Multi-ethnic, European	C	T	56898	0.42	0.37	0.07	3×10^{-7}	0.03	0.01	9×10^{-8}
16	*SCN10A*	3p22.2	rs6800541	Multi-ethnic, European	T	C	56926	0.40	1.21	0.07	1×10^{-62}	0.11	0.01	4×10^{-65}
	SCN5A	3p22.2	rs3922844	African	T	C	-	-	-	-	-	-	-	-
17	*HCN1*	5p12	rs6892594	Multi-ethnic, European	C	T	56931	0.43	0.44	0.07	8×10^{-10}	0.04	0.01	1×10^{-9}
18	*CAV1*	7q31.2	rs3807989	Multi-ethnic, European	G	A	56933	0.41	0.46	0.07	1×10^{-10}	0.04	0.01	8×10^{-11}
19	*FADS1*	11q12.2	rs174546	Multi-ethnic	T	C	-	-	-	-	-	-	-	-
	FADS2	11q12.2	rs1535	European	G	A	56915	0.67	0.48	0.08	5×10^{-10}	0.04	0.01	1×10^{-10}
20	*TBX5*	12q24.21	rs883079	Multi-ethnic, European	T	C	56938	0.28	0.78	0.08	3×10^{-23}	0.07	0.01	2×10^{-24}
21	*MYH6*	14q11.2	rs452036	Multi-ethnic, European	G	A	56928	0.36	0.70	0.07	2×10^{-21}	0.06	0.01	7×10^{-22}

OA: other allele, EA: effect allele, N: sample size, EAF: effect allele frequency, Beta: the changes of (inverse normal transformed) P-wave duration residuals per 1 effect allele increment, SE: standard error. * Locus with minor allele frequency <5% identified from gene-based analysis

Supplemental table 4c: African ancestry analysis

							African							
									Residuals			Inverse normal transformed residuals		
Locus	Closest gene	Location	rsID	Ethnicity	OA	EA	N	EAF	Beta	SE	P	Beta	SE	P
Novel loci														
1	*PKP1*	1q32.1	rs1626370	Multi-ethnic	G	A	-	-	-	-	-	-	-	-
2	*TTN*	2q31.2	rs2042995	Multi-ethnic	T	C	-	-	-	-	-	-	-	-
3	*DLEC1**	3p22.2	rs116202356	Multi-ethnic, European	A	G	-	-	-	-	-	-	-	-
4	*PITX2*	4q25	rs17042171	Multi-ethnic, European	A	C	-	-	-	-	-	-	-	-
5	*ARHGAP10*	4q31.23	rs6845865	Multi-ethnic, European	T	C	-	-	-	-	-	-	-	-
6	*TCF21/TARID*	6q23.2	rs2327429	Multi-ethnic	T	C	-	-	-	-	-	-	-	-
7	*JAZF1*	7p15.1	rs864745	Multi-ethnic	T	C	-	-	-	-	-	-	-	-
8	*CDK6*	7q21.2	rs2282978	Multi-ethnic, European	T	C	-	-	-	-	-	-	-	-
9	*SYNPO2L*	10q22.2	rs3812629	Multi-ethnic, European	G	A	-	-	-	-	-	-	-	-
10	*SOX5*	12p12.1	rs17287293	Multi-ethnic, European	G	A	-	-	-	-	-	-	-	-
11	*HMGA2*	12q14.3	rs8756	Multi-ethnic	A	C	-	-	-	-	-	-	-	-
12	*RPL3L**	16p13.3	rs113956264	Multi-ethnic	T	C	-	-	-	-	-	-	-	-
13	*GOSR2*	17q21.32	rs17608766	Multi-ethnic, European	T	C	-	-	-	-	-	-	-	-
14	*MC4R*	18q21.32	rs12970134	Multi-ethnic	G	A	-	-	-	-	-	-	-	-
Previously reported loci														
15	*CAND2*	3p25.2	rs11718898	Multi-ethnic	C	T	-	-	-	-	-	-	-	-
	CAND2	3p25.2	rs3732675	Multi-ethnic, European	C	T	-	-	-	-	-	-	-	-
16	*SCN10A*	3p22.2	rs6800541	Multi-ethnic, European	T	C	-	-	-	-	-	-	-	-
	SCN5A	3p22.2	rs3922844	African	T	C	5678	0.42	1.80	0.22	5×10^{-16}	0.15	0.02	2×10^{-16}
17	*HCN1*	5p12	rs6892594	Multi-ethnic, European	C	T	-	-	-	-	-	-	-	-
18	*CAV1*	7q31.2	rs3807989	Multi-ethnic, European	G	A	-	-	-	-	-	-	-	-
19	*FADS1*	11q12.2	rs174546	Multi-ethnic	T	C	-	-	-	-	-	-	-	-
	FADS2	11q12.2	rs1535	European	G	A	-	-	-	-	-	-	-	-
20	*TBX5*	12q24.21	rs883079	Multi-ethnic, European	T	C	-	-	-	-	-	-	-	-
21	*MYH6*	14q11.2	rs452036	Multi-ethnic, European	G	A	-	-	-	-	-	-	-	-

OA: other allele, EA: effect allele, N: sample size, EAF: effect allele frequency, Beta: the changes of (inverse normal transformed) P-wave duration residuals per 1 effect allele increment, SE: standard error. * Locus with minor allele frequency <5% identified from gene-based analysis

Supplemental Table 5. Independent signals identified by sequential conditional analysis

								Residuals			Inverse normal transformed residuals		
Chromosome	**Position**	**Closest gene**	**rsID**	**OA**	**EA**	**N**	**EAF**	**Beta**	**SE**	**P**	**Beta**	**SE**	**P**
3	38633923	*SCN5A*	rs11708996	G	C	59302	0.14	1.69	0.10	3×10^{-64}	0.15	0.01	1×10^{-65}
3	38624253	*SCN5A*	rs3922844	T	C	64417	0.67	0.70	0.07	4×10^{-21}	0.06	0.01	3×10^{-22}
3	38593393	*SCN5A*	rs12053903	T	C	64434	0.38	0.64	0.07	1×10^{-17}	0.06	0.01	2×10^{-19}
3	38719935	*SCN5A*	rs9851724	C	T	52466	0.69	0.67	0.08	7×10^{-17}	0.06	0.01	5×10^{-18}
4	111720761	*PITX2*	rs10033464*	T	G	59264	0.90				0.05	0.01	2×10^{-7}
3	38657899	*SCN5A*	rs11710077*	T	A	59288	0.81	-	-	-	0.04	0.01	1×10^{-6}

For P-wave duration residuals, association tests were conditioning on rs1626370, rs2042995, rs6800541, rs11718898, rs17042171, rs6845865, rs6892594, rs2327429, rs3807989, rs2282978, rs3812629, rs174546, rs883079, rs17287293, rs8756, rs452036, rs17608766, rs12970134.

For inverse normal transformed P-wave duration residuals, association tests were conditioning on rs1626370, rs2042995, rs6800541, rs3732675, rs17042171, rs6845865, rs6892594, rs2327429, rs3807989, rs2282978, rs864745, rs3812629, rs174546, rs883079, rs17287293, rs8756, rs452036, rs17608766.

*Only associated with inverse normal transformed P-wave duration residuals

OA: other allele, EA: effect allele, N: sample size, EAF: effect allele frequency, Beta: the changes of (inverse normal transformed) P-wave duration residuals per 1 effect allele increment, SE: standard error.

Supplemental Table 6. Top association results of P-wave duration residuals at previously reported GWAS loci within ±250Kb

Supplemental Table 6a: Multi-ethnic analysis

						Multi-ethnic								
Chrom	**Position**	**GWAS loci**	**Closest gene**	**Reported ethnicity**	**rsID**	**Chrom**	**Position**	**OA**	**EA**	**EAF**	**Beta**	**SE**	**P**	**r^2**
Christophersen 2017														
1	54742618	rs562408	*SSBP3*	Multi-ethnic, European	rs687050	1	54718770	T	C	0.57	0.24	0.07	3×10^{-4}	0.322
2	46533376	rs11894252	*EPAS1*	Multi-ethnic	rs7579899	2	46537604	A	G	0.56	-0.31	0.07	5×10^{-6}	0.974
2	46541176	rs11689011		European						-	-	-	-	-
3	12830775	rs1467026	*CAND2*	Multi-ethnic	rs11718898	3	12848822	T	C	0.67	-0.39	0.08	9×10^{-7}	0.640
3	38621237	rs41312411	*SCN5A*	Multi-ethnic, European	rs6800541	3	38774832	C	T	0.63	-1.18	0.07	4×10^{-63}	0.002
3	38624253	rs3922844		African	rs3922844	3	38624253	T	C	-	-	-	-	-
3	38771925	rs6790396	*SCN10A*	European	rs6800541	3	38774832	C	T	-	-	-	-	-
4	114388820	rs2285703	*CAMK2D*	European	rs28377576	4	114276880	T	C	-	-	-	-	
5	45802079	rs4276421	*HCN1*	Multi-ethnic, European	rs6892594*	5	45427173	T	C	0.45	0.43	0.07	2×10^{-10}	0.723
7	116190597	rs3801995	*CAV1/CAV2*	Multi-ethnic	rs3807989	7	116186241	A	G	0.57	-0.47	0.07	2×10^{-12}	0.484
7	116189376	rs13242816		European						-	-	-	-	-
12	114799974	rs7312625		Multi-ethnic						0.71	-0.80	0.07	9×10^{-28}	0.667
12	114805058	rs148020424	*TBX5*	European	rs883079	12	114793240	C	T	-	-	-	-	-
12	114807035	rs1895582		African						-	-	-	-	-
14	23865885	rs452036	*MYH6*	Multi-ethnic, European	rs452036	14	23865885	G	A	0.38	0.68	0.07	8×10^{-23}	1.000
Verweij 2014														
1	112437344	rs2798334	*KCND3*	European	rs197412	1	112308953	T	C	-	-	-	-	-
3	38767315	rs6801957	*SCN10A*	European	rs6800541	3	38774832	C	T	-	-	-	-	-
11	61604814	rs174577	*FADS2*	European	rs1535	11	61597972	A	G	-	-	-	-	-

* rs6892594 is within ± 500Kb of the previously reported P-wave duration loci

Chrom: chromosome, GWAS loci: previously reported P-wave duration loci, rsID: top variants at the locus, OA: other allele, EA: effect allele, EAF: effect allele frequency, Beta: the changes of P-wave duration residuals per 1 effect allele increment, SE: standard error, r^2: LD between GWAS loci and the top variants in the current findings at the same locus; r^2 is based on all, EUR, or AFR population from Phase 3 (Version 5) of the 1000 Genomes Project, https://ldlink.nci.nih.gov/?tab=ldpair[6]

Supplemental Table 6b: European analysis

										European				
Chrom	**Position**	**GWAS loci**	**Closest gene**	**Reported ethnicity**	**rsID**	**Chrom**	**Position**	**OA**	**EA**	**EAF**	**Beta**	**SE**	**P**	**r^2**
Christophersen 2017														
1	54742618	rs562408	*SSBP3*	Multi-ethnic, European	rs687050	1	54718770	T	C	0.57	0.22	0.07	2×10^{-3}	0.765
2	46533376	rs11894252	*EPAS1*	Multi-ethnic	rs7579899	2	46537604	A	G	-	-	-	-	-
2	46541176	rs11689011		European						0.59	-0.34	0.07	2×10^{-6}	0.975
3	12830775	rs1467026	*CAND2*	Multi-ethnic	rs11718898	3	12848822	T	C	-	-	-	-	-
3	38621237	rs41312411	*SCN5A*	Multi-ethnic, European	rs6800541	3	38774832	C	T	0.60	-1.21	0.07	1×10^{-62}	0.002
3	38624253	rs3922844		African	rs3922844	3	38624253	T	C	-	-	-	-	-
3	38771925	rs6790396	*SCN10A*	European	rs6800541	3	38774832	C	T	0.60	-1.21	0.07	1×10^{-62}	0.980
4	114388820	rs2285703	*CAMK2D*	European	rs28377576	4	114276880	T	C	0.11	0.04	0.11	0.69	0.004
5	45802079	rs4276421	*HCN1*	Multi-ethnic, European	rs6892594*	5	45427173	T	C	0.43	0.44	0.07	8×10^{-10}	0.832
7	116190597	rs3801995	*CAV1/CAV2*	Multi-ethnic	rs3807989	7	116186241	A	G	-	-	-	-	-
7	116189376	rs13242816		European						0.59	-0.46	0.07	1×10^{-10}	0.131
12	114799974	rs7312625		Multi-ethnic						-	-	-	-	-
12	114805058	rs148020424	*TBX5*	European	rs883079	12	114793240	C	T	0.72	-0.78	0.08	3×10^{-23}	0.239
12	114807035	rs1895582		African						-	-	-	-	-
14	23865885	rs452036	*MYH6*	Multi-ethnic, European	rs452036	14	23865885	G	A	0.36	0.70	0.07	2×10^{-21}	1.000
Verweij 2014														
1	112437344	rs2798334	*KCND3*	European	rs197412	1	112308953	T	C	0.40	0.11	0.07	0.14	0.002
3	38767315	rs6801957	*SCN10A*	European	rs6800541	3	38774832	C	T	0.60	-1.21	0.07	1×10^{-62}	0.968
11	61604814	rs174577	*FADS2*	European	rs1535	11	61597972	A	G	0.33	-0.48	0.08	5×10^{-10}	0.945

* rs6892594 is within ± 500Kb of the previously reported P-wave duration loci

Chrom: chromosome, GWAS loci: previously reported P-wave duration loci, rsID: top variants at the locus, OA: other allele, EA: effect allele, EAF: effect allele frequency, Beta: the changes of P-wave duration residuals per 1 effect allele increment, SE: standard error, r^2: LD between GWAS loci and the top variants in the current findings at the same locus; r^2 is based on all, European, or African population from Phase 3 (Version 5) of the 1000 Genomes Project, https://ldlink.nci.nih.gov/?tab=ldpair[6]

Supplemental Table 6c: African analysis

Chrom	Position	GWAS loci	Closest gene	Reported ethnicity	rsID	African							
						Chrom	Position	OA	EA	EAF	Beta	SE	P	r^2
Christophersen 2017														
1	54742618	rs562408	*SSBP3*	Multi-ethnic, European	rs687050	1	54718770	T	C	-	-	-	-	-
2	46533376	rs11894252	*EPAS1*	Multi-ethnic	rs7579899	2	46537604	A	G	-	-	-	-	-
2	46541176	rs11689011		European						-	-	-	-	-
3	12830775	rs1467026	*CAND2*	Multi-ethnic	rs11718898	3	12848822	T	C	-	-	-	-	-
3	38621237	rs41312411	*SCN5A*	Multi-ethnic, European	rs6800541	3	38774832	C	T	-	-	-	-	-
3	38624253	rs3922844		African	rs3922844	3	38624253	T	C	0.42	1.80	0.22	5×10^{-16}	1.000
3	38771925	rs6790396	*SCN10A*	European	rs6800541	3	38774832	C	T	-	-	-	-	-
4	114388820	rs2285703	*CAMK2D*	European	rs28377576	4	114276880	T	C	-	-	-	-	-
5	45802079	rs4276421	*HCN1*	Multi-ethnic, European	rs6892594*	5	45427173	T	C	-	-	-	-	-
7	116190597	rs3801995	*CAV1/CAV2*	Multi-ethnic	rs3807989	7	116186241	A	G	-	-	-	-	-
7	116189376	rs13242816		European						-	-	-	-	-
12	114799974	rs7312625		Multi-ethnic						-	-	-	-	-
12	114805058	rs148020424	*TBX5*	European	rs883079	12	114793240	C	T	-	-	-	-	-
12	114807035	rs1895582		African						0.67	-1.08	0.23	4×10^{-6}	0.879
14	23865885	rs452036	*MYH6*	Multi-ethnic, European	rs452036	14	23865885	G	A	-	-	-	-	-
Verweij 2014														
1	112437344	rs2798334	*KCND3*	European	rs197412	1	112308953	T	C	-	-	-	-	-
3	38767315	rs6801957	*SCN10A*	European	rs6800541	3	38774832	C	T	-	-	-	-	-
11	61604814	rs174577	*FADS2*	European	rs1535	11	61597972	A	G	-	-	-	-	-

* rs6892594 is within ± 500Kb of the previously reported P-wave duration loci

Chrom: chromosome, GWAS loci: previously reported P-wave duration loci, rsID: top variants at the locus, OA: other allele, EA: effect allele, EAF: effect allele frequency, Beta: the changes of P-wave duration residuals per 1 effect allele increment, SE: standard error, r^2: LD between GWAS loci and the top variants in the current findings at the same locus; r^2 is based on all, European, or African population from Phase 3 (Version 5) of the 1000 Genomes Project, https://ldlink.nci.nih.gov/?tab=ldpair[6]

Supplemental Table 7: cis-eQTLs for top loci from meta-analysis

Locus	Top variants at identified loci	Location	rsID	OA	EA	SNP	r^2*	Gene (eQTL)	Right atrial appendage (n=264) slope	SE	P	Left ventricle (n=272) slope	SE	P	ρ	P (z-stat)
Novel loci																
1	*PKP1*	1q32.1	rs1626370	G	A	-	-	-	-	-	-	-	-	-	-	-
2	*TTN*	2q31.2	rs2042995	T	C	rs3045696	0.97	*FKBP7*	**0.16**	**0.04**	**5×10^{-5}**	0.12	0.05	1×10^{-2}	0.491	0.302
3	*DLEC1*	3p22.2	rs116202356	A	G	-	-	-	-	-	-	-	-	-	-	-
4	*PITX2*	4q25	rs17042171	A	C	-	-	-	-	-	-	-	-	-	-	-
5	*ARHGAP10*	4q31.23	rs6845865	T	C	-	-	-	-	-	-	-	-	-	-	-
6	*TCF21/TARID*	6q23.2	rs2327429	T	C	-	-	*TARID*	**0.30**	**0.06**	**8×10^{-7}**	0.22	0.07	1×10^{-3}	0.601	0.176
7	*JAZF1*	7p15.1	rs864745	T	C	-	-	*JAZF1*	**0.23**	**0.05**	**1×10^{-6}**	0.06	0.03	6×10^{-2}	0.309	3×10^{-4}
8	*CDK6*	7q21.2	rs2282978	T	C	-	-	-	-	-	-	-	-	-		
9	*SYNPO2L*	10q22.2	rs3812629	G	A	-	-	*MYOZ1*	**1.09**	**0.08**	**2×10^{-29}**	0.21	0.10	4×10^{-2}	0.300	1×10^{-15}
						-	-	*SYNPO2L*	**-0.17**	**0.04**	**7×10^{-5}**	-0.09	0.03	6×10^{-3}	0.589	0.029
						-	-	*DUSP8P5*	**0.30**	**0.07**	**7×10^{-5}**	0.13	0.06	4×10^{-2}	0.349	0.028
						-	-	*FUT11*	-0.24	0.07	7×10^{-4}	**-0.29**	**0.07**	**3×10^{-5}**	0.512	0.463
10	*SOX5*	12p12.1	rs17287293	G	A	-	-	-	-	-	-	-	-	-	-	-
11	*HMGA2*	12q14.3	rs8756	A	C	-	-	-	-	-	-	-	-	-	-	-
12	*RPL3L*	16p13.3	rs113956264	T	C	-	-	-	-	-	-	-	-	-	-	-
13	*GOSR2*	17q21.32	rs17608766	T	C	-	-	-	-	-	-	-	-	-	-	-
14	*MC4R*	18q21.32	rs12970134	G	A	-	-	-	-	-	-	-	-	-	-	-
Previously reported loci																
15	*CAND2*	3p25.2	rs11718898	C	T	-	-	-	-	-	-	-	-	-	-	-
	CAND2	3p25.2	rs3732675	C	T	-	-	-	-	-	-	-	-	-	-	-
16	*SCN10A*	3p22.2	rs6800541	T	C	-	-	-	-	-	-	-	-	-	-	-
17	*HCN1*	5p12	rs6892594	C	T	rs34666220	0.99	*HCN1*	**-0.21**	**0.05**	**5×10^{-5}**	-[†]	-	-	-	-
18	*CAV1*	7q31.2	rs3807989	G	A	-	-	-	-	-	-	-	-	-	-	-
19	*FADS1*	11q12.2	rs174546	T	C	-	-	*FADS2*	**-0.38**	**0.06**	**2×10^{-10}**	**-0.35**	**0.05**	**2×10^{-10}**	0.618	0.467
						-	-	*FADS1*	0.14	0.07	0.04	**0.21**	**0.04**	**7×10^{-8}**	0.450	0.198
						rs174568	0.99	*TMEM258*	**-0.16**	**0.04**	**3×10^{-5}**	-0.11	0.04	2×10^{-3}	0.265	0.297
20	*TBX5*	12q24.21	rs883079	T	C	-	-	-	-	-	-	-	-	-	-	-
21	*MYH6*	14q11.2	rs452036	G	A	-	-	-	-	-	-	-	-	-	-	-

*r^2 are calculated based on all populations from Phase 3 (Version 5) of the 1000 Genomes Project (https://ldlink.nci.nih.gov)[6]

[†]eQTL is not available in left ventricle.

Significant cis-eQTLs (in bold) for the top variants or their proxies (r^2>0.8) from GTEx version 7 heart tissues, left ventricle and right atrial appendage. If the lead variant is significant cis-QTL, we report the results for the lead variant. Otherwise, we report the results of the best proxy (the one with the highest r^2 with the top variant. Significance was defined by a false discovery rate ≤5%.

rsID: Top variant at each locus, OA: other allele, EA: effect allele, SNP: rsID of the best proxy for the cis-eQTL results, Gene(eQTL): gene from cis-eQTL results, r^2: linkage equilibrium r^2 between the top variant (rsID) and proxy variant(s), slope and P: slope and P value were estimated from a linear regression model between genotype and normalized gene expression - details of laboratory and analysis methods can be found at GTEx Protal (www.gtexportal.org). The effect allele in the linear regression is corresponding to the P-wave duration increasing allele in our primary analysis. ρ: the correlation coefficient of normalized gene expression level from 179 individuals with expression data for both heart tissues. P (z-stat): p-value from z-statistics, and z-statistics is estimated by $(slope_{right\ atrial\ appendage} - slope_{left\ ventricle})^2 / (SE_{right\ atrial\ appendage}^2 + SE_{left\ ventricle}^2 - 2\rho \cdot SE_{right\ atrial\ appendage} \cdot SE_{left\ ventricle})]$. We used the Bonferroni correction to establish the P (z-stat) significance threshold for differences in association at P<0.005 (=0.05/10 significant cis-eQTLs).

Supplemental Table 8: Lookups for other electrocardiogram traits and atrial fibrillation risk at P-wave duration loci*

Supplemental Table 8a: PR interval

Locus	Closest gene	Location	rsID	OA	EA	Summary		PR interval			
						Related to atrial fibrillation risk	Related to ECG trait loci	Reported variants	r^2	Pubmed ID	Reported Genes
Novel loci											
1	*PKP1*	1q32.1	rs1626370	G	A	-	No				
2	*TTN*	2q31.2	rs2042995	T	C	↑	Yes (PR interval)	rs2042995	1.000	29748316	*TTN*
3	*DLEC1*	3p22.2	rs116202356	A	G	↓	Yes (PR interval, QRS)	rs116202356	1. 000	29748316	*DLEC1*
4	*PITX2*	4q25	rs17042171	A	C	↓	No				
5	*ARHGAP10*	4q31.23	rs6845865	T	C	-	Yes (QT, RR)				
6	*TCF21*	6q23.2	rs2327429	T	C	↑	No				
7	*JAZF1*	7p15.1	rs864745	T	C	-	Yes (RR)				
8	*CDK6*	7q21.2	rs2282978	T	C	↓	No				
9	*SYNPO2L*	10q22.2	rs3812629	G	A	↓	Yes (RR)				
10	*SOX5/C12orf67*	12p12.1	rs17287293	G	A	↑	Yes (PR interval, RR)	rs17287293	1.000	30046033, 29748316	*C12orf67, SOX5. LINC00477*
11	*HMGA2*	12q14.3	rs8756	A	C	-	Yes (RR)				
12	*RPL3L*	16p13.3	rs113956264	T	C	-	No				
13	*GOSR2*	17q21.32	rs17608766	T	C	↑	Yes (QRS)				
14	*MC4R*	18q21.32	rs12970134	G	A	↑	No				
Previously reported loci											
15	*CAND2*	3p25.2	rs11718898	C	T	↓	No				
	CAND2	3p25.2	rs3732675	C	T	↓	No				
16	*SCN10A*	3p22.2	rs6800541	T	C	↓	Yes (PR interval, QRS, RR)	rs6800541	1.000	20062060	*SCN10A*
17	*HCN1*	5p12	rs6892594	C	T	-	No				
18	*CAV1*	7q31.2	rs3807989	G	A	↓	Yes (PR interval, PR segment, QRS)	rs3807989	1.000	31217584, 30046033, 20062063, 25055868, 29127183, 20062060, 24850809, 29748316	*CAV1, CAV2*
19	*FADS1*	11q12.2	rs174546	T	C	-	Yes (QT, RR)				
20	*TBX5*	12q24.21	rs883079	T	C	↓	Yes (PR interval, QRS)	rs883079	1.000	29748316	*TBX5*
21	*MYH6*	14q11.2	rs452036	G	A	↑	Yes (RR)				

*For atrial fibrillation risk, the association results are from Roselli et al. 2018.[8] Significance threshold was set at p<0.0024 (0.05/21 loci) for AF risk. For ECG traits, we display variants or their proxies (r^2 ≥0.8) with the highest r^2 at a top P-wave duration locus-related variant.
OA: other allele, EA: effect allele, r^2: r^2 between rsID and the reported variants, obtained from Ldlink, https://ldlink.nci.nih.gov, based on all population from Phase 3 (Version 5) of the 1000 Genomes Project.[6]

Supplemental Table 8b: PR segment

Locus	Closest gene	Location	rsID	OA	EA	Summary		PR segment			
						Related to atrial fibrillation risk	Related to ECG trait loci	Reported variants	r^2	Pubmed ID	Reported Genes
Novel loci											
1	*PKP1*	1q32.1	rs1626370	G	A	-	No				
2	*TTN*	2q31.2	rs2042995	T	C	↑	Yes (PR interval)				
3	*DLEC1*	3p22.2	rs116202356	A	G	↓	Yes (PR interval, QRS)				
4	*PITX2*	4q25	rs17042171	A	C	↓	No				
5	*ARHGAP10*	4q31.23	rs6845865	T	C	-	Yes (QT, RR)				
6	*TCF21*	6q23.2	rs2327429	T	C	↑	No				
7	*JAZF1*	7p15.1	rs864745	T	C	-	Yes (RR)				
8	*CDK6*	7q21.2	rs2282978	T	C	↓	No				
9	*SYNPO2L*	10q22.2	rs3812629	G	A	↓	Yes (RR)				
10	*SOX5/C12orf67*	12p12.1	rs17287293	G	A	↑	Yes (PR interval, RR)				
11	*HMGA2*	12q14.3	rs8756	A	C	-	Yes (RR)				
12	*RPL3L*	16p13.3	rs113956264	T	C	-	No				
13	*GOSR2*	17q21.32	rs17608766	T	C	↑	Yes (QRS)				
14	*MC4R*	18q21.32	rs12970134	G	A	↑	No				
Previously reported loci											
15	*CAND2*	3p25.2	rs11718898	C	T	↓	No				
	CAND2	3p25.2	rs3732675	C	T	↓	No				
16	*SCN10A*	3p22.2	rs6800541	T	C	↓	Yes (PR interval, QRS, RR)				
17	*HCN1*	5p12	rs6892594	C	T	-	No				
18	*CAV1*	7q31.2	rs3807989	G	A	↓	Yes (PR interval, PR segment, QRS)	rs3807989	1.000	24850809	*CAV1, MET*
19	*FADS1*	11q12.2	rs174546	T	C	-	Yes (QT, RR)				
20	*TBX5*	12q24.21	rs883079	T	C	↓	Yes (PR interval, QRS)				
21	*MYH6*	14q11.2	rs452036	G	A	↑	Yes (RR)				

*For atrial fibrillation risk, the association results are from Roselli et al. 2018.[8] Significance threshold was set at p<0.0024 (0.05/21 loci) for AF risk. For ECG traits, we display variants or their proxies ($r^2 \geq 0.8$) with the highest r^2 to a top P-wave duration locus-related variant.

OA: other allele, EA: effect allele, r^2: r^2 between rsID and the reported variants, obtained from Ldlink, https://ldlink.nci.nih.gov, based on all population from Phase 3 (Version 5) of the 1000 Genomes Project[6]

Supplemental Table 8c: QRS

Locus	Closest gene	Location	rsID	OA	EA	Summary		QRS			
						Related to atrial fibrillation risk	Related to ECG trait loci	Reported variants	r^2	Pubmed ID	Reported Genes
Novel loci											
1	*PKP1*	1q32.1	rs1626370	G	A	-	No				
2	*TTN*	2q31.2	rs2042995	T	C	↑	Yes (PR interval)				
3	*DLEC1*	3p22.2	rs116202356	A	G	↓	Yes (PR interval, QRS)	rs116202356	1	30012220	*DLEC1*
4	*PITX2*	4q25	rs17042171	A	C	↓	No				
5	*ARHGAP10*	4q31.23	rs6845865	T	C	-	Yes (QT, RR)				
6	*TCF21*	6q23.2	rs2327429	T	C	↑	No				
7	*JAZF1*	7p15.1	rs864745	T	C	-	Yes (RR)				
8	*CDK6*	7q21.2	rs2282978	T	C	↓	No				
9	*SYNPO2L*	10q22.2	rs3812629	G	A	↓	Yes (RR)				
10	*SOX5/C12orf67*	12p12.1	rs17287293	G	A	↑	Yes (PR interval, RR)				
11	*HMGA2*	12q14.3	rs8756	A	C	-	Yes (RR)				
12	*RPL3L*	16p13.3	rs113956264	T	C	-	No				
13	*GOSR2*	17q21.32	rs17608766	T	C	↑	Yes (QRS)	rs17608766	1.000	27577874, 27659466, 21076409, 30012220	*GOSR2*
14	*MC4R*	18q21.32	rs12970134	G	A	↑	No				
Previously reported loci											
15	*CAND2*	3p25.2	rs11718898	C	T	↓	No				
	CAND2	3p25.2	rs3732675	C	T	↓	No				
16	*SCN10A*	3p22.2	rs6800541	T	C	↓	Yes (PR interval, PR segment, QRS, RR)	rs6795970	0.942	20062063, 23463857, 27659466, 30012220	*SCN10A*
17	*HCN1*	5p12	rs6892594	C	T	-	No				
18	*CAV1*	7q31.2	rs3807989	G	A	↓	Yes (PR interval, PR segment, QRS)	rs3807989	1.000	30012220 31641117	*CAV1*
19	*FADS1*	11q12.2	rs174546	T	C	-	Yes (QT, RR)				
20	*TBX5*	12q24.21	rs883079	T	C	↓	Yes (PR interval, QRS)	rs883079	1.000	27659466, 21076409, 27577874, 30012220, 31217584	*TBX5*
21	*MYH6*	14q11.2	rs452036	G	A	↑	Yes (RR)				

*For atrial fibrillation risk, the association results are from Roselli et al. 2018.[8] Significance threshold was set at p<0.0024 (0.05/21 loci) for AF risk. For ECG traits, we display variants or their proxies (r^2≥0.8) with the highest r^2 to a top P-wave duration locus-related variant.

OA: other allele, EA: effect allele, r^2: r^2 between rsID and the reported variants, obtained from Ldlink, https://ldlink.nci.nih.gov, based on all population from Phase 3 (Version 5) of the 1000 Genomes Project[6]

Supplemental Table 8d: QT

Locus	Closest gene	Location	rsID	OA	EA	Summary		QT			
						Related to atrial fibrillation risk	Related to ECG trait loci	Reported variants	r^2	Pubmed ID	Reported Genes
Novel loci											
1	*PKP1*	1q32.1	rs1626370	G	A	-	No				
2	*TTN*	2q31.2	rs2042995	T	C	↑	Yes (PR interval)				
3	*DLEC1*	3p22.2	rs116202356	A	G	↓	Yes (PR interval, QRS)				
4	*PITX2*	4q25	rs17042171	A	C	↓	No				
5	*ARHGAP10*	4q31.23	rs6845865	T	C	-	Yes (QT, RR)	rs6845865	1.000	20031603	*ARHGAP10*
6	*TCF21*	6q23.2	rs2327429	T	C	↑	No				
7	*JAZF1*	7p15.1	rs864745	T	C	-	Yes (RR)				
8	*CDK6*	7q21.2	rs2282978	T	C	↓	No				
9	*SYNPO2L*	10q22.2	rs3812629	G	A	↓	Yes (RR)				
10	*SOX5/C12orf67*	12p12.1	rs17287293	G	A	↑	Yes (PR interval, RR)				
11	*HMGA2*	12q14.3	rs8756	A	C	-	Yes (RR)				
12	*RPL3L*	16p13.3	rs113956264	T	C	-	No				
13	*GOSR2*	17q21.32	rs17608766	T	C	↑	Yes (QRS)				
14	*MC4R*	18q21.32	rs12970134	G	A	↑	No				
Previously reported loci											
15	*CAND2*	3p25.2	rs11718898	C	T	↓	No				
	CAND2	3p25.2	rs3732675	C	T	↓	No				
16	*SCN10A*	3p22.2	rs6800541	T	C	↓	Yes (PR interval, PR segment, QRS, RR)				
17	*HCN1*	5p12	rs6892594	C	T	-	No				
18	*CAV1*	7q31.2	rs3807989	G	A	↓	Yes (PR interval, PR segment, QRS)				
19	*FADS1*	11q12.2	rs174546	T	C	-	Yes (QT, RR)	rs174546	1.000	30679814	*FADS1*
20	*TBX5*	12q24.21	rs883079	T	C	↓	Yes (PR interval, QRS)				
21	*MYH6*	14q11.2	rs452036	G	A	↑	Yes (RR)				

*For atrial fibrillation risk, the association results are from Roselli et al. 2018.[8] Significant threshold was set at p<0.0024 (0.05/21 loci) for AF risk. For ECG traits, we display variants or their proxies ($r^2 \geq 0.8$) with the highest r^2 to a top P-wave duration locus-related variant.

OA: other allele, EA: effect allele, r^2: r^2 between rsID and the reported variants, obtained from Ldlink, https://ldlink.nci.nih.gov, based on all population from Phase 3 (Version 5) of the 1000 Genomes Project[6]

Supplemental Table 8e: Heart Rate (RR interval)

Locus	Closest gene	Location	rsID	OA	EA	Summary		Heart Rate (RR interval)			
						Related to atrial fibrillation risk	Related to ECG trait loci	Reported variants	r^2	Pubmed ID	Reported Genes
Novel loci											
1	*PKP1*	1q32.1	rs1626370	G	A	-	No				
2	*TTN*	2q31.2	rs2042995	T	C	↑	Yes (PR interval)				
3	*DLEC1*	3p22.2	rs116202356	A	G	↓	Yes (PR interval, QRS)				
4	*PITX2*	4q25	rs17042171	A	C	↓	No				
5	*ARHGAP10*	4q31.23	rs6845865	T	C	-	Yes (QT, RR)	rs6845865	1.000	27798624	*ARHGAP10, EDNRA*
6	*TCF21*	6q23.2	rs2327429	T	C	↑	No				
7	*JAZF1*	7p15.1	rs864745	T	C	-	Yes (RR)	rs1635852	0.955	28379579	*JAZF1*
8	*CDK6*	7q21.2	rs2282978	T	C	↓	No				
9	*SYNPO2L*	10q22.2	rs3812629	G	A	↓	Yes (RR)	rs4746139	0.885	30940143	*AGAP5, BMS1P4, C10orf55, CAMK2G, CHCHD1, FUT11, GLUD1P3, NDST2, PLAU, SEC24C, SYNPO2L, ZSWIM8, ZSWIM8-AS1*
10	*SOX5/C12orf67*	12p12.1	rs17287293	G	A	↑	Yes (PR interval, RR)	rs17287293	1.000	23583979, 20639392	*LINC00477, C12orf67*
11	*HMGA2*	12q14.3	rs8756	A	C	-	Yes (RR)	rs8756	1.000	30940143	*HMGA2*
12	*RPL3L*	16p13.3	rs113956264	T	C	-	No				
13	*GOSR2*	17q21.32	rs17608766	T	C	↑	Yes (QRS)				
14	*MC4R*	18q21.32	rs12970134	G	A	↑	No				
Previously reported loci											
15	*CAND2*	3p25.2	rs11718898	C	T	↓	No				
	CAND2	3p25.2	rs3732675	C	T	↓	No				
16	*SCN10A*	3p22.2	rs6800541	T	C	↓	Yes (PR interval, PR segment, QRS, RR)	rs6795970	0.942	28379579	*SCN10A*
17	*HCN1*	5p12	rs6892594	C	T	-	No				

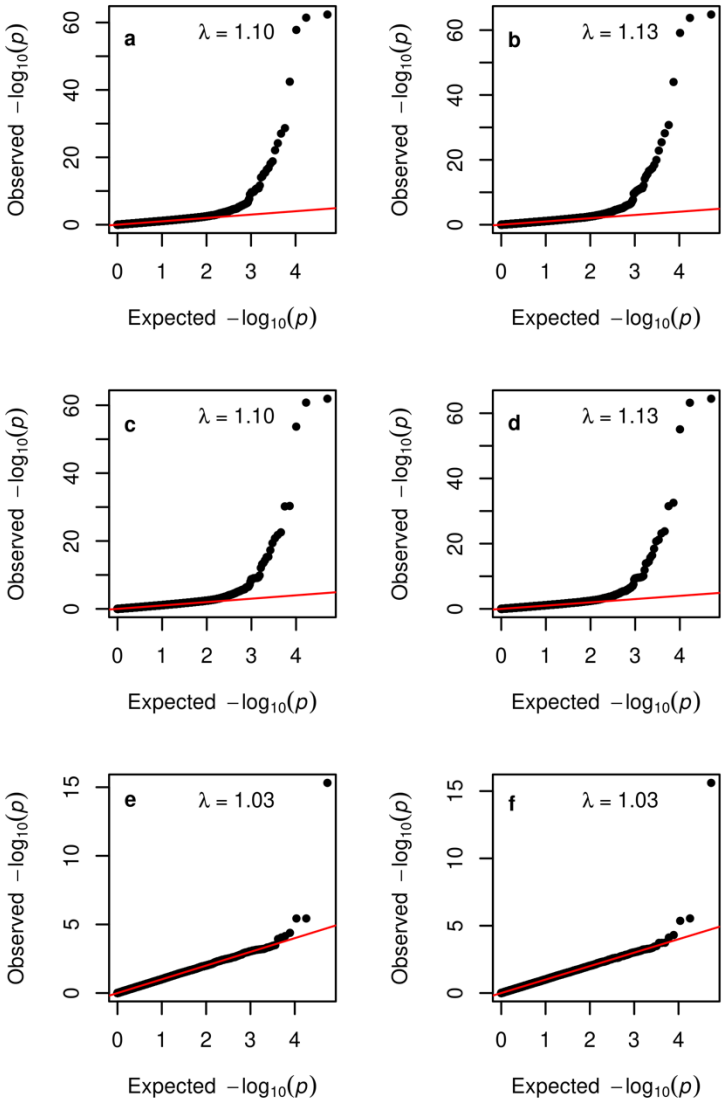
18	*CAV1*	7q31.2	rs3807989	G	A	↓	Yes (PR interval, PR segment, QRS)				
19	*FADS1*	11q12.2	rs174546	T	C	-	Yes (QT, RR)	rs174547	0.998	20639392	*FADS1*
20	*TBX5*	12q24.21	rs883079	T	C	↓	Yes (PR interval, QRS)				
21	*MYH6*	14q11.2	rs452036	G	A	↑	Yes (RR)	rs452036		20639392, 23183192	*MYH6*

*For atrial fibrillation risk, the association results are from Roselli et al. 2018.[8] Significant threshold was set at p<0.0024 (0.05/21 loci) for AF risk.
For ECG traits, we display variants or their proxies ($r^2 \geq 0.8$) with the highest r^2 to a top P-wave duration locus-related variant.

OA: other allele, EA: effect allele, r^2: r^2 between rsID and the reported variants, obtained from Ldlink, https://ldlink.nci.nih.gov, based on all population from Phase 3 (Version 5) of the 1000 Genomes Project[6]

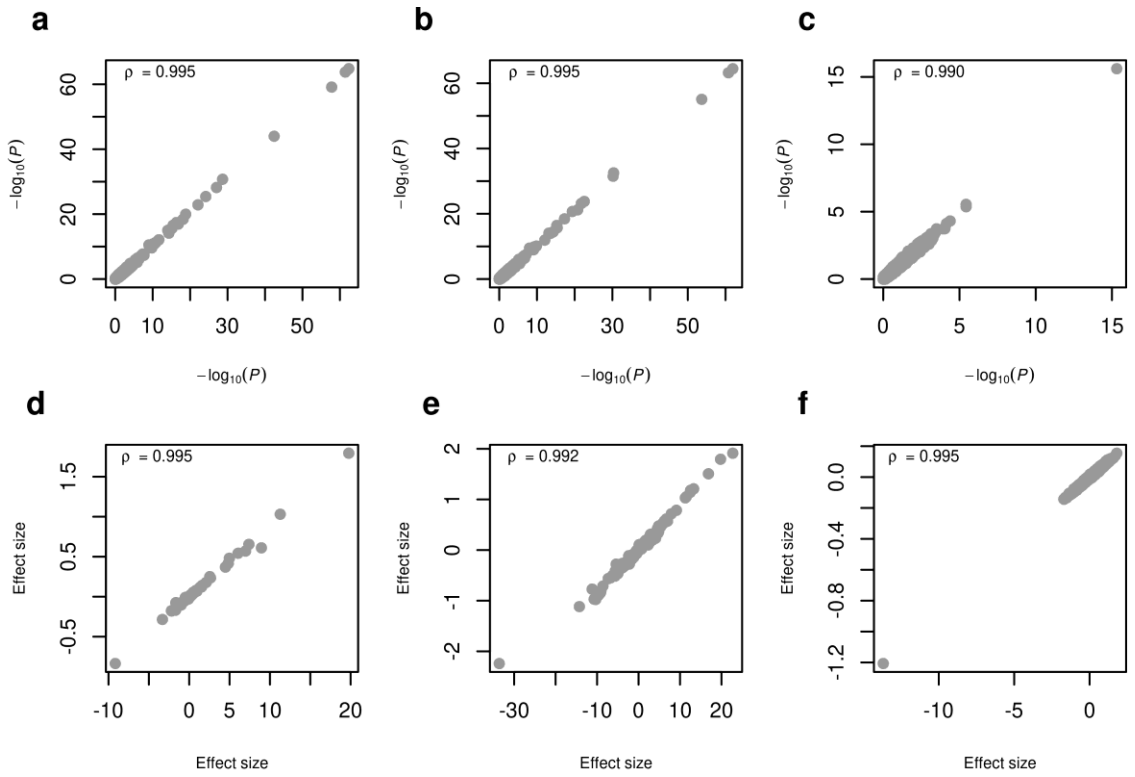
Supplemental Figures

Supplemental Figure 1 Quantile-Quantile plots from single variant meta-analyses of P-wave duration.



P-values are from single common variant meta-analysis for multi-ethnic P-wave duration residuals (a) multi-ethnic inverse normal transformed P-wave duration residuals (b) European P-wave duration residuals (c) European inverse normal transformed P-wave duration residuals (d) African P-wave duration residuals (e) African inverse normal transformed P-wave duration residuals (f).

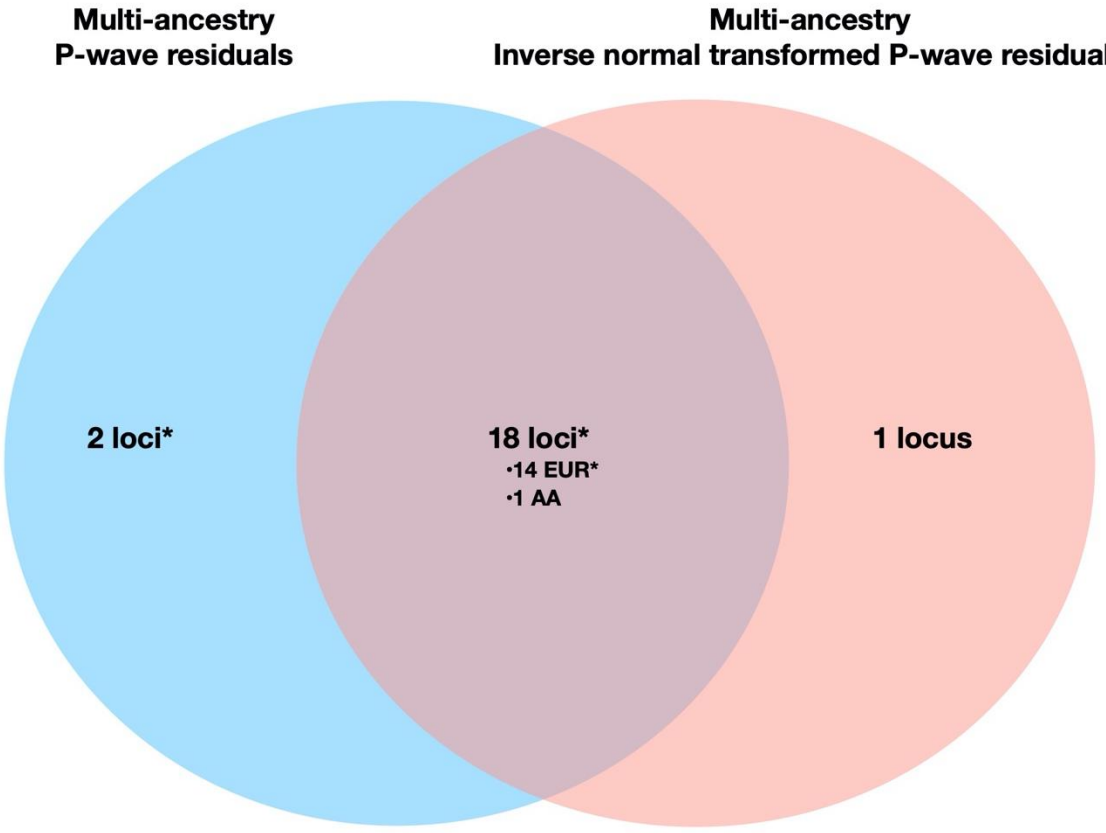
Supplemental Figure 2 Correlation between single variant association results from P-wave residuals and inverse normal transformed P-wave duration residuals.



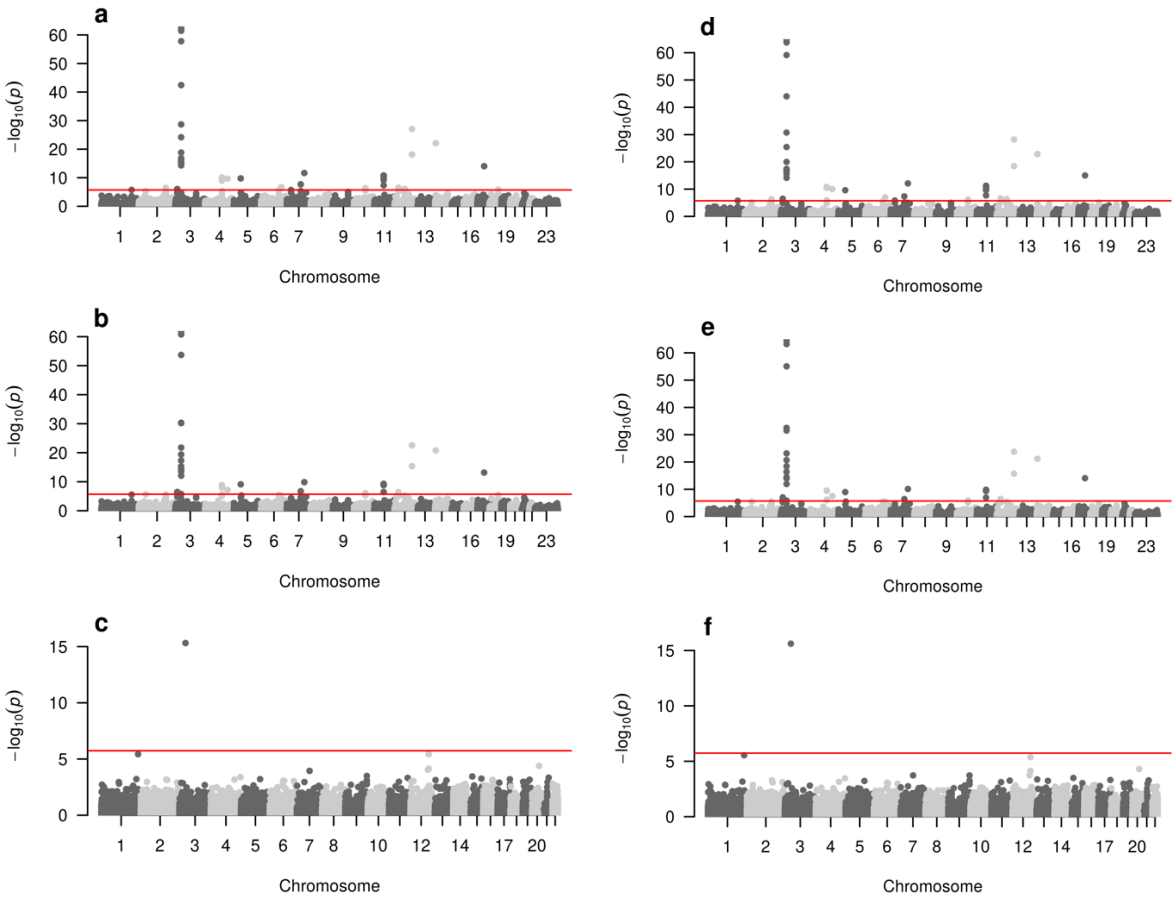
P and effect size are from single common variant meta-analysis of P-wave duration in multi-ethnic group (**a,d**) European population (**b,e**) and African population (**c,f**). X-axis refers to the results from meta-analyses of P-wave duration residuals, and Y-axis refers to the results from meta-analyses of inverse normal transformed P-wave duration residuals.

Supplemental Figure 3 Exome-wide significant loci across meta-analyses of P-wave duration residuals and inverse normal transformed P-wave duration residuals.

The Venn diagram shows the overlap of exome-wide significant loci across meta-analyses of P-wave duration residuals (light blue) and inverse normal transformed P-wave duration residuals (pale red) in the multi-ancestry analysis. A total of 21 loci exceeded the exome-wide significance threshold in the multi-ancestry analysis. Fourteen of the 21 overall loci were also observed in the European-specific analysis. Of these, one locus reached exome-wide significance in the African ancestry analysis. Multi-ethnic meta-analyses and ancestry-specific meta-analyses were performed in a parallel manner. * One variant is low-frequency variant from gene-based analysis



Supplemental Figure 4 Manhattan plots of single variant meta-analyses



Single variant meta-analyses for P-wave duration residuals (left) and inverse normal transformed P-wave duration residuals (right) from the multi-ethnic (**a, d**), European (**b, e**), and African (**c, f**) ancestry

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