SUPPLEMENTAL MATERIAL

Supplementary Figures

Supplementary Figure 1. Associations between genetically predicted PR segment and P wave durations and EHR phenotypes.

Supplementary Tables

Supplementary Table 1: Characteristics of the eMERGE population.
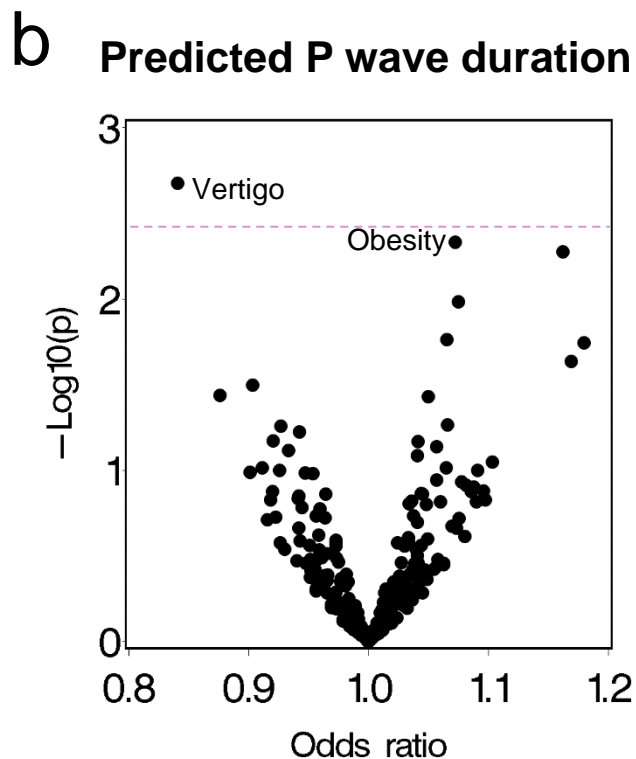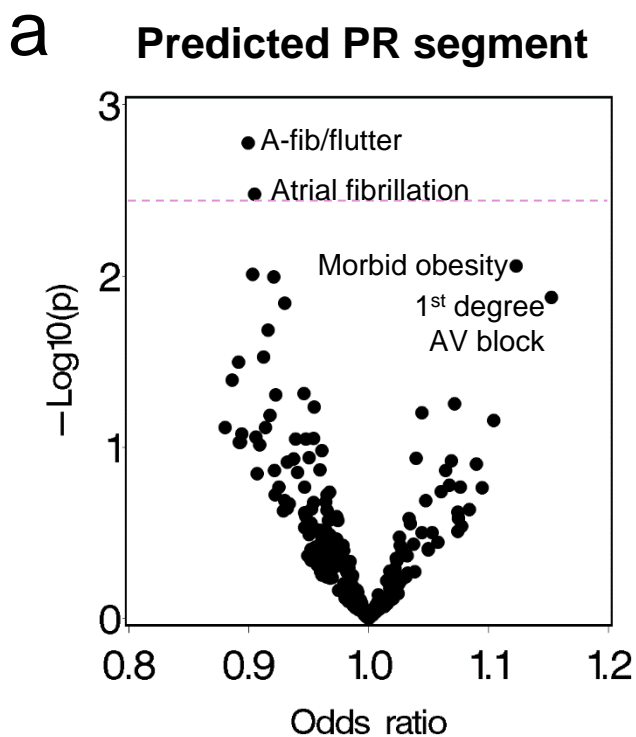
Supplementary Table 2: List of SNPS identified by prior GWAS used to compute genetic risk scores for the PR interval and atrial fibrillation.

Supplementary Table 3: List of SNPS identified by prior GWAS used to compute genetic risk scores for body mass index (BMI).

Supplementary Table 4: Characteristics of the ARIC population.

Supplementary Table 5: Demographics for the eMERGE atrial fibrillation cases and controls.

Supplementary Figure 1

a **Predicted PR segment**

b **Predicted P wave duration**

Supplementary Figure 1. Plot of p-value versus odds-ratio (OR) from logistic regression analyses of the association between a genetically predicted a) PR segment or b) P wave duration and 261 eMERGE phenotypes, adjusted for sex, gender and principal components. ORs represent the risk per standard deviation change in the predicted value.   For all graphs, each point represents a phenotype and green colored points have an FDR q<0.1. The purple line denotes the expected false positive rate (=1/261).

Supplementary Table 1: Characteristics of the eMERGE population.

Characteristic		
Gender [n (%)]		
Males	6,253 (48.2)	
Females	6,725 (51.8)	
Birth Decade		
median (IQR)	1940 (1920-1950)	
Distinct PheWAS codes per subject		
median (IQR)	44 (21-76)	
Phenotypes used for genetic correlation analyses	**Cases**	**Controls**
Hypertension	6,354	3,425
Essential hypertension	6,321	3,425
Disorders of lipid metabolism	6,042	3,896
Hyperlipidemia	5,966	3,896
Osteoarthrosis	3,989	5,348
Pain in limb	3,851	5,357
Peripheral enthesopathies and allied syndromes	3,473	4,805
Osteoarthrosis NOS	3,391	5,128
Hypercholesterolemia	3,180	3,611
Ischemic Heart Disease	3,160	5,606
Acute upper respiratory infections of multiple or unspecified sites	2,984	5,486
Coronary atherosclerosis	2,717	5,282
Overweight, obesity and other hyperalimentation	2,610	6,730
Diabetes mellitus	2,488	6,532
GERD	2,442	5,621
Type 2 diabetes	2,408	6,504
Obesity	2,301	6,265
Benign neoplasm of colon	2,244	6,592
Diverticulosis and diverticulitis	2,179	4,194
Hemorrhoids	2,049	4,612
Dizziness and giddiness (Light-headedness and vertigo)	2,036	6,247
Diverticulosis	1,966	3,975
Anxiety, phobic and dissociative disorders	1,870	5,101
Glaucoma	1,866	3,866
Other headache syndromes	1,711	6,695
Other peripheral nerve disorders	1,698	6,587
Atherosclerosis	1,695	3,770
Impacted cerumen	1,611	4,998

Atrial fibrillation and flutter	1,600	3,166
Atrial fibrillation	1,547	3,128
Peripheral vascular disease	1,539	4,415
Sprains and strains of back and neck	1,533	2,484
Diseases of sebaceous glands	1,533	5,898
Tobacco use disorder	1,527	7,094
Nausea and vomiting	1,442	6,713
Peripheral vascular disease, unspecified	1,361	3,812
Atherosclerosis of the extremities	1,318	3,128
Other arthropathies	1,227	6,186
Urinary incontinence	1,098	3,990
Otitis media and Eustachian tube disorders	1,074	4,941
Angina pectoris	1,029	3,755
Other chronic ischemic heart disease, unspecified	953	3,382
Sebaceous cyst	924	4,526
Atherosclerosis of native arteries of the extremities with intermittent claudication	890	1,878
Dementias	889	2,179
Varicose veins	824	3,203
Other upper respiratory disease	813	3,322
Otitis media	801	3,790
Adjustment reaction	777	3,079
Other persistent mental disorders due to conditions classified elsewhere	760	2,709
Varicose veins of lower extremity	748	3,034
Disorders of function of stomach	729	3,831
Symptoms involving cardiovascular system	678	3,201
Fracture of unspecified bones	662	3,831
Dyspepsia and other specified disorders of function of stomach	655	3,484
Corns and callosities	649	3,284
Other aneurysm	617	2,780
Morbid obesity	602	3,600
Cellulitis and abscess of leg, except foot	598	3,668
Alzheimer's disease	590	1,860
Hyposmolality and/or hyponatremia	583	3,375
Type 2 diabetes with neurological manifestations	525	3,479
Lymphadenitis	501	3,679

Supplementary Table 2: List of SNPS available in each data set for use in computing genetic risk scores for either the PR interval or atrial fibrillation. Shown are the published weights used from computing GRSs. In addition, association statistics for either the PR interval or AF, respectively, are shown.

Phenotype	SNP	Beta (s.e.) for the PR interval from prior GWAS*	OR (95% CI) for AF in the eMERGE data set
PR interval	rs11897119	1.4 (0.2)	0.98 (0.89-1.08)
	rs11708996	3.0 (0.3)	0.92 (0.81-1.06)
	rs6800541	3.8 (0.2)	0.89 (0.81-0.98)
	rs7692808	-2.0 (0.2)	1.05 (0.95-1.17)
	rs251253	-1.5 (0.2)	0.92 (0.83-1.02)
	rs3807989	2.3 (0.2)	0.92 (0.84-1.01)
	rs4944092	-1.2 (0.2)	1.06 (0.96-1.18)
	rs1896312	2.0 (0.2)	0.98 (0.88-1.09)

			Association in ARIC data set		
Phenotype	SNP	OR (95% CI) for AF previously reported by GWAS**	PR interval Beta (s.e.)	PR segment Beta (s.e.)	P wave duration Beta (s.e.)
Atrial fibrillation	rs6666258	1.18 (1.13–1.23)	-0.69 (0.45)	-0.43 (0.44)	-0.28 (0.23)
	rs3903239	1.14 (1.10–1.18)	0.63 (0.42)	0.64 (0.40)	0.03 (0.21)
	rs6817105	1.64 (1.55–1.73)	1.37 (0.66)	0.91 (0.64)	0.54 (0.33)
	rs2040862	1.15 (1.09–1.21)	0.00 (0.55)	-0.14 (0.53)	0.13 (0.27)
	rs3807989	0.88 (0.84–0.91)	2.18 (0.43)	1.51 (0.42)	0.61 (0.21)
	rs10821415	1.13 (1.08–1.18)	-0.29 (0.42)	-0.44 (0.41)	0.18 (0.21)
	rs10824026	0.85 (0.81–0.90)	-0.39 (0.58)	-1.10 (0.56)	0.67 (0.29)
	rs1152591	1.13 (1.09–1.18)	0.71 (0.43)	0.55 (0.41)	0.19 (0.21)
	rs7164883	1.16 (1.10–1.22)	-1.30 (0.57)	-1.32 (0.55)	0.06 (0.28)
	rs2106261	1.24 (1.17–1.30)	-0.37 (0.55)	-0.62 (0.54)	0.28 (0.28)

* Pfeufer A, van Noord C, Marciante KD, Arking DE, Larson MG, Smith AV et al. Genome-wide association study of PR interval. Nat Genet 2010; 42: 153–159.

**Ellinor PT, Lunetta KL, Albert CM, Glazer NL, Ritchie MD, Smith AV et al. Meta-analysis identifies six new susceptibility loci for atrial fibrillation. Nat Genet 2012; 44: 670–675.

Supplementary Table 3: List of previously* published SNPs and weights
used to compute a BMI genetic risk score.
*Locke AE, Kahali B, Berndt SI, Justice AE, Pers TH, Day FR *et al.* Genetic
studies of body mass index yield new insights for obesity biology. *Nature* 2015;
518: 197–206.

SNP	Beta
rs1558902	0.082
rs6567160	0.056
rs13021737	0.060
rs10938397	0.040
rs543874	0.048
rs2207139	0.045
rs11030104	0.041
rs3101336	0.033
rs7138803	0.032
rs10182181	0.031
rs3888190	0.031
rs1516725	0.045
rs12446632	0.040
rs2287019	0.036
rs16951275	0.031
rs3817334	0.026
rs2112347	0.026
rs12566985	0.024
rs3810291	0.028
rs7141420	0.024
rs13078960	0.030
rs10968576	0.025
rs17024393	0.066
rs657452	0.023
rs12429545	0.033
rs12286929	0.022
rs13107325	0.048
rs11165643	0.022
rs7903146	0.023
rs10132280	0.023
rs17405819	0.022
rs6091540	0.019
rs1016287	0.023
rs4256980	0.021
rs17094222	0.025
rs12401738	0.021
rs7599312	0.022
rs2365389	0.020
rs205262	0.022
rs2820292	0.020
rs12885454	0.021
rs9641123	0.019

rs12016871	0.030
rs16851483	0.048
rs1167827	0.020
rs758747	0.023
rs1928295	0.019
rs9925964	0.019
rs11126666	0.021
rs2650492	0.021
rs6804842	0.019
rs12940622	0.018
rs7164727	0.018
rs11847697	0.049
rs4740619	0.018
rs492400	0.016
rs13191362	0.028
rs3736485	0.018
rs17001654	0.031
rs11191560	0.031
rs2080454	0.017
rs7715256	0.016
rs2176040	0.014
rs1528435	0.018
rs2075650	0.026
rs1000940	0.019
rs2033529	0.019
rs11583200	0.018
rs7239883	0.016
rs2836754	0.016
rs9400239	0.019
rs10733682	0.017
rs11688816	0.017
rs11057405	0.031
rs9914578	0.020
rs977747	0.017
rs2121279	0.025
rs29941	0.018
rs11727676	0.036
rs3849570	0.019
rs9374842	0.019
rs6477694	0.017
rs4787491	0.016
rs1441264	0.018
rs7899106	0.040
rs2176598	0.020
rs2245368	0.032
rs17203016	0.021
rs17724992	0.019
rs7243357	0.022
rs16907751	0.035

rs1808579	0.017
rs13201877	0.023
rs2033732	0.019
rs9540493	0.017
rs1460676	0.020
rs6465468	0.017

Supplementary Table 4: Characteristics of the ARIC population.
See Methods for metabolic trait definitions.

Characteristic	Value
Gender [n (%)]	
Males	3,040 (45.2)
Females	3,691 (54.8)
Age at first visit (years)	
median (IQR)	54 (49-59)
Metabolic traits [n (%)]	
Waist circumference	3,242 (48.1)
Insulin Resistance	444 (6.6)
Hypertension	1,341 (19.9)
Triglycerides	1,983 (29.5)
HDL cholesterol	2,698 (44.1)
Metabolic syndrome	1,435 (21.3)
EKG parameters [mean (s.d.)]	
PR interval duration (ms)	159 (23)
P wave duration (ms)	105 (12)
PR segment duration (ms)	55 (28)

Supplementary Table 5: Demographics for the eMERGE atrial fibrillation cases and controls. Comorbidities are based on ICD-9 pheWAS codes, as described in the methods.

Characteristic	AF cases (n=1,547)	AF controls (n=3,128)
Gender [n (%)]		
Males	867 (56.0)	1,642 (52.5)
Females	680 (44.0)	1,486 (47.5)
Birth Decade		
median (IQR)	1925 (1915-1935)	1935 (1925-1945)
Comorbidities[1] [n (%)]		
Essential hypertension	1249 (80.7)	1467 (46.9)
Coronary atherosclerosis	851 (55.0)	380 (12.1)
Congestive heart failure	809 (52.3)	111 (3.5)
Hemorrhage due to anticoagulants	789 (51.0)	151 (4.8)
Cerebrovascular disease	602 (38.9)	360 (11.5)
Heart valve disorders	536 (34.6)	152 (4.9)
Renal failure	499 (32.3)	195 (6.2)
Type 2 diabetes	499 (32.3)	526 (16.8)
Chronic airway obstruction	442 (28.6)	256 (8.2)
Myocardial infarction	394 (25.5)	84 (2.7)
Cardiomegaly	365 (23.6)	54 (1.7)
Tobacco use disorder	246 (15.9)	361 (11.5)