FinnGen

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Genotyping and imputation in FinnGen

FinnGen samples were genotyped with Illumina and Affymetrix arrays (Illumina Inc., San Diego, and Thermo Fisher Scientific, Santa Clara, CA, USA) and put through the same rigorous QC steps as described above. Genotype imputation was carried out by using the population-specific SISu v3 imputation reference panel with Beagle 4.1 (version 08Jun17.d8b, https://faculty.washington.edu/browning/beagle/b4_1.html) as described in the following protocol: dx.doi.org/10.17504/protocols.io.nmndc5e. Post-imputation QC involved excluding variants with imputation INFO <0.7.

Genotyping and imputation in FINRISK

26,404 FINRISK samples were genotyped using several arrays: the HumanCoreExome BeadChip, the Human610-Quad BeadChip, the Affymetrix6.0, and the Infinium HumanOmniExpress (Illumina Inc., San Diego and Affymetrix, Inc., Santa Clara, CA, USA). Genotype calls were generated together with other available data sets using zCall at the Institute for Molecular Medicine Finland (FIMM). After sample-wise quality control (exclude samples with ambiguous gender, missingness (>5%), excess heterozygosity (+-4SD), non-European ancestry) and variant-wise quality control (exclude SNPs with high missingness (>2%), low HWE P-value (<1e-6), minor allele count (MAC) <3 (in case Zcall'ed chip data) or MAC <10 (chip data called using Illumina GenCall) steps, the samples were pre-phased using Eagle2 (version 2.3). Genotype imputation was carried out by using a Finnish population-specific reference panel consisting of 2690 high-coverage WGS and 5092 WES samples with IMPUTE2 (version 2.3.2) that allows the usage of two panels at the same time (the 'merge_ref_panels' option). Post-imputation quality control involved excluding variants imputed with imputation INFO < 0.7. Chromosome X variants were also excluded from the downstream analyses. We excluded one individual of each sample-pair with kinship >0.125, and calculated principal components for the unrelated individuals. The 26,404 samples contained the 2012 FINRISK cohort; this study used only FINRISK cohorts from 1992, 1997, 2002, and 2007, comprising 21,813 unrelated individuals.

Polygenic risk scores

In LDpred,[1] using a linkage disequilibrium (LD) reference panel matching the genome-wide association study (GWAS) discovery population is recommended. We applied the Finnish panel SISu v2, however, type 2 diabetes (T2D) PRSs calculated with i) SISuv2 and ii) 503 Europeans from the 1000 Genomes phase 3[2] as the LD reference showed high correlation (>0.9). Due to the high LD in the isolated Finnish population, we selected an LD-radius approximately twice the radius recommended, which is M/3,000, where M is the total number of single nucleotide polymorphisms used in the analysis. Variants with minor allele frequency less than 1% are excluded by the software.

We calculated the polygenic risk scores by summing the dosage of each risk allele carried by an individual (ranging from 0 to 2 for each variant, dosage used for incorporating imputation uncertainty), weighting each variant by its natural logarithm of the relative risk extracted from the genome-wide association study. For each individual *i*, this results in a single value on a continuous scale:

$$\text{PRS}_i = \sum_{j=1}^{M} \hat{\beta}_j \times dosage_{ij}$$

where $\hat{\beta}_j$ is the weight for variant *j* obtained from GWAS summary statistics. Within the whole FINRISK dataset, the PRS the highest C-index was chosen for the subsequent analyses (Supplementary Table 4). Adjusted survival curves were plotted with the R package *survminer*, using the calculation parameter "conditional", which after rebalancing averages for the polygenic risk score categories. The restricted mean survival times[3] (RMST; age 85 as the upper limit) were estimated by fitting flexible parametric survival models, which generated similar effect sizes as the Cox proportional hazards models.

Clinical risk calculators

In the FINRISK analyses, the association between PRS and disease was tested for incident cases only. The number of prevalent cases excluded was 954 for coronary heart disease, 671 for type 2 diabetes (T2D), 351 for atrial fibrillation (AF), 164 for breast cancer, and 59 for prostate cancer. For clinical risk factor variables missingness was at most 1.8%; individuals with missing data were removed from each respective clinical risk assessment. For calculating the 10-year risk for hard atherosclerotic cardiovascular disease (ASCVD) according to the Pooled Cohort Equations by ACC/AHA (2013), were excluded 23 individuals with missing data in any of the risk factors.

Clinical high risk for T2D was defined by the criteria for testing diabetes or prediabetes in asymptomatic adults, based on American Diabetes Association's current clinical practice recommendations.[4] These criteria consist of a combination of BMI ≥25kg/m^2 and one or more additional risk factors, of which the following were applicable in our study: first-degree relative with diabetes, history of cardiovascular disease, hypertension (≥140/90 mmHg), HDL <0.90 mmol/l, triglyceride level >2.82 mmol/l, and severe obesity (BMI ≥35kg/m^2). Individuals who with impaired fasting glucose (≥5.6 mmol/L) were also defined as having high risk. In assessing this risk, history of cardiovascular disease was defined as physician-diagnosed coronary heart disease or stroke (see Supplementary Table 2 for definition of coronary heart disease; stroke was any of I61, I63, I64 except I63.6 (International Classification of Diseases, 10th revision; ICD-10) or 431, 4330A, 4331A, 4339A, 4340A, 4341A, 4349A, 436 (ICD-9) as the underlying or direct cause of death, or as the main or side diagnosis at hospital discharge. 82 individuals with missing data on BMI were excluded from these analyses involving clinical risk assessment of T2D.

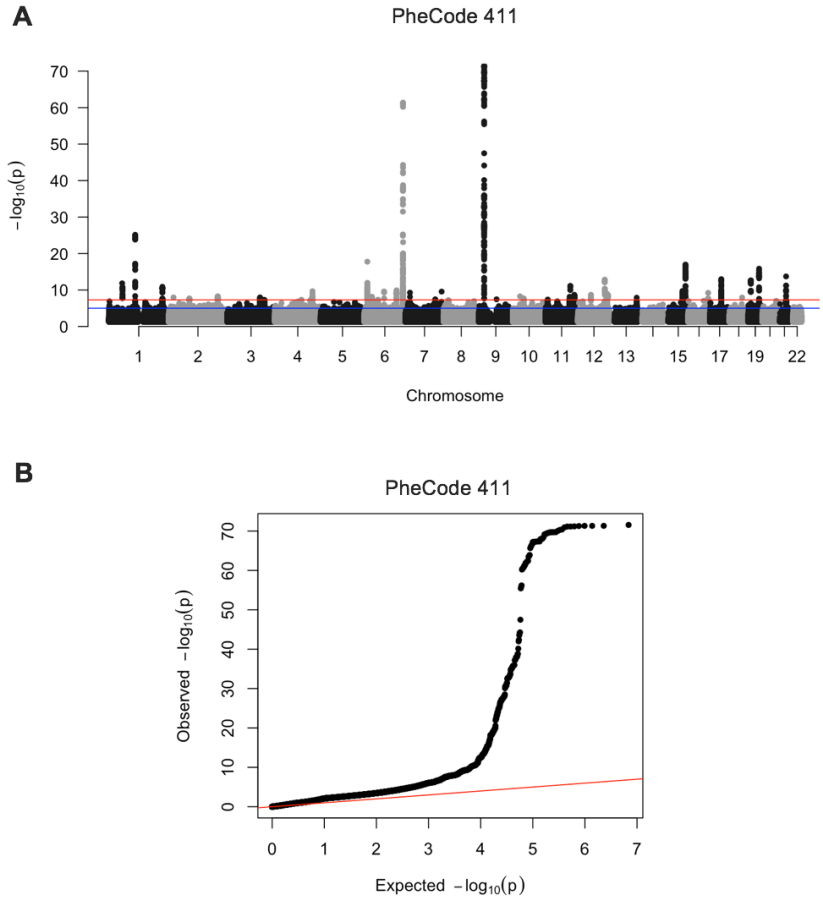
When taking all calculator components from the original study, the original CHARGE-AF score showed poor calibration with a mean 5-year risk 0.02% in individuals aged ≥45. To improve calibration, we obtained the mean component from FINRISK individuals aged 45 to 74, which resulted in a 5-year mean risk of 4.2% (standard deviation 4.3%). We did not revise the baseline hazard, as the original baseline

hazard ≈0.972 was similar to ours (≈0.977). 85 individuals with missing data for the risk variables were excluded.

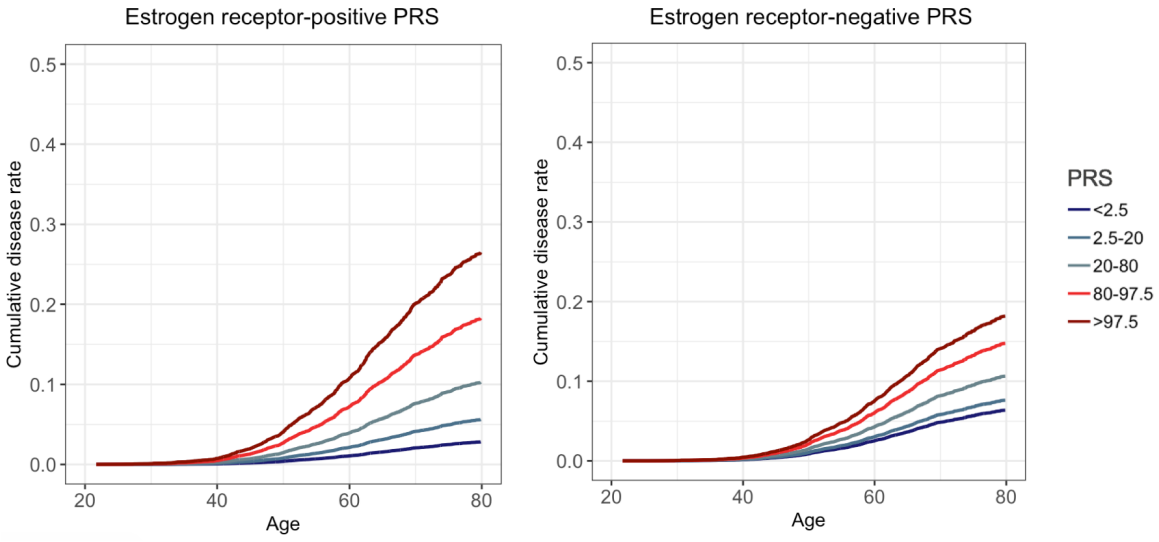
Supplementary References

1. Vilhjalmsson BJ, Yang J, Finucane HK, et al. Modeling Linkage Disequilibrium Increases Accuracy of Polygenic Risk Scores. Am J Hum Genet 2015;97:576-92.
2. Genomes Project Consortium, Auton A, Brooks LD, et al. A global reference for human genetic variation. Nature 2015;526:68-74.
3. Royston P, Parmar MK. Restricted mean survival time: an alternative to the hazard ratio for the design and analysis of randomized trials with a time-to-event outcome. BMC Med Res Methodol 2013;13:152.
4. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2019. Diabetes Care 2019;42:S13-S28.
5. Zhou W, Nielsen JB, Fritsche LG, et al. Efficiently controlling for case-control imbalance and sample relatedness in large-scale genetic association studies. Nat Genet 2018;50:1335-41.

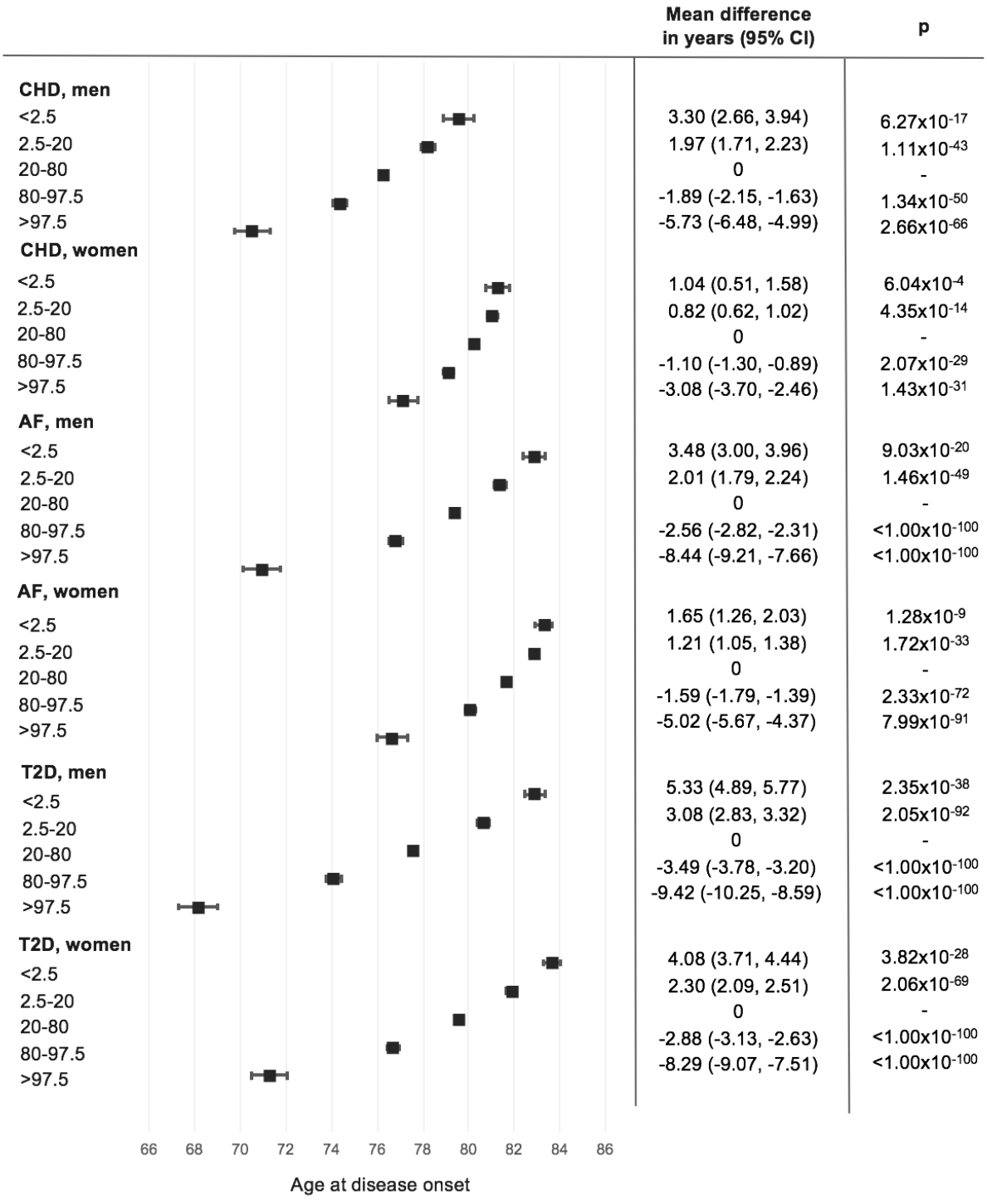
Supplementary Figure 1. Manhattan plot (A) and quantile-quantile plot (B) for the genome-wide association study for PheCode 411 (Ischemic heart disease) by Zhou et al.[5] These summary statistics were used for constructing the polygenic risk score for coronary heart disease.



Supplementary Figure 2. With any breast cancer as the outcome in FinnGen, adjusted survival curves for estrogen receptor-specific polygenic risk scores (PRS). The PRS for any breast cancer showed high correlation with the estrogen receptor-positive PRS (r = 0.93) and moderate correlation with estrogen receptor-negative PRS (0.54).

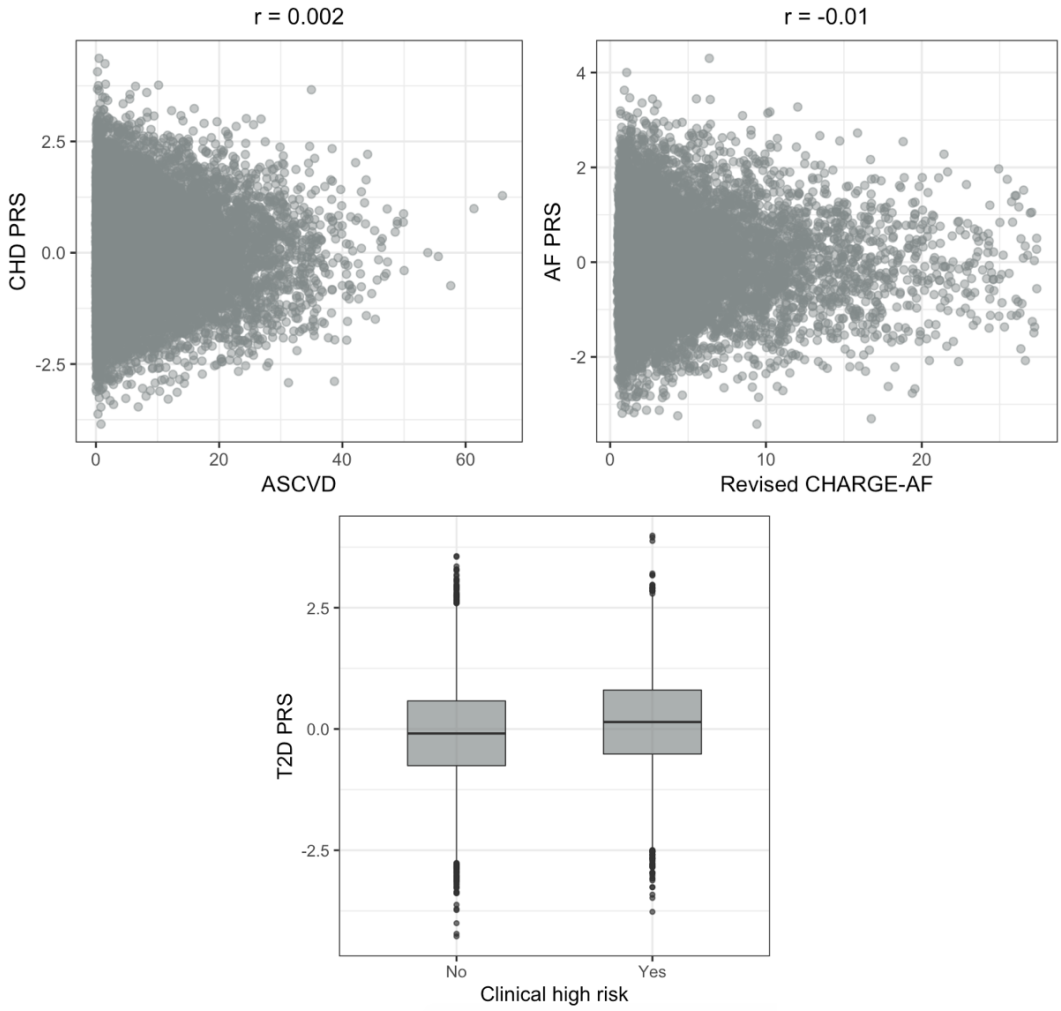


Supplementary Figure 3. Difference in age at disease onset by sex, across polygenic risk score categories (FinnGen).



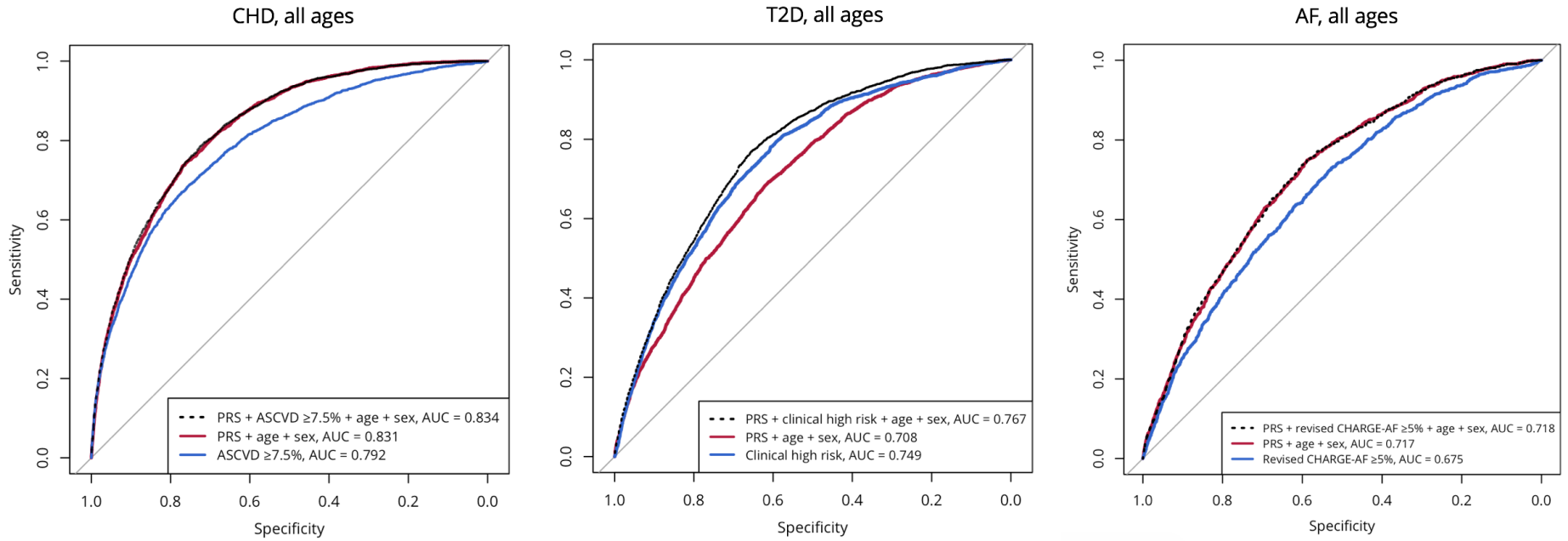
CHD = coronary heart disease, AF = atrial fibrillation or flutter, T2D = type 2 diabetes. The estimands for age at onset are restricted mean survival times (RMST).

Supplementary Figure 4. Correlation between polygenic and clinical risk in FINRISK, using respective incident disease cases and controls.



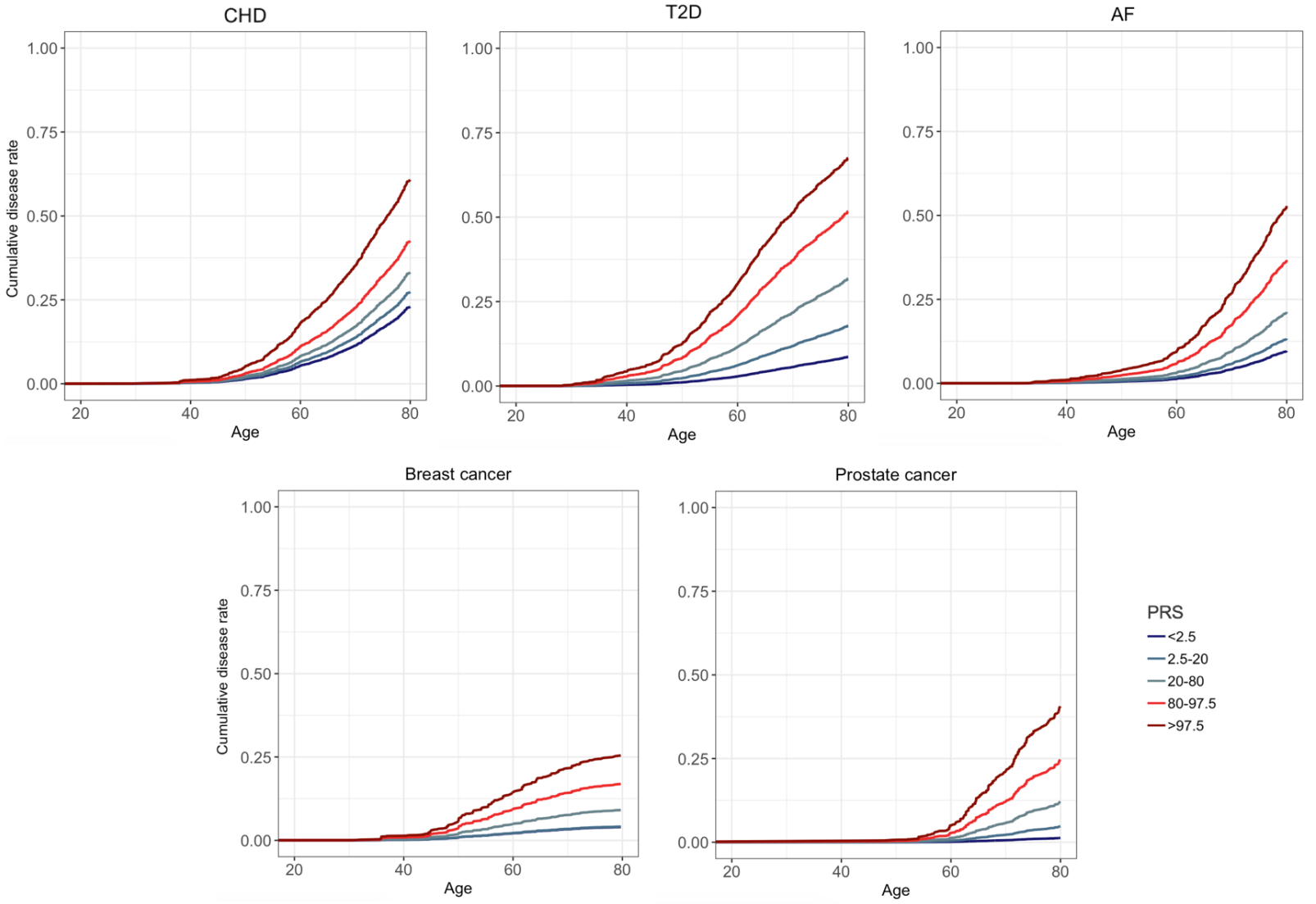
CHD = coronary heart disease, PRS = polygenic risk score, AF = atrial fibrillation or flutter, T2D = type 2 diabetes, BMI = body mass index, WHR = waist-hip ratio. ASCVD = the 10-year risk calculator for hard atherosclerotic cardiovascular disease (ASCVD), according to the Pooled Cohort Equations by ACC/AHA (2013). Revised CHARGE-AF = revised version of the CHARGE-AF, a risk calculator for 5-year risk of AF. Clinical high risk for T2D defined as BMI ≥25kg/m2 and one of more additional clinical risk factors.[4]

Supplementary Figure 5. The area under the receiver operating characteristic curves (AUC) for high PRS, high clinical risk, or their combination.



CHD = coronary heart disease (N = 20,165), T2D = type 2 diabetes, AF = atrial fibrillation or flutter (N = 10,666). High PRS = above the 90th percentile. ASCVD = the 10-year risk calculator for hard atherosclerotic cardiovascular disease (ASCVD), according to the Pooled Cohort Equations by ACC/AHA (2013). Clinical high risk for T2D defined as BMI ≥25kg/m^2 and one of more additional clinical risk factors.[16] Revised CHARGE-AF = revised version of the CHARGE-AF, a risk calculator for the 5-year risk of AF.

Supplementary Figure 6. Adjusted survival curves in FINRISK, showing cumulative risk of incident disease in by polygenic risk score (PRS) categories.



The FINRISK cohorts (n = 21,813) comprised of 2,197 incident cases of CHD, 1,431 cases of AF, 2,516 cases of T2D, 404 cases of breast cancer, and 444 cases of prostate cancer.

Table S1. The prospective epidemiological and disease-based cohorts, and hospital biobank samples in FinnGen Data Freeze 2.

Cohort	N
Auria biobank*	9,967
Blood Service biobank	1,3222
Borealis biobank*	1,368
Botnia Family	1,216
Botnia New	6
Botnia PPP	4,856
Botnia Sib-Helsinki	431
Corogene	4,495
Eastern Finland biobank*	1,965
FinHealth 2017	5,783
FINRISK 1992-2012	29,550
GeneRISK	6,960
Health 2000	6,602
Health 2011	711
Helsinki biobank*	21,014
Kuusamo 2011	145
Migraine	7,732
SUPER	4,402
Tampere biobank*	1,973
THL Diabetes	6,983
Twins	5,919
Sum	**135,300**

*Hospital-based biobanks

Table S2. Disease endpoint definitions.

	Additional definitions	Only main diagnosis accepted	ICD-10	ICD-9	ICD-8	ICD-10 exclu-sions	Cause of death ICD-10	Cause of death ICD-9	Cause of death ICD-8	Cause of death ICD-10 exclu-sions	Cause of death ICD-9 exclu-sions	Topo-graphical codes*
Coronary heart disease	Myocardial infarction|Myocardial infarction, strict|Complications following myocardial infarction|Prior myocardial infactrion|Angina pectoris|Other coronary atherosclerosis|Coronary artery bypass graft**|Coronary angioplasty**											
Major coronary heart disease event	Myocardial infarction|Coronary artery bypass graft|Coronary angioplasty	Yes	I20.0 | I21 | I22	410 | 411.0	410 | 411.0		I2[1-5] | I46 | R96 | R98	41[0-4] | 798	41[0-4] | 798		798.0A	
Myocardial infarction, strict		Yes	I21 | I22	410	410		I21 | I22	410	410			
Myocardial infarction			I21 | I22	410	410		I21 | I22	410	410			
Complications following myocardial infarction			I23	-	-		I23	-	-			
Old myocardial infarction			I25.2	412	412		I25.3	412	412			
Angina pectoris			I20	413 | 411[0-1]	413		I20	413 | 411[0-1]	413			
Other coronary atheroclerosis			I25 | I24 | Z95.1 | T82.2	414 | 996.0A	414	I25.3	I25 | I24 | Z95.1 | T82.2	414 | 996.0A	414	I25.3		

Atrial fibrillation and flutter	Eligibility for special reimbursement for apixaban, dabigatran, edoxaban, rivaroxaban or dronedarone for ICD-10 I48	I48	427.3	427.92		I48	427.3	427.92	
Malignant neoplasm of breast / breast cancer									C50
Malignant neoplasm of prostate / prostate cancer									C61
Type 2 diabetes* **	Any type 2 diabetes diagnosis defined below | Medication purchases for ATC A10B, Blood glucose lowering drugs, excluding insulins.				E10[0-9]				
Type 2 diabetes with coma		E11.0	250.2A	-		E11.0	250.2A		
Type 2 diabetes with ketoacidosis		E11.1	250.1A	-		E11.1	250.1A		
Type 2 diabetes with renal complications		E11.2	250.3A	-		E11.2	250.3A		
Type 2 diabetes with ophthalmic complications		E11.3	250.4A	-		E11.3	250.4A		
Type 2 diabetes with neurological complications		E11.4	250.5A	-		E11.4	250.5A		
Type 2 diabetes with peripheral circulatory complications		E11.5	250.6A	-		E11.5	250.6A		
Type 2 diabetes with other specified/ multiple/unspecified complications	Eligibility for medication reimbursement with ICD-10 E11	E11[6-8]	250.7A | 250.8A	-		E11[6-8]	250.7A | 250.8A		
Type 2 diabetes without complications		E11.9	250.0A	-		E11.9	250.0A		

* The International Classification of Diseases for Oncology, Third Edition (ICD-O-3). **Procedure code identified at hospital discharge or from the nationwide register of invasive cardiac procedures. *** In FinnGen analyses, individuals with type 1 diabetes were excluded from cases (ICD-10 E10[0-9], ICD-9 250[0-8]B as a hospital discharge diagnosis or cause of death, or E10 for medication reimbursement)

Table S3. Genome-wide association studies used for constructing the polygenic risk scores and the number of variants in the final scores.

	GWAS summary statistics source	Article link	Data download link	Most recent access to data download	SNPs in discovery GWAS	SNPs in PRS calculation	LD radius	Additional information
Coronary heart disease	UKBB SAIGE	https://www.nature.com/articles/s41588-018-0184-y	https://www.dropbox.com/sh/wuj4y8wsqjz78om/AAACfAJK54KtvnzSTAoaZTLma?dl=0	Nov 2, 2018	28 345 446	6 412 950	4 000	PheCode 411 Ischemic heart disease
Type 2 diabetes	Mahajan et al 2018	https://www.nature.com/articles/s41588-018-0241-6	http://www.diagram-consortium.org/downloads.html	Dec 21, 2018	23 465 133	6 437 380	4 000	Not adjusted for BMI
Atrial fibrillation and flutter	Nielsen et al 2018	https://www.nature.com/articles/s41588-018-0171-3	http://csg.sph.umich.edu/willer/public/afib2018/	Dec 21, 2018	34 740 187	6 171 733	4 000	
Breast cancer	Michailidou et al 2017	https://www.nature.com/articles/nature24284	http://bcac.ccge.medschl.cam.ac.uk/bcacdata/oncoarray/gwas-icogs-and-oncoarray-summary-results/	Dec 21, 2018	11 792 358	6 390 808	4 000	
Breast cancer, estrogen receptor-positive	Michailidou et al 2017	https://www.nature.com/articles/nature24284	http://bcac.ccge.medschl.cam.ac.uk/bcacdata/oncoarray/gwas-icogs-and-oncoarray-summary-results/	Dec 21, 2018	11 784 434	6 390 799	4 000	
Breast cancer, estrogen receptor-negative	Michailidou et al 2017	https://www.nature.com/articles/nature24284	http://bcac.ccge.medschl.cam.ac.uk/bcacdata/oncoarray/gwas-icogs-and-oncoarray-summary-results/	Dec 21, 2018	11 784 725	6 390 805	4 000	
Prostate cancer	Schumacher et al 2018	https://www.nature.com/articles/s41588-018-0142-8	http://practical.icr.ac.uk/blog/?page_id=8088	Dec 21, 2018	20 734 509	6 606 785	4 000	

Table S4. The LDpred algorithm uses a tuning parameter p for denoting the fraction of variants assumed to be causal for the disease. The PRS with the highest C-index (bolded) in FINRISK was chosen for the subsequent analyses.

	Fraction of causal markers	C-index
Coronary heart disease	0.0001*	0.8163
	0.0003*	0.8162
	0.001*	0.8163
	0.003	**0.8203**
	0.01	0.8195
	0.03	0.8188
	0.1	0.8184
	0.3	0.8183
	1	0.8183
	inf	0.8183
Type 2 diabetes	0.0001*	0.7022
	0.0003*	0.7043
	0.001*	0.7033
	0.003*	0.7033
	0.01*	0.7089
	0.03*	0.7091
	0.1	0.7374
	0.3	**0.7417**
	1	0.7402
	inf	0.7398
Atrial fibrillation or flutter	0.0001*	0.7912
	0.0003*	0.7915
	0.001*	0.7921
	0.003*	0.7916
	0.01*	0.7942
	0.03	**0.8135**
	0.1	0.8107
	0.3	0.8082
	1	0.8057
	inf	0.8055
Prostate cancer	0.0001*	0.8076
	0.0003*	0.8077
	0.001*	0.8096
	0.003	0.8140
	0.01	**0.8416**
	0.03	0.8341
	0.1	0.8270
	0.3	0.8237
	1	0.8224
	inf	0.8223
Breast cancer	0.0001*	0.6426
	0.0003*	0.6403
	0.001*	0.6454
	0.003*	0.6490
	0.01*	0.6422

	0.03	**0.7042**
	0.1	0.6955
	0.3	0.6892
	1	0.6852
	inf	0.6853
Breast cancer, estrogen receptor-positive	0.0001*	0.6404
	0.0003*	0.6421
	0.001*	0.6434
	0.003*	0.6450
	0.01*	0.6479
	0.03	**0.6990**
	0.1	0.6912
	0.3	0.6868
	1	0.6834
	inf	0.6833
Breast cancer, estrogen receptor-negative	0.0001*	0.6403
	0.0003*	0.6410
	0.001*	0.6405
	0.003	**0.6511**
	0.01	0.6472
	0.03	0.6449
	0.1	0.6438
	0.3	0.6435
	1	0.6434
	inf	0.6432

*One or multiple chromosomes failed to converge.

Table S5. Baseline characteristics for FINRISK.

	FINRISK 1992	FINRISK 1997	FINRISK 2002	FINRISK 2007
	N = 4,745	N = 6,733	N = 5,427	N = 4,908
Follow-up in years, mean (SD)	22.3 (4.3)	17.5 (3.7)	13.3 (2.0)	8.7 (1.0)
Age, mean (SD)	44.3 (11.4)	48.2 (13.4)	48.3 (13.1)	51.1 (13.9)
Age ≤50, %	65.9	54.9	52.4	45.2
Women, %	53.8	51.0	53.4	53.3
Current smokers, %	28.0	23.6	26.3	19.9
TC, mean (SD)	5.6 (1.1)	5.5 (1.1)	5.6 (1.1)	5.3 (1.0)
LDL, mean (SD)	3.5 (1.0)	3.5 (0.9)	3.4 (1.0)	3.2 (0.9)
HDL, mean (SD)	1.4 (0.3)	1.4 (0.4)	1.5 (0.4)	1.4 (0.4)
TG, mean (SD)	1.5 (1.1)	1.5 (1.0)	1.4 (1.0)	1.4 (0.9)
SBP, mean (SD)	135.3 (19.3)	136.0 (19.9)	135.2 (20.0)	136.2 (20.3)
BMI, mean (SD)	26.1(4.4)	26.6 (4.5)	26.9 (4.7)	27.2 (4.9)
WHR, mean (SD)	0.8 (0.1)	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)
Blood pressure-lowering treatment, %	9.0	13.0	14.3	21.3
Lipid-lowering treatment, %	1.5	3.2	7.1	14.6
Positive family history for any diabetes, %	N/A	25.8	26.4	28.7
Positive family history for early MI, %	23.6	25.5	25.6	15.5
Prevalent CHD, %	3.3	5.3	5.0	6.4
Prevalent MI, %	0.8	1.3	1.0	1.7
Prevalent AF, %	0.9	1.8	1.7	2.9
Prevalent T2D, %	0.4	2.8	3.8	4.5
Prevalent breast cancer in women, %	1.0	1.2	1.3	2.3
Prevalent prostate cancer in men, %	0.0	0.6	0.5	1.2
Incident CHD, %	14.2	13.8	8.8	5.3
Incident MI, %	5.6	5.7	3.7	2.0
Incident AF, %	9.5	9.1	6.0	4.0
Incident T2D, %	15.7	13.2	10.1	7.2
Incident breast cancer in women, %	5.3	4.1	3.0	1.5
Incident prostate cancer in men, %	5.5	5.6	3.6	2.0

TC = total cholesterol, LDL = low-density lipoprotein (using the Friedewald equation), HDL = high-density lipoprotein, TG = triglycerides, SBP = systolic blood pressure, BMI = body mass index, WHR = waist-hip ratio, CHD = coronary heart disease, MI = myocardial infarction, T2D = type 2 diabetes, AF = atrial fibrillation or flutter. Units: lipid measurements mmol/l, SBP mmHg, BMI kg/m2.

Table S6. Impact of family history on polygenic risk score (PRS) effect size estimates (per standard deviation increment).

	HR (95% CI)	p
CHD PRS	1.27 (1.22-1.32)	4.77×10^{-28}
Family history of early MI	1.49 (1.36-1.63)	7.57×10^{-18}
CHD PRS + family history of early MI		
CHD PRS	1.26 (1.21-1.31)	5.24×10^{-26}
Family history of early MI	1.45 (1.32-1.59)	1.21×10^{-15}
T2D PRS	1.57 (1.50-1.66)	1.24×10^{-68}
Family history of any diabetes	1.62 (1.47-1.78)	1.67×10^{-22}
T2D PRS + family history of any diabetes		
T2D PRS	1.54 (1.46-1.62)	2.24×10^{-62}
Family history of early MI	1.49 (1.35-1.64)	8.27×10^{-16}

CHD = coronary heart disease, T2D = type 2 diabetes. T2D models adjusted for BMI.

Table S7. Hazard ratios (HR) and 95% confidence intervals (CI) per standard deviation increment in FINRISK.

	HR (95% CI)	p
Coronary heart disease	1.25 (1.18-1.32)	1.74×10^{-14}
Type 2 diabetes	1.70 (1.63-1.78)	$<1.00 \times 10^{-100}$
Atrial fibrillation or flutter	1.62 (1.54-1.70)	8.85×10^{-78}
Breast cancer	1.75 (1.59-1.92)	2.61×10^{-30}
Prostate cancer	1.88 (1.71-2.06)	4.74×10^{-41}

Table S8. Hazard ratios (HR) and 95% confidence intervals (CI) for polygenic risk score (PRS) bins in FINRISK.

	HR (95% CI)	p	N cases / N contols
CHD PRS			
<2.5	0.65 (0.47-0.89)	0.008	39 / 466
2.5-20	0.81 (0.72-0.92)	0.001	313 / 3,220
20-80	1 (reference)	-	1,274 / 10,838
80-97.5	1.35 (1.22-1.50)	2.45×10^{-8}	471 / 3,062
>97.5	2.42 (1.97-2.97)	2.21×10^{-17}	100 / 405
T2D PRS			
<2.5	0.23 (0.14-0.38)	7.14×10^{-9}	16 / 513
2.5-20	0.50 (0.43-0.58)	2.80×10^{-21}	224 / 3,476
20-80	1 (reference)	-	1,406 / 11,278
80-97.5	1.90 (1.73-2.08)	4.44×10^{-43}	719 / 2,981
>97.5	2.99 (2.52-3.54)	1.44×10^{-36}	151 / 378
AF PRS			
<2.5	0.44 (0.26-0.73)	0.002	15 / 478
2.5-20	0.60 (0.50-0.72)	1.69×10^{-8}	143 / 3,303
20-80	1 (reference)	-	779 / 11,035
80-97.5	1.94 (1.72-2.19)	4.28×10^{-27}	406 / 3,039
>97.5	3.19 (2.56-3.98)	8.67×10^{-25}	88 / 405
Breast cancer PRS			
<2.5	0.43 (0.16-1.16)	0.09	4 / 280
2.5-20	0.44 (0.30-0.65)	3.58×10^{-5}	29 / 1,954
20-80	1 (reference)	-	221 / 6,577
80-97.5	1.94 (1.56-2.42)	3.90×10^{-9}	123 / 1,860
>97.5	3.05 (2.04-4.55)	5.34×10^{-8}	27 / 257
Prostate cancer PRS			
<2.5	0.10 (0.01-0.73)	0.02	1 / 256
2.5-20	0.38 (0.25-0.58)	4.90×10^{-6}	25 / 1,770
20-80	1 (reference)	-	233 / 5,921
80-97.5	2.14 (1.74-2.64)	6.58×10^{-13}	146 / 1,649
>97.5	3.93 (2.79-5.53)	3.90×10^{-15}	39 / 218

CHD = coronary heart disease, AF = atrial fibrillation or flutter, T2D = type 2 diabetes, PRS = polygenic risk score