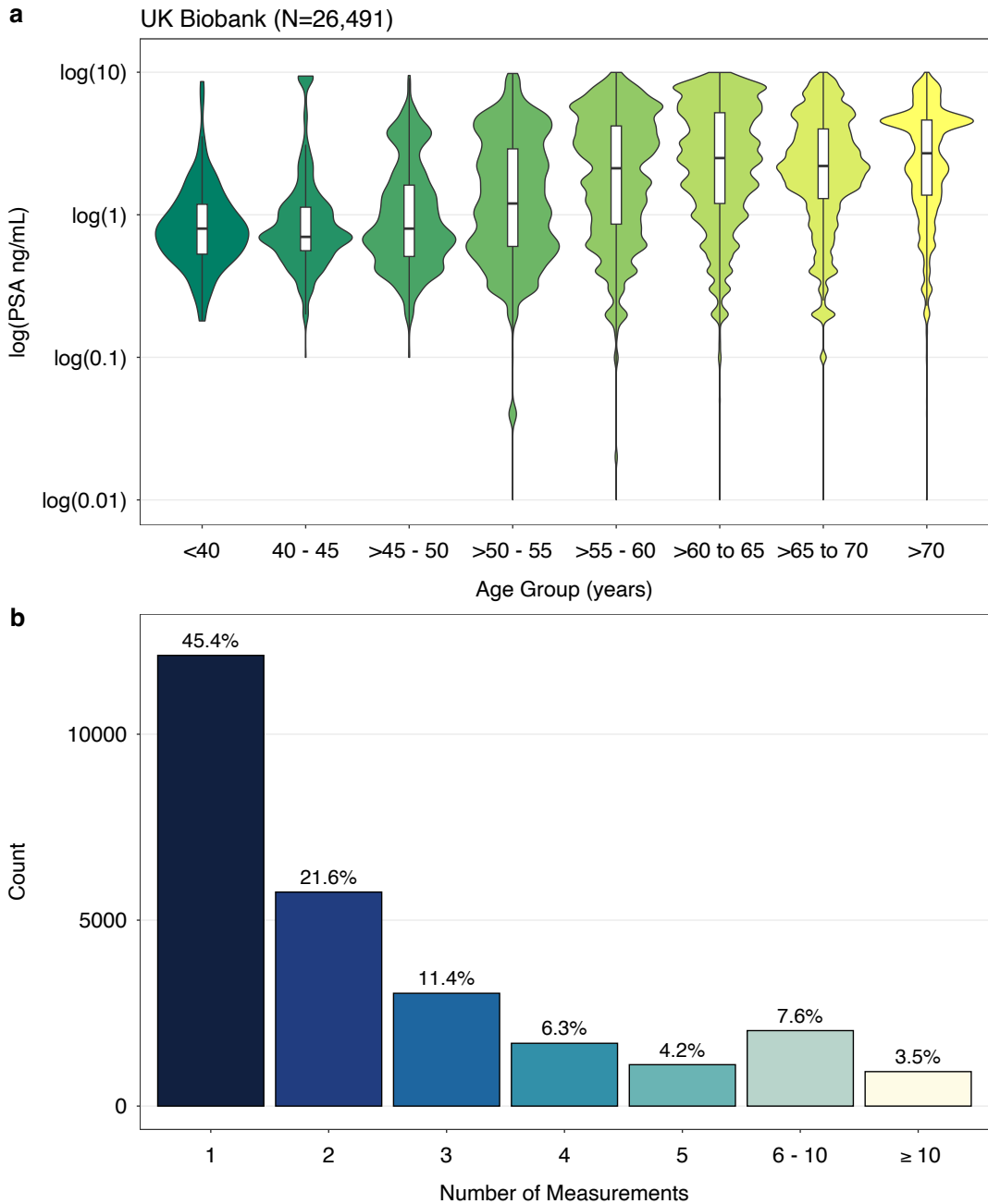


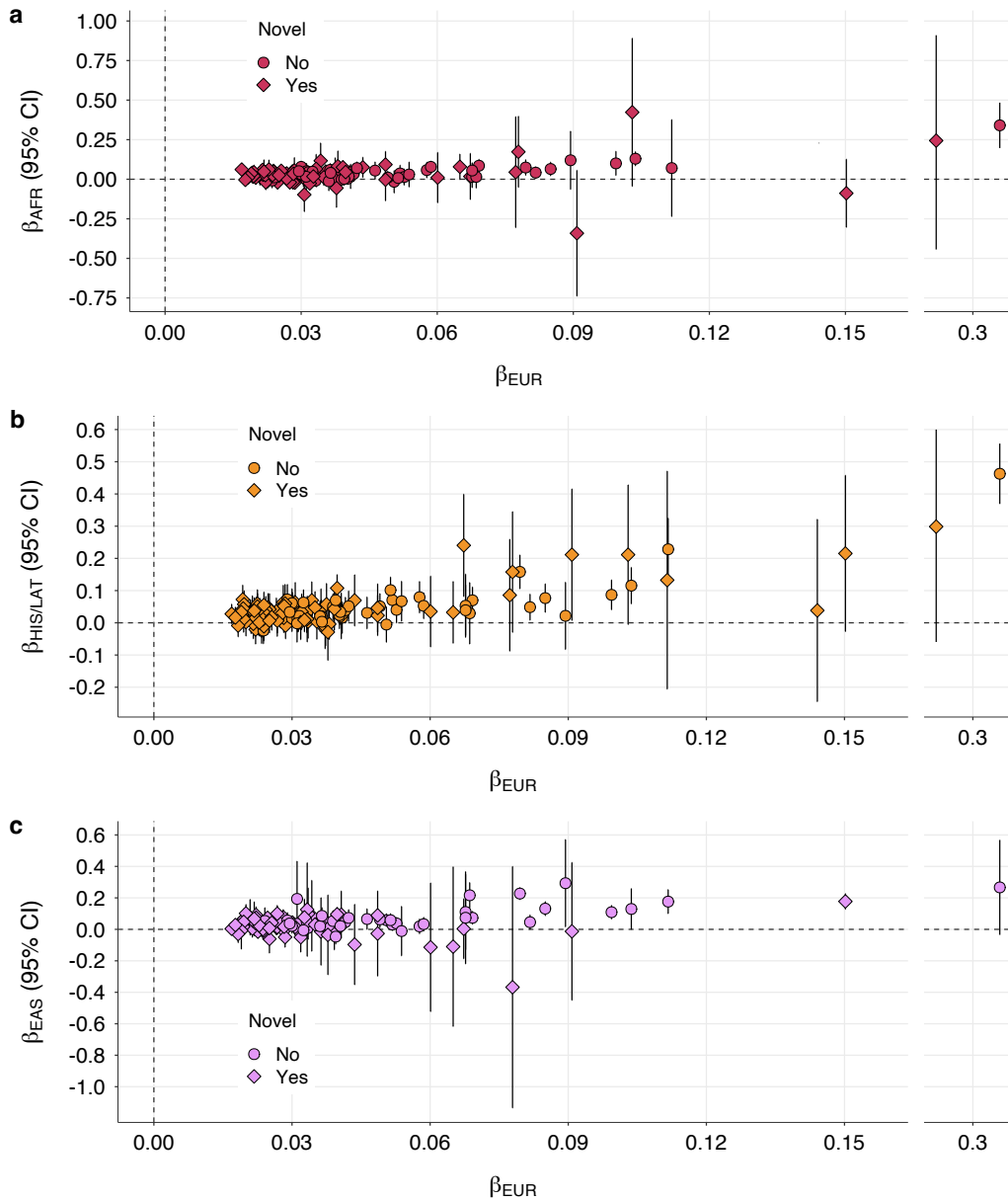
Genetically adjusted PSA levels for prostate cancer screening

In the format provided by the
authors and unedited

Supplementary Figure 1: PSA values in men of European ancestry in the UK Biobank. **a**, Violin plots and box plots visualize the distribution of PSA values across age groups. Lower and upper box plot hinges correspond to the first and third quartiles, or 25th and 75th percentiles, respectively. The upper and lower whiskers extend from each hinge to as a multiple of the inter-quartile range (IQR*1.5). **b**, Bar plots show the counts of UK Biobank participants with different numbers of PSA measurements, with the corresponding proportion of total GWAS sample size (N=26,491) accounted by each category.



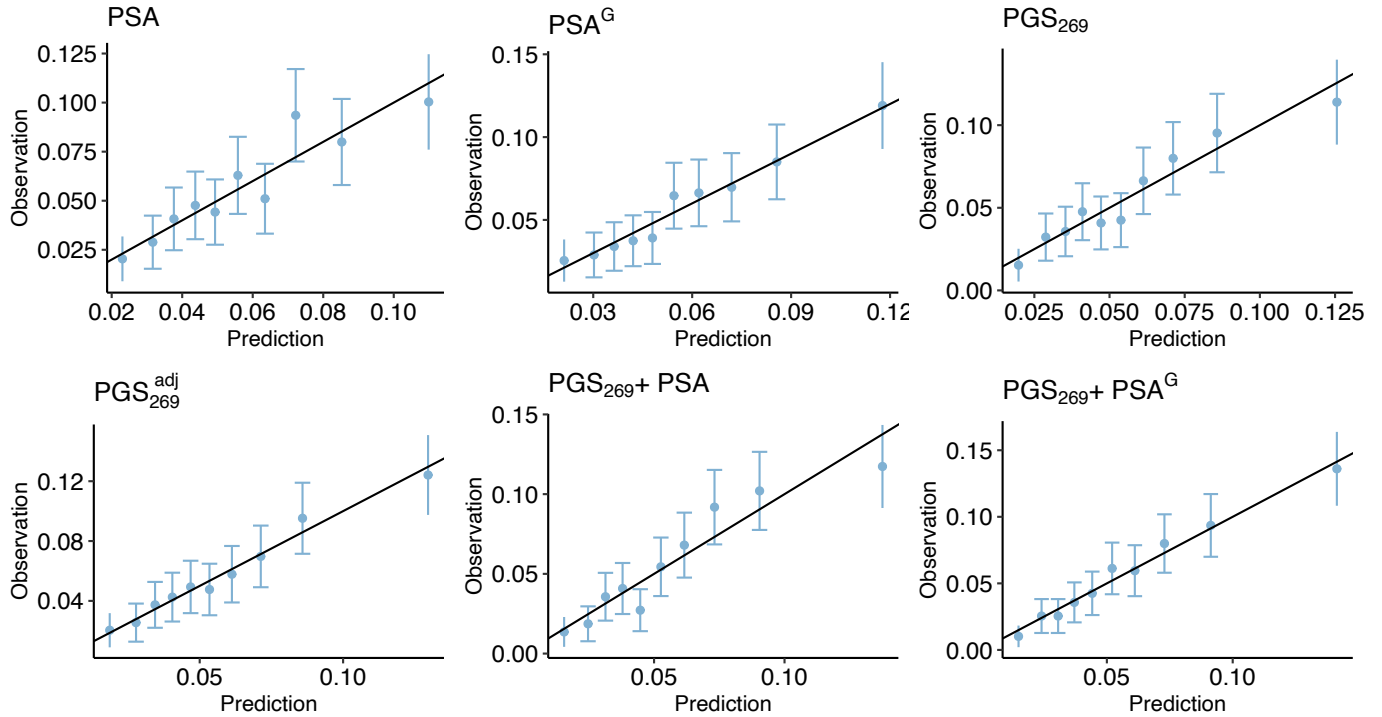
Supplementary Figure 2: Cross-ancestry comparison of effect sizes for 128 PSA index variants. Each panel compares effect sizes (β) in the European ancestry (EUR) inverse-variance-weighted fixed-effects meta-analysis ($n=85,824$) with effect sizes and corresponding 95% confidence intervals (CI) from **a**, African ancestry (β_{AFR} ; $n=3,509$) **b**, Hispanic/Latino ($\beta_{\text{HIS/LAT}}$; $n=3,098$) **c**, East Asian ancestry (β_{EAS} ; $n=3,337$) inverse-variance weighted fixed-effects meta-analyses. Index variants with $P < 5 \times 10^{-8}$ were selected from the multi-ancestry GWAS meta-analysis ($N=95,768$) using linkage disequilibrium (LD) clumping ($\text{LD } r^2 < 0.01$ within 10Mb windows). Correlations between effect sizes were estimated using Spearman's rho (ρ) for all variants and excluding those in the 19q13.33 (*KLK3*) region. All p-values are two-sided.



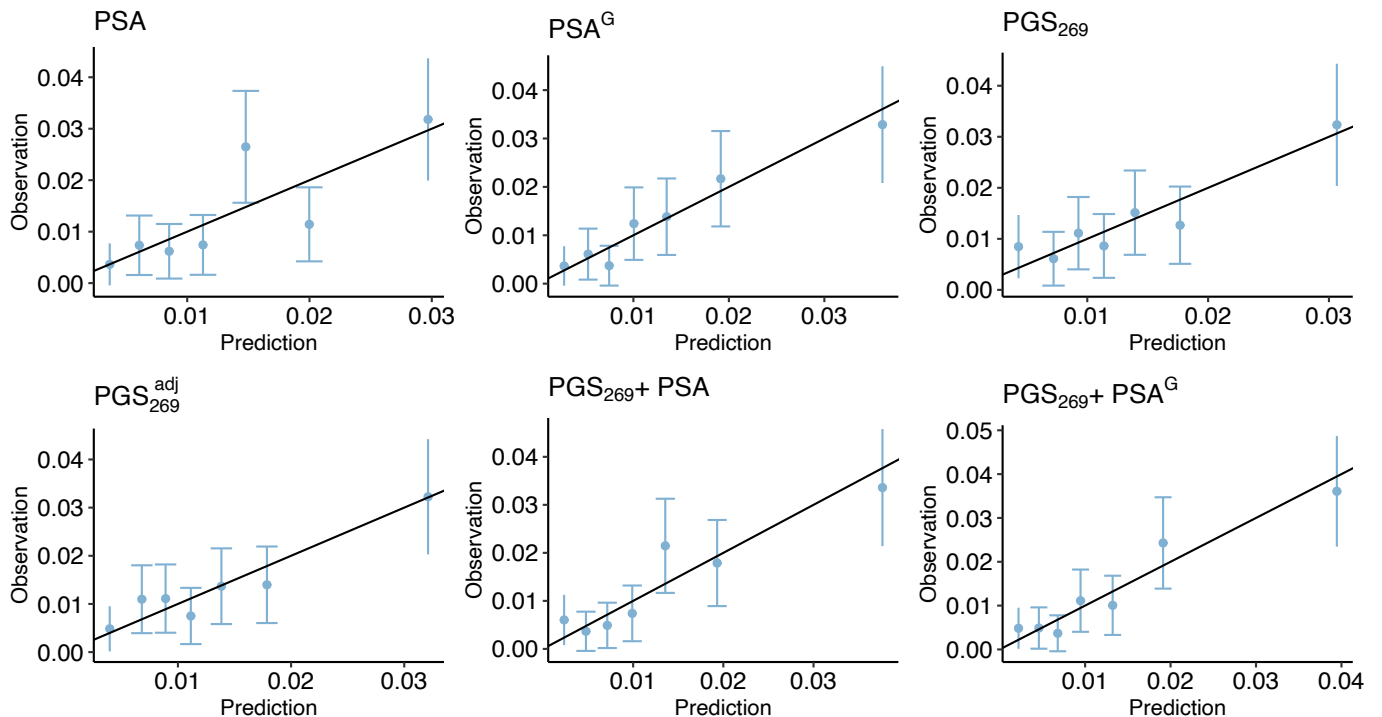
	ρ (all variants)	p – value (all variants)	ρ (exclude 19q13.33)	p – value (exclude 19q13.33)
AFR	0.273	1.95×10^{-3}	0.285	2.12×10^{-3}
HIS/LAT	0.479	1.14×10^{-8}	0.399	9.84×10^{-6}
EAS	0.166	0.069	0.097	0.31

Supplementary Figure 3: Calibration plots show the concordance between observed and predicted values generated from logistic regression models for overall incident prostate cancer (335 cases and 5548 controls) and aggressive prostate cancer (75 cases and 5548 controls) in the pooled, multi-ancestry population in the Prostate Cancer Prevention Trial (PCPT). Error bars show the 95% confidence intervals for the predictions within each bin.

PCPT: Prostate Cancer (Pooled)

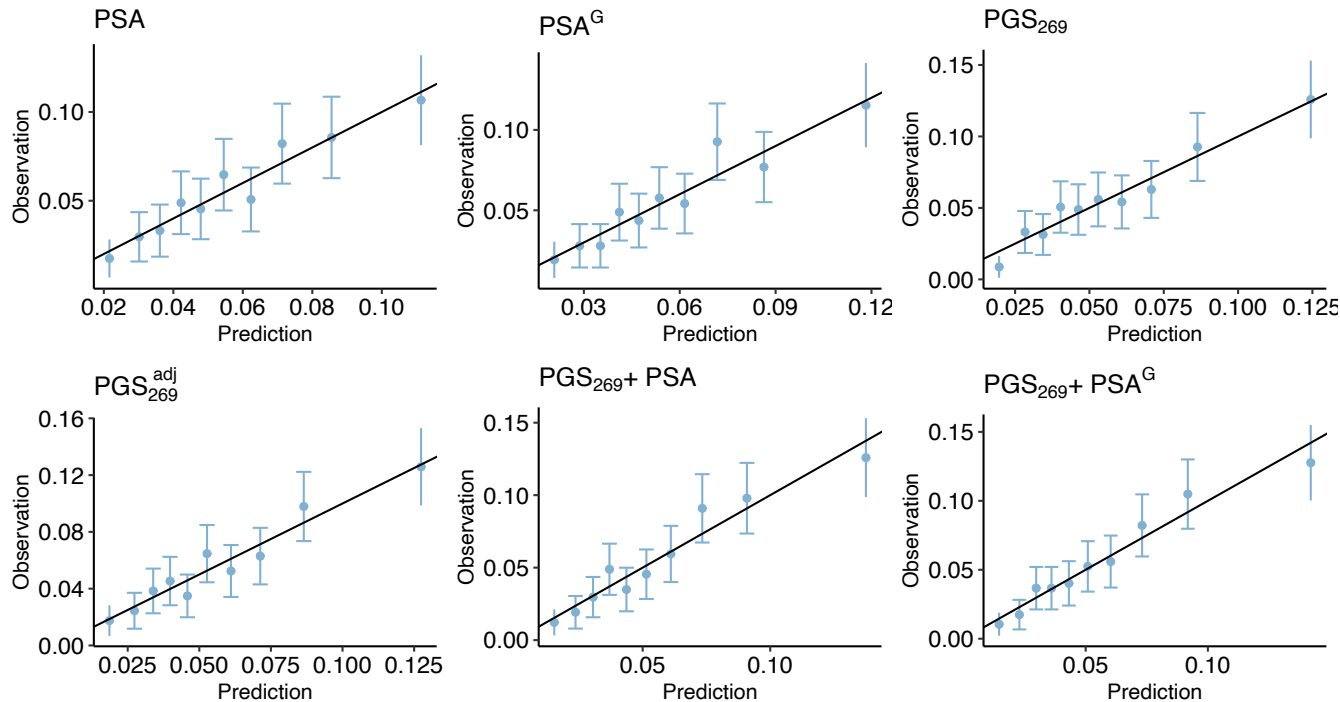


PCPT: Aggressive Prostate Cancer (Pooled)

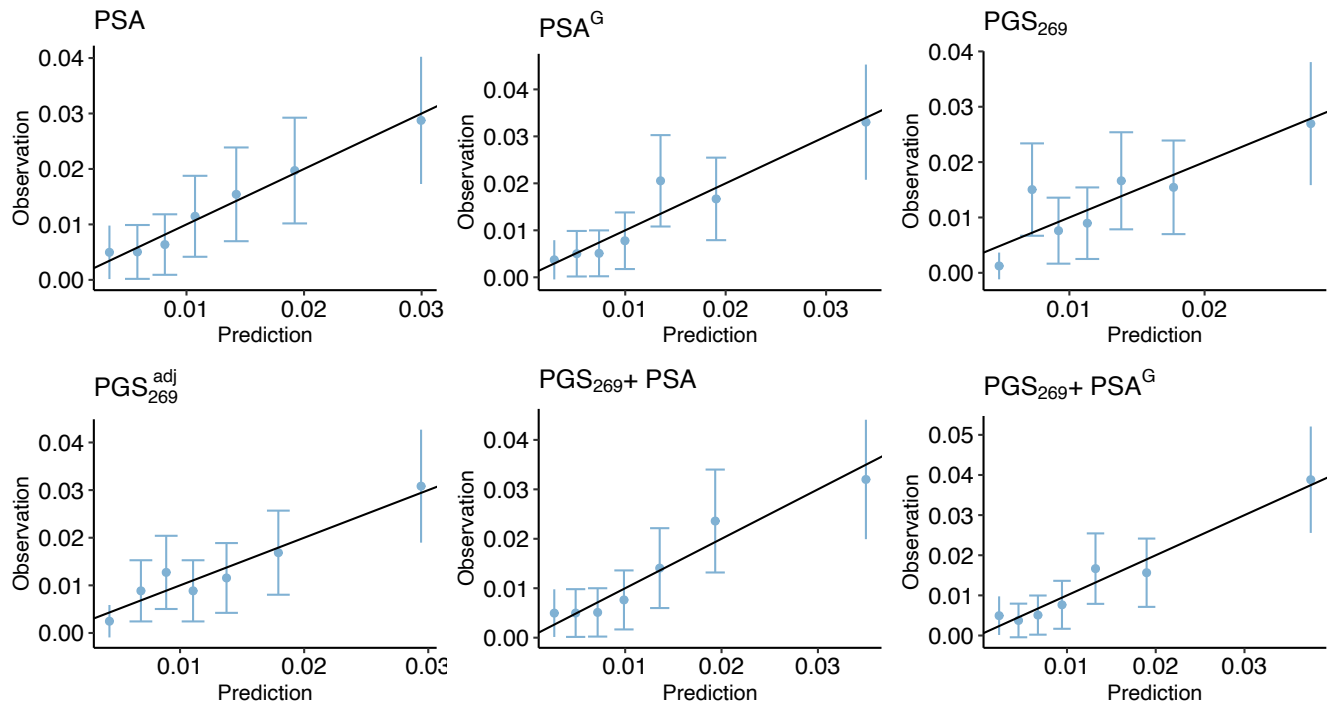


Supplementary Figure 4: Calibration plots show the concordance between observed and predicted values generated from logistic regression models for incident prostate cancer (323 cases and 5402 controls) and aggressive prostate cancer (71 cases and 5402 controls) in men of European ancestry in the Prostate Cancer Prevention Trial (PCPT). Error bars show the 95% confidence intervals for the predictions within each bin.

PCPT: Prostate Cancer (EUR)

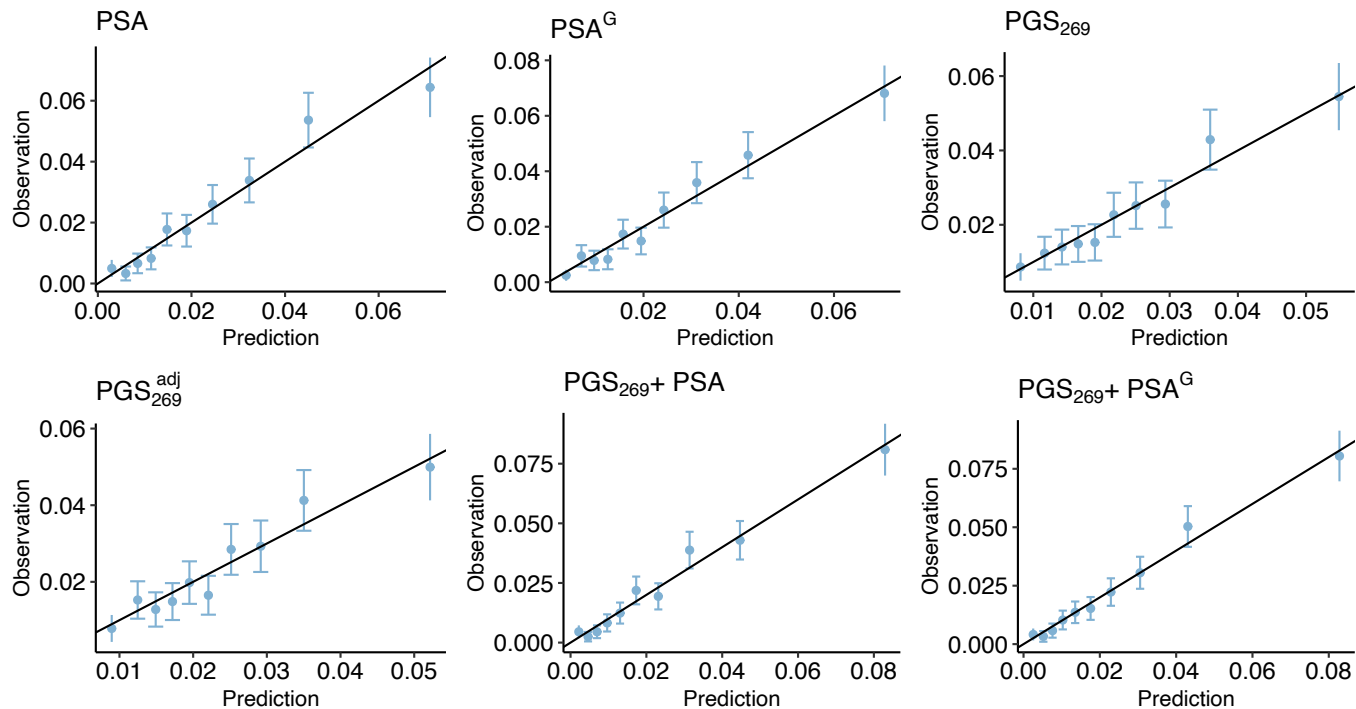


PCPT: Aggressive Prostate Cancer (EUR)

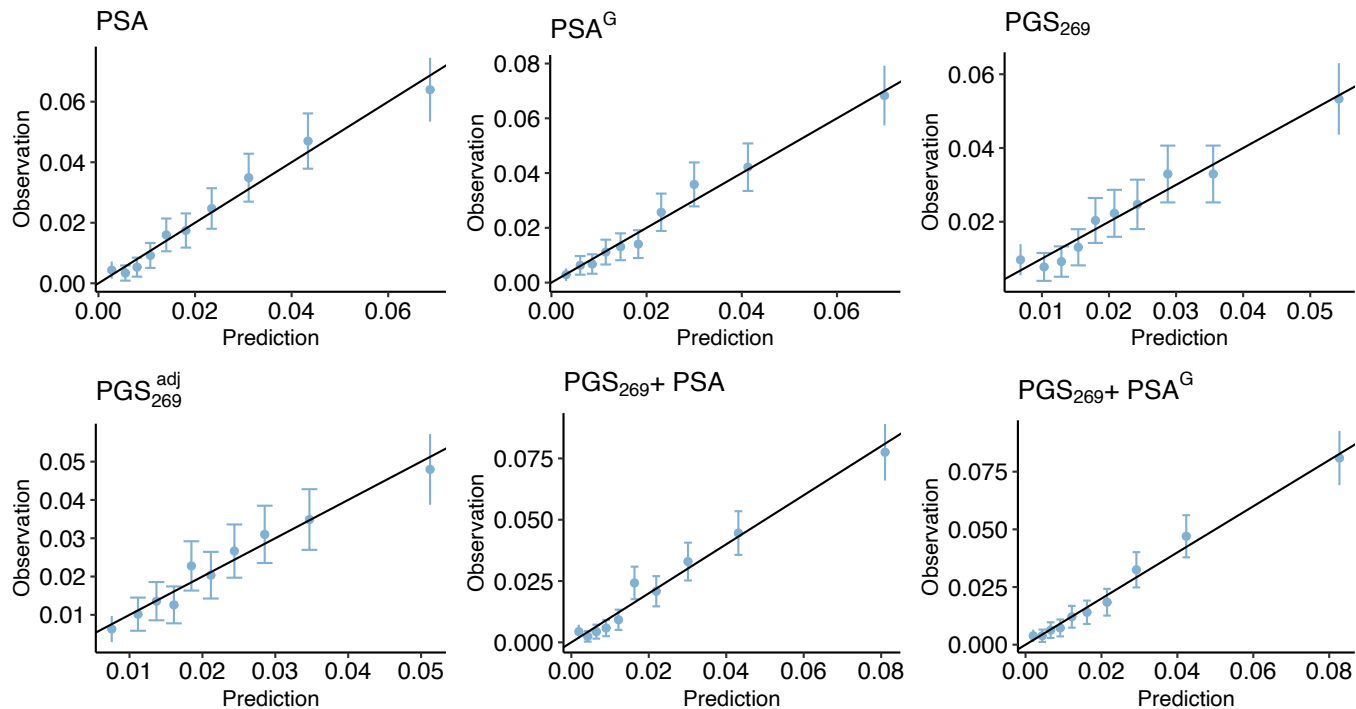


Supplementary Figure 5: Calibration plots show the concordance between observed and predicted values generated from logistic regression models for incident prostate cancer in the Selenium and Vitamin E Cancer Prevention Trial (SELECT). The pooled analysis includes 572 prostate cancer cases and 23,667 controls. European ancestry (EUR $\geq$ 0.80) group includes 467 cases and 20,173 controls. Error bars show the 95% confidence intervals for the predictions within each bin.

SELECT: Prostate Cancer (Pooled)

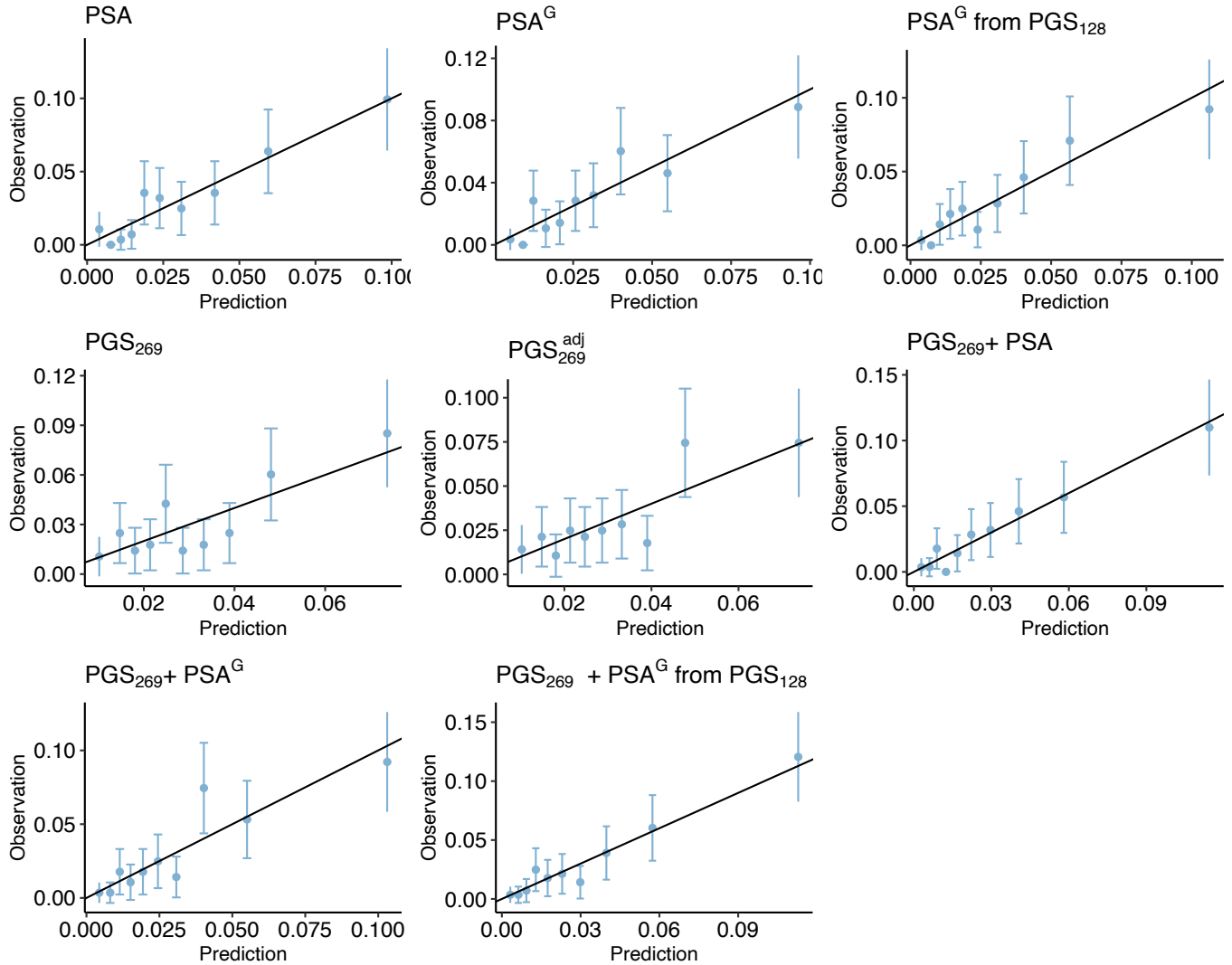


SELECT: Prostate Cancer (EUR)



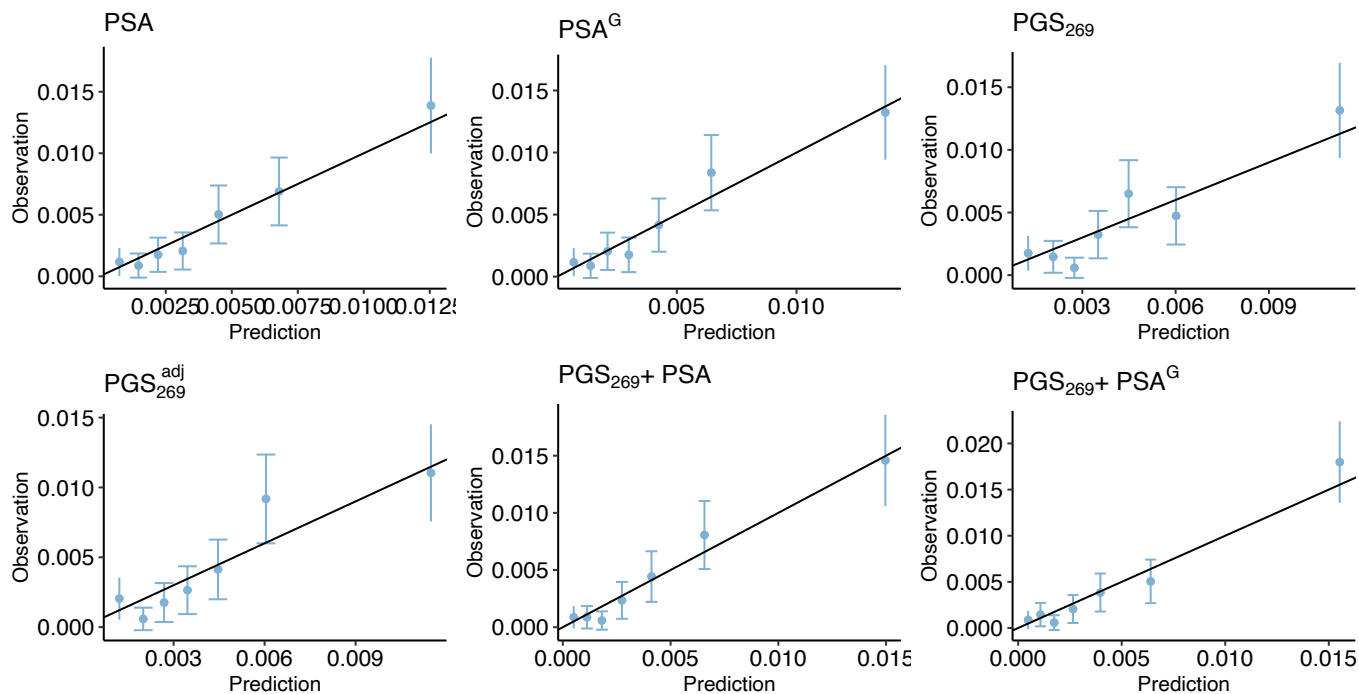
Supplementary Figure 6: Calibration plots show the concordance between observed and predicted values generated from logistic regression models for prostate cancer in the Selenium and Vitamin E Cancer Prevention Trial (SELECT). Pooled African ancestry group includes men of African ancestry ($AFR \geq 0.80$) and admixed African and European ancestry ($0.20 < AFR/EUR < 0.80$), for a total of 88 cases and 2733 controls. Error bars show the 95% confidence intervals for the predictions within each bin.

SELECT: Prostate Cancer (AFR pooled)

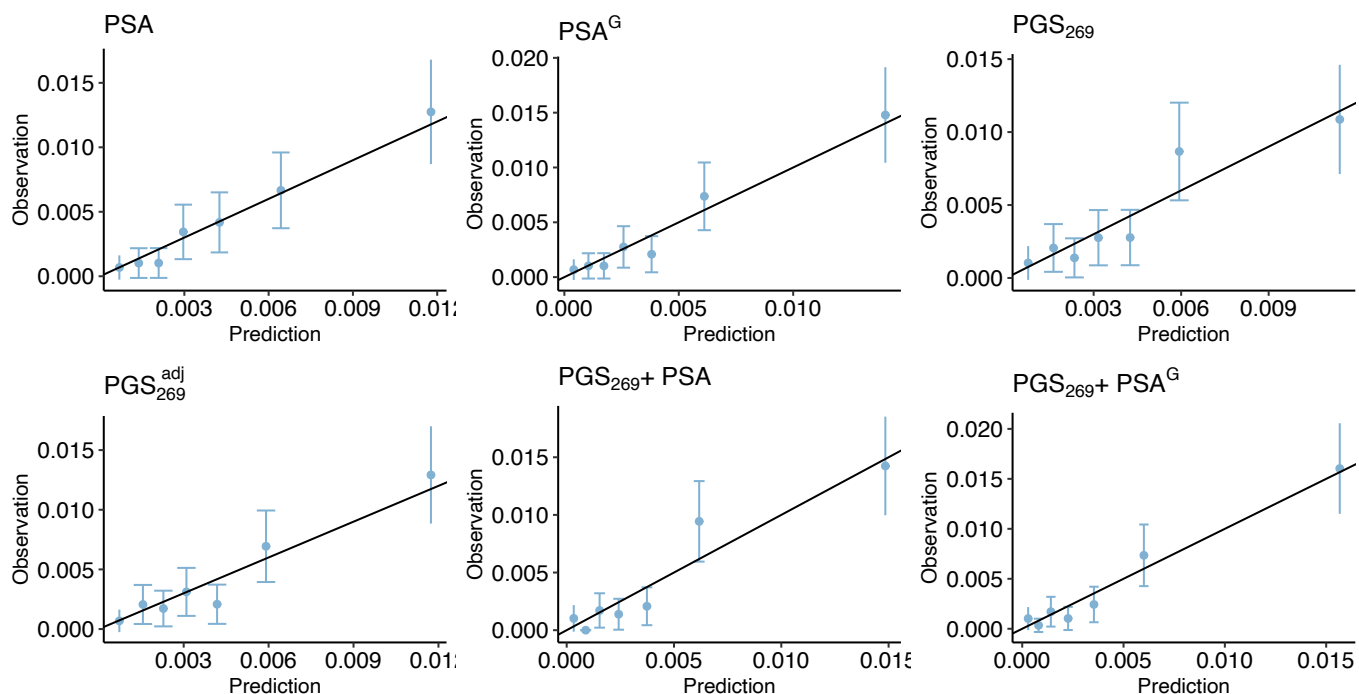


Supplementary Figure 7: Calibration plots show the concordance between observed and predicted values generated from logistic regression models for incident aggressive prostate cancer in the Selenium and Vitamin E Cancer Prevention Trial (SELECT). The pooled analysis included 106 cases and 23,667 controls. European ancestry (EUR ≥ 0.80) group includes 85 cases and 20,173 controls. Error bars show the 95% confidence intervals for the predictions within each bin.

SELECT: Aggressive Prostate Cancer (Pooled)

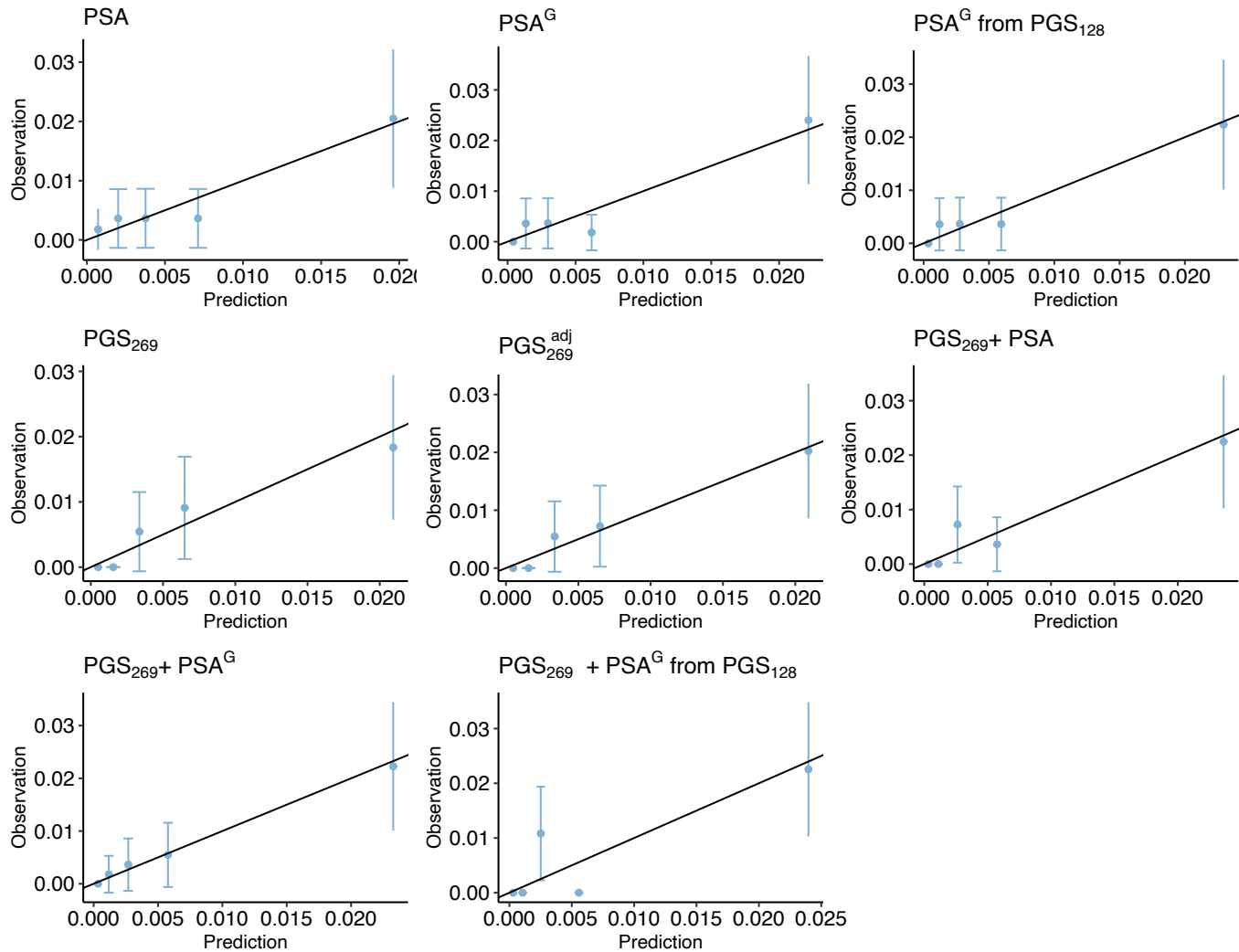


SELECT: Aggressive Prostate Cancer (EUR)



Supplementary Figure 8: Calibration plots show the concordance between observed and predicted values generated from logistic regression models for incident aggressive prostate cancer in the Selenium and Vitamin E Cancer Prevention Trial (SELECT). Pooled African ancestry subgroup includes men of African ancestry ($AFR \geq 0.80$) and admixed African and European ancestry ($0.20 < AFR/EUR < 0.80$), for a total of 18 cases and 2733 controls. Error bars show the 95% confidence intervals for the predictions within each bin. Error bars are absent for bins that had too few observations.

SELECT: Aggressive Prostate Cancer (AFR pooled)



Supplementary Table 1: Heritability (h^2) of PSA levels in men of European ancestry without prostate cancer. Estimates are compared between methods that use individual-level data and GWAS summary statistics, as well as between different approaches to modelling longitudinal PSA values. Multiple PSA measurements per individual were summarized as the median. The second approach involved fitting a linear mixed model to longitudinal PSA data and estimating the heritability of the individual-specific random intercept derived from this model.

Phenotype	Method	Genetic Relatedness Matrix Parameters				h²	(95% CI)
		Kinship	LD r²	INFO	(N _{SNP})		
UKB median log(PSA) n=26,491	GCTA	0.025	0.80	0.80	(2,109,931)	0.405	(0.353 - 0.456)
			0.80	Typed	(563,257)	0.372	(0.326 - 0.418)
	LDAK	0.025	0.80	0.80	(2,109,931)	0.302	(0.266 - 0.339)
			0.98	0.95	(2,629,389)	0.244	(0.213 - 0.276)
			0.98	Typed	(563,257)	0.295	(0.261 - 0.329)
			0.80	0.80	(2,109,931)	0.408	(0.359 - 0.457)
	GCTA	0.05	0.80	Typed	(563,257)	0.376	(0.332 - 0.420)
			0.80	0.80	(2,109,931)	0.296	(0.261 - 0.331)
UKB random intercept n=26,491	LDAK	0.05	0.98	0.95	(2,629,389)	0.239	(0.209 - 0.269)
			0.98	Typed	(563,257)	0.288	(0.256 - 0.320)
	GCTA	0.025	0.80	0.80	(2,109,931)	0.351	(0.300 - 0.402)
			0.80	Typed	(563,257)	0.327	(0.280 - 0.373)
	LDAK	0.025	0.80	0.80	(2,109,931)	0.270	(0.233 - 0.307)
			0.98	0.95	(2,629,389)	0.210	(0.179 - 0.242)
			0.98	Typed	(563,257)	0.255	(0.221 - 0.289)
			0.80	0.80	(2,109,931)	0.358	(0.309 - 0.407)
	GCTA	0.05	0.80	Typed	(563,257)	0.333	(0.289 - 0.377)
			0.80	0.80	(2,109,931)	0.259	(0.224 - 0.294)
	LDAK	0.05	0.98	0.95	(2,629,389)	0.207	(0.178 - 0.237)
			0.98	Typed	(563,257)	0.251	(0.220 - 0.283)
Summary Statistics	Method	Reference Panel		INFO	(N _{SNP})	h²	(95% CI)
		Variants	LD Dataset				
UKB median log(PSA) n=26,491	LDAK	HapMap3	UKB GBR	0.30	(1,127,342)	0.385	(0.310 - 0.460)
				0.30	(1,127,337) ¹	0.349	(0.275 - 0.424)
				0.95	(1,118,359) ¹	0.350	(0.275 - 0.425)
Meta-analysis log(PSA) n=85,824	HDL	HapMap3	UKB GBR	0.30	(1,029,876)	0.252	(0.207 - 0.298)
	LDSR	HapMap3	1000G EUR	0.30	(1,133,218)	0.206	(0.154 - 0.257)
	LDAK	HapMap3	UKB GBR	0.30	(1,168,859)	0.332	(0.307 - 0.357)
				0.30	(1,168,854) ¹	0.300	(0.287 - 0.311)
	HDL	HapMap3	UKB EUR	0.30	(1,029,876)	0.195	(0.157 - 0.233)
LDSR	HapMap3	1000G EUR	0.30	(1,136,374)	0.188	(0.151 - 0.225)	

¹ Excluding variants with large effect, using cutoff=0.01 for maximum variance explained

INFO Minimum imputation quality

HDL High-definition likelihood method, as described in Ning et al. (PMID: 32601477)

GBR British white individuals

LDSR LD score regression

Supplementary Table 2: Genome-wide association study (GWAS) of PSA levels in the UK Biobank (N=26,491). Genome-wide significant ($P < 5 \times 10^{-8}$) lead variants were identified using LD-based clumping at $r^2 < 0.01$ in ± 10 Mb windows. All GWAS p-values are two-sided and derived from linear regression models.

Region	Position (b37)	Nearest Gene	Variant ID	EA	OA	EAF	β^1	(SE)	P	P _{RI}
1p22.3	88197017	<i>PKN2-AS1</i>	rs12731909	C	T	0.484	0.041	(0.007)	9.12E-10	3.81E-09
2p21	43594483	<i>THADA</i>	rs79625619	T	A	0.100	-0.063	(0.011)	1.27E-08	3.48E-08
2p16.1	60762502	<i>BCL11A</i>	rs2556378	T	G	0.161	0.058	(0.009)	1.45E-10	3.56E-10
2p15	63277843	<i>OTX1</i>	rs58235267	G	C	0.484	0.038	(0.007)	1.50E-08	5.41E-07
3q27.3	186754957	<i>ST6GAL1</i>	rs3936289	C	T	0.242	0.041	(0.008)	1.58E-07	7.07E-09
5p15.33	1341101	<i>CLPTM1L</i>	rs31487	C	G	0.444	-0.064	(0.007)	1.78E-21	6.11E-17
6p21.32	32682812	<i>HLA-DQB1-AS1</i>	rs9275602	A	C	0.191	-0.048	(0.009)	1.83E-08	9.64E-07
6p21.1	43710381	<i>POLR1C</i>	rs10807290	C	T	0.475	0.045	(0.007)	2.21E-11	1.13E-07
7p15.2	27989768	<i>JAZF1</i>	rs739704	A	G	0.253	-0.043	(0.008)	2.02E-08	1.26E-04
8p21.2	23535219	<i>NKX3-1</i>	rs13262167	C	A	0.414	0.067	(0.007)	1.01E-22	1.26E-19
8q24.21	128318755	<i>CASC8 – PCAT1</i>	rs10107982	C	T	0.277	-0.053	(0.008)	1.23E-12	6.15E-09
8q24.21	128413305	<i>CASC8</i>	rs6983267	T	G	0.481	-0.054	(0.007)	8.70E-16	2.45E-14
10q11.22	51549496	<i>MSMB</i>	rs10993994	T	C	0.386	0.087	(0.007)	1.06E-36	4.87E-26
10q26.12	122633607	<i>WDR11</i>	rs7080550	G	C	0.365	0.049	(0.007)	1.54E-12	2.91E-10
10q26.12	123048008	<i>LINC01153</i>	rs10886900	G	A	0.231	0.103	(0.008)	1.75E-38	2.49E-32
10q26.13	123186164	<i>RN7SKP167</i>	rs201552570	C	CA	0.052	-0.118	(0.015)	7.02E-15	4.56E-13
10q26.13	123349324	<i>FGFR2</i>	rs45631563	T	A	0.046	0.090	(0.016)	2.62E-08	3.30E-05
11p13	34770077	<i>EHF – APIP</i>	rs10742324	C	G	0.291	-0.054	(0.007)	3.54E-13	8.78E-10
12q24.21	115094260	<i>TBX3</i>	rs11067228	G	A	0.451	-0.045	(0.007)	1.65E-11	2.46E-09
13q14.3	51130374	<i>DLEU1</i>	rs35681675	TC	T	0.389	0.042	(0.007)	1.37E-09	1.29E-08
17q12	36097775	<i>HNF1B</i>	rs11263761	G	A	0.481	-0.062	(0.007)	4.32E-20	8.87E-15
18q23	76765837	<i>SALL3</i>	rs6506878	T	G	0.320	-0.041	(0.007)	1.35E-08	6.75E-07
19q13.33	51323947	<i>KLK1</i>	rs2659104	A	G	0.317	0.055	(0.007)	3.39E-14	9.62E-10
19q13.33	51340794	<i>KLK15</i>	rs2659053	A	G	0.394	0.082	(0.007)	5.38E-33	1.83E-27
19q13.33	51360768	<i>KLK3</i>	rs266877	A	G	0.048	-0.094	(0.016)	2.29E-09	3.49E-09
19q13.33	51361757	<i>KLK3</i>	rs17632542	C	T	0.077	-0.375	(0.012)	1.69E-202	4.16E-155
19q13.33	51399496	<i>KLKP1</i>	rs2659110	T	C	0.114	-0.076	(0.011)	6.39E-13	9.41E-15
20q11.21-q11.22	32127671	<i>CBFA2T2</i>	rs2150165	T	A	0.104	0.069	(0.011)	3.60E-10	4.72E-07
Xp22.11	24065653	<i>EIF2S3 – KLHL15</i>	rs12389566	T	C	0.331	0.033	(0.005)	1.73E-10	8.78E-08
Xq13.1	70117073	<i>TEX11</i>	rs186347618	T	A	0.368	0.039	(0.005)	7.89E-15	6.66E-13

¹ Per allele change in log(PSA)

Abbreviations:

EA Effect allele for which the change in log(PSA) is modelled

OA Other allele

EAF Effect allele frequency

P_{RI} P-value from the GWAS of individual-specific random intercepts estimated in

Supplementary Table 3: Association estimates for 128 index variants associated with PSA levels in the multi-ancestry meta-analysis (N=95,768).

Genome-wide significant ($P < 5 \times 10^{-8}$) index variants were selected from fixed-effects, inverse-variance weighted meta-analysis results generated by METAL using linkage disequilibrium (LD) clumping at $r^2 < 0.01$ within ± 10 Mb windows. Associations are compared between METAL (P_{METAL}), where heterogeneity is quantified using Cochran's Q statistic ($P_{\text{Het-Q}}$), and MR-MEGA (P_{MEGA}), an alternative approach to cross-ancestry meta-analysis that uses meta-regression to quantify heterogeneity due to ancestry ($P_{\text{Het-Anc}}$) separately from residual heterogeneity due to other factors ($P_{\text{Het-Res}}$). All p-values are two-sided.

Region	Position (b37)	Variant ID	Effect Allele	Other Allele	Fixed-effects Meta-analysis (METAL)					Meta-Regression (MR-MEGA)			New ²
					EAF	β^1	SE	P_{METAL}	$P_{\text{Het-Q}}$	P_{MEGA}	$P_{\text{Het-Anc}}$	$P_{\text{Het-Res}}$	
1p32.3	51237409	rs12569177	C	G	0.428	0.026	(0.004)	3.2E-13	0.89	3.5E-11	0.59	0.80	yes
1p22.3	88199778	rs12131120	T	A	0.493	0.033	(0.004)	1.6E-19	0.38	3.9E-18	0.12	0.36	no
1p13.2	112264274	rs2076591	C	T	0.216	0.032	(0.004)	2.6E-13	0.094	4.9E-12	0.10	0.77	yes
1q21.3	154868055	rs4845681	T	G	0.412	0.022	(0.004)	7.7E-09	0.15	5.3E-07	0.74	0.13	yes
1q25.3	184191716	rs12046452	C	T	0.622	0.021	(0.004)	9.0E-09	0.95	8.7E-07	0.95	0.19	yes
1q32.1	205632217	rs71152447	G	GGCCGAC AGCCCTTC TGCTGGCT CGGTGGG GCCCAGC	0.047	0.163	(0.024)	9.9E-12	0.27	1.2E-09	0.80	0.025	no
1q32.1	205636334	rs4951018	C	A	0.230	0.032	(0.004)	2.7E-13	0.52	2.5E-12	0.058	0.092	no
1q41	219694903	rs12034581	C	A	0.495	0.025	(0.004)	2.5E-12	0.074	3.5E-11	0.14	0.49	yes
1q41	219954267	rs6664688	G	A	0.216	0.025	(0.005)	3.9E-08	0.025	1.9E-07	0.084	1.2E-03	yes
2p24.2	18911674	rs12710685	G	C	0.105	0.033	(0.006)	2.3E-08	0.26	1.7E-06	0.73	0.57	yes
2p24.1	20880833	rs10193919	T	C	0.345	0.031	(0.004)	1.5E-15	0.84	3.7E-13	0.95	0.25	yes
2p23.3	25463871	rs734693	T	C	0.715	0.023	(0.004)	3.9E-08	0.054	7.4E-08	0.040	0.37	yes
2p21	43072828	rs1123695	G	C	0.659	0.031	(0.004)	3.3E-16	0.80	6.7E-14	0.89	0.81	yes
2p21	43618819	rs11899863	C	T	0.902	0.045	(0.006)	1.7E-13	0.48	2.2E-11	0.56	0.078	yes
2p16.1	60759747	rs2556375	G	T	0.176	0.057	(0.005)	1.8E-32	0.33	5.2E-30	0.54	0.42	no
2p15	63277843	rs58235267	G	C	0.482	0.026	(0.004)	4.9E-13	0.014	1.1E-12	0.016	0.57	yes
2p13.2	72059504	rs11679946	T	C	0.674	0.022	(0.004)	2.6E-08	0.23	1.3E-06	0.79	0.35	yes
2q33.1	198929083	rs34388051	A	G	0.671	0.022	(0.004)	2.2E-08	0.62	1.4E-06	0.65	0.52	yes
3q13.2	113290793	rs4682495	A	C	0.573	0.021	(0.004)	2.9E-09	0.12	1.6E-07	0.40	0.081	no
3q21.3	128067275	rs11709611	C	T	0.120	0.036	(0.006)	2.0E-10	0.97	2.7E-08	0.98	0.90	yes
3q23	141115219	rs1582874	C	T	0.442	0.030	(0.004)	1.0E-16	0.36	1.1E-14	0.37	0.79	no

3q25.33	160130592	rs10673842	TTATC	T	0.522	0.023	(0.004)	2.2E-08	0.11	2.9E-07	0.15	0.46	yes
3q27.2	185246981	rs4012714	A	G	0.579	0.025	(0.004)	1.1E-08	0.11	7.7E-08	0.11	0.81	yes
3q27.3	186746994	rs12629450	C	G	0.171	0.031	(0.005)	2.6E-10	0.65	2.2E-08	0.58	0.69	yes
3q28	189482770	rs6765473	T	C	0.881	0.037	(0.006)	3.2E-10	0.31	6.0E-09	0.23	0.73	yes
4p15.2	24410024	rs4276269	G	A	0.263	0.023	(0.004)	2.0E-08	0.91	1.5E-06	0.82	0.59	yes
4q31.22	146890261	rs9968429	G	A	0.370	0.032	(0.004)	6.3E-18	0.061	1.0E-16	0.056	0.29	no
4q32.1	157497921	rs13115840	A	G	0.355	0.031	(0.004)	4.3E-17	0.70	2.7E-14	0.86	0.56	no
5p15.33	1285974	rs7705526	A	C	0.331	0.023	(0.004)	1.2E-08	0.46	6.0E-07	0.47	0.97	no
5p15.33	1322087	rs401681	C	T	0.560	0.059	(0.004)	7.0E-54	0.47	1.5E-52	0.12	0.84	no
5q14.3	92052005	rs7732515	A	T	0.227	0.033	(0.004)	3.5E-14	0.52	5.3E-12	0.86	0.46	yes
5q35.2	172945918	rs889017	C	A	0.230	0.024	(0.004)	2.6E-08	0.081	1.3E-07	0.074	0.19	yes
6p22.3	15463139	rs926309	T	G	0.374	0.026	(0.004)	1.6E-12	0.81	1.4E-10	0.69	0.88	yes
6p22.3	16515154	rs236961	T	C	0.353	0.026	(0.004)	8.6E-12	0.10	7.6E-11	0.10	0.44	yes
6p22.1	29915061	rs2248162	C	T	0.666	0.025	(0.004)	3.6E-10	0.26	9.7E-09	0.24	0.36	yes
6p21.31	34212537	rs551980123	TG	T	0.043	0.069	(0.011)	1.6E-10	0.14	2.1E-08	0.91	0.14	yes
6p21.1	43711981	rs1535507	T	C	0.164	0.048	(0.005)	1.5E-22	0.063	1.4E-22	1.8E-03	0.044	no
6q22.33	129168057	rs73583119	A	T	0.929	0.193	(0.035)	3.5E-08	0.12	-	-	-	yes
7p15.3	20909622	rs204592	G	A	0.517	0.022	(0.004)	1.2E-09	0.24	1.9E-08	0.21	0.45	yes
7p15.3	21839896	rs6956349	T	C	0.427	0.021	(0.004)	8.6E-09	0.78	6.1E-07	0.67	0.56	yes
7p15.2	27281792	rs17437810	A	G	0.021	0.077	(0.013)	8.0E-09	0.98	8.5E-07	0.96	0.55	yes
7p15.2	27483166	rs10250340	A	G	0.321	0.023	(0.004)	2.0E-09	0.047	1.4E-08	0.073	0.030	yes
7p15.2	27975919	rs67152137	G	C	0.740	0.048	(0.004)	8.6E-31	0.29	1.9E-28	0.13	0.78	no
8p21.2	23437981	rs2928681	C	A	0.413	0.031	(0.004)	3.5E-18	0.10	5.7E-17	0.045	0.66	no
8p21.2	23529521	rs1160267	G	A	0.430	0.070	(0.004)	6.3E-83	0.89	9.6E-78	0.78	0.69	no
8q12.1	57138676	rs36112366	T	G	0.886	0.037	(0.006)	7.3E-11	0.73	6.9E-09	0.60	0.84	yes
8q12.1	57834357	rs4738555	C	T	0.434	0.031	(0.004)	3.2E-17	0.22	2.1E-16	0.028	0.76	no
8q21.13	81811566	8:81811566_CA_C	CA	C	0.590	0.024	(0.004)	7.6E-11	0.13	9.1E-10	0.090	0.54	yes
8q23.1	108849527	rs1494920	T	C	0.604	0.020	(0.004)	4.8E-08	0.84	1.7E-06	0.46	0.55	yes
8q24.21	127817460	rs7843726	G	C	0.145	0.030	(0.005)	1.7E-08	0.073	2.0E-07	0.14	0.24	yes
8q24.21	128093297	rs1016343	T	C	0.205	0.035	(0.004)	3.6E-15	0.67	9.2E-13	0.94	0.80	yes
8q24.21	128318755	rs10107982	T	C	0.728	0.046	(0.004)	4.1E-30	0.85	6.9E-27	0.98	0.25	no

8q24.21	128413305	rs6983267	G	T	0.512	0.051	(0.004)	2.6E-45	0.49	7.1E-43	0.45	0.31	no
9q22.32	99146751	rs7020681	C	T	0.214	0.027	(0.005)	1.4E-09	6.1E-03	8.2E-10	5.6E-03	0.74	yes
9q33.1	118258080	rs150402584	T	TG	0.129	0.035	(0.006)	9.0E-10	0.14	1.6E-08	0.17	0.37	yes
9q33.1	120475302	rs4986790	A	G	0.942	0.065	(0.008)	7.1E-17	0.51	6.7E-15	0.51	0.73	no
9q33.2	123643426	rs59482735	T	TAA	0.321	0.032	(0.005)	2.9E-12	0.23	2.2E-10	0.44	0.087	no
10p12.31	22363979	rs3011633	C	T	0.221	0.040	(0.004)	5.9E-20	0.71	1.1E-17	0.36	0.81	no
10p12.2	23398448	rs1857279	C	G	0.662	0.025	(0.004)	3.9E-11	0.90	5.3E-09	0.71	0.41	yes
10p12.1	28096754	rs2815506	A	G	0.804	0.036	(0.005)	4.9E-15	0.55	3.2E-13	0.50	0.44	no
10q11.23	51549496	rs10993994	T	C	0.402	0.086	(0.004)	7.3E-87	0.16	3.0E-84	0.20	0.68	no
10q25.2	111991733	rs562417881	G	GT	0.840	0.035	(0.006)	5.6E-09	0.21	2.5E-07	0.43	0.36	yes
10q26.12	122631067	rs9325569	A	G	0.340	0.051	(0.004)	9.9E-41	0.40	1.2E-38	0.39	0.72	no
10q26.12	123049264	rs10886902	C	T	0.231	0.099	(0.004)	8.2E-118	0.92	6.2E-116	0.83	0.58	no
10q26.13	123135200	rs10788173	C	T	0.403	0.021	(0.004)	2.9E-08	0.27	4.5E-07	0.19	0.86	yes
10q26.13	123185303	rs10749415	A	G	0.920	0.108	(0.008)	1.8E-45	0.72	1.7E-42	0.75	0.42	no
10q26.13	123349324	rs45631563	T	A	0.045	0.089	(0.009)	7.9E-23	0.28	4.5E-20	0.97	0.082	no
10q26.13	126737579	rs3012065	C	T	0.320	0.022	(0.004)	2.2E-08	0.70	1.6E-06	0.76	0.99	yes
11p15.5	197557	rs7103852	G	A	0.878	0.041	(0.007)	1.2E-09	0.86	7.2E-08	0.64	0.60	yes
11p13	34718279	rs553481604	G	GT	0.697	0.031	(0.005)	1.7E-11	0.59	5.4E-10	0.21	7.4E-03	no
11p13	34780936	rs10466455	C	T	0.397	0.038	(0.004)	8.0E-26	0.19	2.0E-23	0.20	0.80	no
11q13.5	76153279	rs58015965	G	A	0.688	0.021	(0.004)	4.0E-08	0.84	1.9E-06	0.49	0.78	yes
11q22.2	102396607	rs12285347	C	T	0.452	0.038	(0.004)	2.6E-25	0.17	5.5E-24	0.13	0.98	no
11q22.2	102438778	rs7129424	A	G	0.559	0.024	(0.004)	2.5E-11	0.42	1.8E-09	0.54	0.52	yes
12p13.31	9222286	rs1805664	T	C	0.334	0.022	(0.004)	9.2E-09	0.12	1.1E-07	0.18	0.96	yes
12q14.3	66393756	rs74097857	T	C	0.872	0.033	(0.006)	1.2E-09	0.75	8.7E-08	0.54	0.24	yes
12q21.31	84994000	rs61928422	T	C	0.169	0.027	(0.005)	1.1E-08	0.027	9.6E-09	0.015	0.27	yes
12q24.21	115099805	rs10774760	G	A	0.504	0.042	(0.004)	2.4E-30	0.98	3.3E-27	0.84	0.78	no
12q24.21	115155460	rs11067251	G	T	0.584	0.022	(0.004)	1.9E-09	0.10	1.4E-08	0.077	0.96	yes
12q24.23	118855432	rs1045542	G	A	0.907	0.047	(0.006)	1.2E-13	0.69	1.8E-11	0.76	0.47	yes
13q14.3	51087443	rs202346	A	C	0.253	0.044	(0.004)	1.8E-27	0.38	4.0E-26	0.025	0.53	no
13q14.3	51165912	rs12869529	A	G	0.960	0.064	(0.009)	9.4E-12	0.80	9.6E-10	0.69	0.031	yes
13q14.3	51445360	rs9563006	A	G	0.443	0.024	(0.004)	5.6E-11	0.81	1.9E-10	0.034	0.78	no

13q22.1	74055303	rs1361057	C	T	0.261	0.023	(0.004)	3.3E-08	0.30	1.6E-06	0.53	0.43	yes
13q32.1	95799006	rs61965887	A	G	0.062	0.059	(0.008)	3.7E-14	0.74	2.5E-12	0.51	0.57	yes
14q13.3	37240591	rs712329	G	A	0.432	0.021	(0.004)	2.0E-08	0.031	1.2E-07	0.083	0.22	yes
14q32.13	94838142	rs112635299	G	T	0.979	0.106	(0.013)	1.2E-15	0.26	3.4E-14	0.19	0.36	yes
14q32.13	95104745	rs72695000	C	T	0.825	0.054	(0.005)	7.4E-28	0.76	4.5E-26	0.19	0.12	no
15q22.31	66941399	rs8038722	G	A	0.499	0.020	(0.004)	3.2E-08	0.68	3.9E-06	1.00	0.65	yes
16p13.3	4318206	rs251739	G	A	0.506	0.033	(0.004)	6.6E-20	0.13	2.0E-17	0.46	0.13	no
16p13.13	11201428	rs9933507	C	T	0.430	0.023	(0.004)	3.8E-10	0.84	5.2E-08	0.90	0.74	yes
16q23.1	77507275	rs7206309	C	T	0.316	0.039	(0.004)	1.6E-22	0.53	3.5E-20	0.54	0.56	no
16q24.1	86554784	rs13334022	T	C	0.109	0.042	(0.006)	3.4E-11	0.17	5.7E-10	0.14	0.45	yes
17p13.3	1994071	rs3760230	C	G	0.433	0.020	(0.004)	2.8E-08	0.63	1.7E-06	0.58	0.56	yes
17p13.1	7571752	rs78378222	G	T	0.012	0.112	(0.018)	2.8E-10	0.90	3.6E-08	0.86	0.85	yes
17p13.1	7793367	rs34009884	C	CTG	0.104	0.035	(0.006)	1.1E-08	0.20	1.7E-07	0.26	0.29	yes
17p12	12320741	rs7219536	T	C	0.495	0.025	(0.004)	5.7E-12	0.23	2.0E-10	0.30	0.60	yes
17p12	12556260	rs9889266	C	A	0.574	0.023	(0.004)	8.9E-10	0.62	4.4E-08	0.65	0.97	yes
17q12	36099952	rs10908278	A	T	0.525	0.052	(0.004)	2.1E-46	0.017	2.8E-44	0.16	0.017	no
18q23	76777252	rs71279357	A	T	0.725	0.035	(0.005)	1.8E-12	0.80	1.3E-10	0.57	0.97	yes
19q12	32055024	rs11084590	C	T	0.691	0.035	(0.004)	3.4E-18	0.39	2.4E-16	0.48	0.91	no
19q13.32	46229711	rs6509234	G	T	0.822	0.028	(0.005)	7.7E-09	0.066	1.0E-07	0.18	0.28	yes
19q13.33	49206462	rs681343	T	C	0.483	0.020	(0.004)	4.4E-08	0.70	2.4E-06	0.65	0.70	yes
19q13.33	51225544	rs890863	G	A	0.656	0.023	(0.004)	1.1E-08	0.44	3.1E-07	0.43	0.22	yes
19q13.33	51323501	rs1054713	A	G	0.324	0.037	(0.004)	4.8E-22	5.9E-04	2.1E-22	8.7E-04	0.076	no
19q13.33	51340794	rs2659053	A	G	0.405	0.078	(0.004)	5.4E-94	0.035	2.3E-92	5.2E-03	0.031	no
19q13.33	51349841	rs113920094	C	T	0.007	0.144	(0.025)	6.5E-09	0.072	3.4E-08	0.076	0.98	yes
19q13.33	51360398	rs374546878	GA	G	0.762	0.165	(0.023)	1.7E-12	0.12	-	-	-	yes
19q13.33	51361757	rs17632542	T	C	0.924	0.368	(0.007)	3.2e-638	0.21	7.0e-641	2.8E-15	4.4E-09	no
19q13.33	51365466	rs2735837	G	A	0.871	0.098	(0.006)	7.2E-58	1.5E-12	6.7E-67	3.6E-12	0.51	no
19q13.33	51373744	rs12983994	T	C	0.050	0.071	(0.008)	1.1E-17	1.3E-03	3.2E-19	2.0E-04	0.32	no
19q13.33	51378275	rs112103380	C	G	0.008	0.212	(0.024)	1.7E-18	0.89	5.3E-16	0.88	0.38	yes
19q13.33	51383072	rs198978	G	T	0.642	0.044	(0.004)	8.4E-31	1.5E-03	5.1E-30	0.034	0.077	yes
19q13.41	51421334	rs141135092	C	G	0.976	0.091	(0.015)	1.2E-09	0.11	1.9E-09	0.025	0.43	yes

19q13.41	51441425	rs80122351	G	T	0.804	0.030	(0.005)	1.2E-10	0.37	5.2E-09	0.56	7.5E-03	no
20q11.21	31950845	rs291671	G	A	0.114	0.053	(0.006)	1.2E-18	0.23	1.3E-16	0.31	3.1E-03	yes
21q22.2	40289167	rs2836750	T	G	0.401	0.027	(0.004)	1.6E-12	0.46	4.3E-11	0.22	0.97	yes
22q13.31	45996298	rs13268	A	G	0.976	0.080	(0.013)	1.6E-10	0.45	1.4E-08	0.69	0.43	yes
Xp22.31	8912815	rs112062538	C	T	0.261	0.029	(0.003)	4.7E-19	0.57	5.8E-18	0.10	0.71	yes
Xp22.2	16844831	rs62586587	G	A	0.614	0.031	(0.003)	3.6E-25	0.56	1.9E-23	0.054	0.027	no
Xp22.13	17831188	rs200615037	TTG	T	0.950	0.066	(0.007)	3.5E-22	0.87	2.8E-20	0.34	0.021	no
Xp22.11	24109619	rs7065158	A	G	0.311	0.036	(0.003)	1.1E-29	0.080	1.6E-27	0.099	0.25	no
Xp11.22	51242364	rs5987424	A	G	0.384	0.017	(0.003)	2.1E-08	0.16	3.4E-07	0.15	0.41	yes
Xp11.21	55936822	rs10855058	A	G	0.322	0.019	(0.003)	7.6E-09	0.054	2.5E-08	0.048	0.20	yes
Xq13.1	68996186	rs2520386	G	A	0.735	0.023	(0.003)	4.2E-11	0.64	1.3E-09	0.18	0.50	yes
Xq13.1	70125103	rs62608084	A	G	0.334	0.032	(0.003)	1.7E-24	0.43	4.8E-25	3.8E-03	0.089	yes
Xq26.2	132935739	rs4829762	T	C	0.704	0.024	(0.003)	5.9E-12	0.59	3.7E-10	0.35	0.90	yes
Xq26.3	133703924	rs5930651	T	C	0.665	0.017	(0.003)	1.0E-08	0.62	4.3E-07	0.43	0.99	yes

¹ Per allele change in log(PSA)

² Variants that were independent of previously reported PSA associations at LD $r^2 < 0.01$ within ± 10 Mb were considered novel

Abbreviations:

EAF Effect allele frequency

Note: MR-MEGA results are not available for variants that were present in too few studies

Supplementary Table 4: Population-specific association estimates for 128 index variants associated with PSA in the multi-ancestry meta-analysis (N=95,768). For each variant, effect sizes (β) and corresponding two-sided p-values are reported from an invese-variance-weighted fixed-effects meta-analysis performed within each ancestry group using METAL.

Region	Position (b37)	Variant ID	Effect Allele	Other Allele	EUR (N=85,824)			AFR (N=3,509)			HIS/LAT (N=3,098)			EAS (N=3,337)			New ²
					EAF	β^1	P _{METAL}	EAF	Effect	P _{METAL}	EAF	β^1	P _{METAL}	EAF	β^1	P _{METAL}	
1p32.3	51237409	rs12569177	C	G	0.431	0.027	2.78E-12	0.565	0.023	0.21	0.362	0.036	0.088	0.215	0.011	0.62	yes
1p22.3	88199778	rs12131120	T	A	0.478	0.033	2.13E-18	0.862	0.018	0.50	0.565	0.025	0.24	0.923	0.089	0.011	no
1p13.2	112264274	rs2076591	C	T	0.207	0.028	1.45E-09	0.398	0.050	8.07E-03	0.177	0.064	0.019	0.184	0.078	1.58E-03	yes
1q21.3	154868055	rs4845681	T	G	0.393	0.023	1.84E-09	0.533	0.014	0.45	0.535	-0.024	0.24	0.852	0.023	0.39	yes
1q25.3	184191716	rs12046452	C	T	0.622	0.021	4.05E-08	0.797	0.026	0.26	0.639	0.030	0.17	0.503	0.013	0.50	yes
1q32.1	205632217	rs71152447	G	GGCCGACA GCCCTTCT GCTGGCTC GGTGGGG CCCAGC	0.013	0.112	5.05E-03	0.010	0.071	0.65	0.051	0.228	3.42E-06	0.078	0.176	5.46E-06	no
1q32.1	205636334	rs4951018	C	A	0.224	0.033	5.03E-13	0.132	0.007	0.82	0.321	0.036	0.099	0.340	0.008	0.70	no
1q41	219694903	rs12034581	C	A	0.477	0.025	6.82E-11	0.821	0.013	0.60	0.622	0.005	0.80	0.655	0.073	2.49E-04	yes
1q41	219954267	rs6664688	G	A	0.185	0.019	7.72E-05	0.393	0.041	0.028	0.277	0.073	1.36E-03	0.454	0.057	2.89E-03	yes
2p24.2	18911674	rs12710685	G	C	0.098	0.037	6.92E-09	0.135	0.008	0.76	0.118	-0.019	0.55	0.178	0.026	0.31	yes
2p24.1	20880833	rs10193919	T	C	0.347	0.031	2.07E-14	0.118	0.010	0.73	0.327	0.043	0.047	0.437	0.029	0.13	yes
2p23.3	25463871	rs734693	T	C	0.745	0.023	2.68E-07	0.504	-0.015	0.42	0.691	0.059	8.65E-03	0.352	0.042	0.041	yes
2p21	43072828	rs1123695	G	C	0.662	0.030	4.07E-14	0.824	0.031	0.19	0.725	0.048	0.036	0.442	0.043	0.026	yes
2p21	43618819	rs11899863	C	T	0.900	0.044	6.10E-12	0.910	0.075	0.021	0.935	0.070	0.086	0.995	-0.097	0.46	yes
2p16.1	60759747	rs2556375	G	T	0.172	0.058	8.88E-30	0.172	0.058	0.020	0.221	0.080	1.36E-03	0.221	0.019	0.43	no
2p15	63277843	rs58235267	G	C	0.476	0.029	6.68E-14	0.453	-0.022	0.24	0.512	-0.009	0.67	0.679	0.045	0.030	yes
2p13.2	72059504	rs11679946	T	C	0.680	0.022	4.67E-08	0.764	0.024	0.28	0.718	-0.021	0.37	0.431	0.040	0.039	yes
2q33.1	198929083	rs34388051	A	G	0.679	0.021	3.04E-07	0.820	0.042	0.10	0.594	0.008	0.71	0.470	0.038	0.052	yes
3q13.2	113290793	rs4682495	A	C	0.580	0.024	5.95E-10	0.571	0.012	0.52	0.612	-0.024	0.24	0.339	0.008	0.69	no
3q21.3	128067275	rs11709611	C	T	0.116	0.036	1.25E-09	0.192	0.036	0.12	0.109	0.042	0.19	0.011	-0.013	0.90	yes
3q23	141115219	rs1582874	C	T	0.440	0.031	2.00E-16	0.796	0.042	0.063	0.405	0.013	0.52	0.233	-0.003	0.90	no
3q25.33	160130592	rs10673842	TTATC	T	0.530	0.025	2.41E-08	0.579	-0.019	0.37	0.460	0.048	0.028	0.271	0.001	0.97	yes
3q27.2	185246981	rs4012714	A	G	0.574	0.028	8.53E-10	0.560	-0.018	0.43	0.589	0.016	0.51	0.730	-0.009	0.73	yes

3q27.3	186746994	rs12629450	C	G	0.169	0.032	3.92E-10	0.139	0.020	0.48	0.185	0.034	0.23	0.231	0.003	0.91	yes
3q28	189482770	rs6765473	T	C	0.881	0.034	9.06E-09	0.967	0.117	0.040	0.845	0.070	0.017	0.986	0.086	0.45	yes
4p15.2	24410024	rs4276269	G	A	0.265	0.023	8.32E-08	0.255	0.010	0.65	0.255	0.031	0.19	0.222	0.028	0.22	yes
4q31.22	146890261	rs9968429	G	A	0.361	0.030	2.25E-14	0.438	0.078	2.49E-05	0.358	0.014	0.51	0.506	0.039	0.037	no
4q32.1	157497921	rs13115840	A	G	0.355	0.031	3.01E-15	0.172	0.051	0.040	0.363	0.013	0.54	0.457	0.035	0.063	no
5p15.33	1285974	rs7705526	A	C	0.334	0.024	5.30E-08	0.200	-0.008	0.74	0.309	0.023	0.30	0.386	0.045	0.052	no
5p15.33	1322087	rs401681	C	T	0.562	0.059	2.19E-49	0.417	0.078	2.35E-05	0.581	0.053	9.58E-03	0.672	0.033	0.13	no
5q14.3	92052005	rs7732515	A	T	0.224	0.034	2.45E-13	0.331	0.045	0.023	0.184	0.004	0.89	0.020	0.099	0.23	yes
5q35.2	172945918	rs889017	C	A	0.213	0.022	1.59E-06	0.550	0.020	0.28	0.189	0.029	0.27	0.162	0.091	5.38E-04	yes
6p22.3	15463139	rs926309	T	G	0.385	0.027	4.98E-12	0.275	0.037	0.080	0.290	0.012	0.60	0.187	0.014	0.56	yes
6p22.3	16515154	rs236961	T	C	0.347	0.028	5.18E-12	0.415	-0.020	0.29	0.442	0.025	0.23	0.367	0.035	0.079	yes
6p22.1	29915061	rs2248162	C	T	0.659	0.025	1.14E-09	0.700	0.022	0.27	0.782	0.042	0.092	0.956	-0.061	0.19	yes
6p21.31	34212537	rs551980123	TG	T	0.044	0.067	8.96E-10	0.023	0.017	0.81	0.019	0.240	2.96E-03	0.015	0.004	0.97	yes
6p21.1	43711981	rs1535507	T	C	0.156	0.051	6.93E-22	0.067	-0.016	0.66	0.155	-0.005	0.85	0.325	0.059	4.24E-03	no
6q22.33	129168057	rs73583119	A	T	6E-04	-	-	0.926	0.181	3.98E-07	0.995	0.452	7.66E-03	1E-04	-	-	yes
7p15.3	20909622	rs204592	G	A	0.532	0.020	1.47E-07	0.269	0.027	0.19	0.493	0.041	0.041	0.350	0.056	4.82E-03	yes
7p15.3	21839896	rs6956349	T	C	0.438	0.021	4.41E-08	0.117	0.018	0.53	0.298	0.029	0.18	0.027	0.077	0.18	yes
7p15.2	27281792	rs17437810	A	G	0.021	0.077	1.21E-08	0.006	0.045	0.80	0.015	0.086	0.33	NA	NA	NA	yes
7p15.2	27483166	rs10250340	A	G	0.323	0.024	3.00E-09	0.353	0.053	6.51E-03	0.284	-0.011	0.63	0.277	-0.017	0.44	yes
7p15.2	27975919	rs67152137	G	C	0.764	0.049	2.56E-28	0.707	0.011	0.60	0.601	0.051	0.012	0.154	0.063	0.017	no
8p21.2	23437981	rs2928681	C	A	0.418	0.033	4.82E-18	0.443	-0.009	0.64	0.338	0.012	0.59	0.282	0.048	0.024	no
8p21.2	23529521	rs1160267	G	A	0.424	0.069	2.53E-72	0.696	0.085	2.55E-05	0.448	0.070	9.02E-04	0.315	0.073	4.22E-04	no
8q12.1	57138676	rs36112366	T	G	0.884	0.038	2.64E-10	0.971	0.028	0.61	0.894	0.058	0.080	0.914	0.005	0.89	yes
8q12.1	57834357	rs4738555	C	T	0.445	0.032	1.28E-16	0.325	0.045	0.023	0.401	0.021	0.31	0.223	-0.013	0.56	no
8q21.13	81811566	8:81811566_ CA_C	CA	C	0.588	0.022	2.25E-08	0.732	0.059	4.97E-03	0.468	0.015	0.45	0.619	0.053	6.25E-03	yes
8q23.1	108849527	rs1494920	T	C	0.619	0.019	1.02E-06	0.513	0.035	0.059	0.569	0.027	0.20	0.372	0.024	0.23	yes
8q24.21	127817460	rs7843726	G	C	0.139	0.031	2.98E-08	0.036	-0.097	0.074	0.126	0.063	0.047	0.261	0.015	0.50	yes
8q24.21	128093297	rs1016343	T	C	0.201	0.035	4.99E-14	0.215	0.047	0.036	0.155	0.004	0.89	0.289	0.032	0.12	yes
8q24.21	128318755	rs10107982	T	C	0.720	0.046	5.80E-28	0.874	0.055	0.049	0.790	0.031	0.22	0.908	0.066	0.048	no
8q24.21	128413305	rs6983267	G	T	0.508	0.052	1.49E-42	0.865	0.037	0.17	0.569	0.071	5.77E-04	0.384	0.030	0.12	no

9q22.32	99146751	rs7020681	C	T	0.196	0.032	1.93E-11	0.543	-0.026	0.17	0.166	0.002	0.95	0.041	-0.050	0.30	yes
9q33.1	118258080	rs150402584	T	TG	0.100	0.037	3.91E-09	0.163	0.003	0.90	0.133	-0.014	0.63	0.381	0.054	5.67E-03	yes
9q33.1	120475302	rs4986790	A	G	0.942	0.068	4.77E-17	0.925	0.015	0.66	0.958	0.053	0.29	0.992	0.110	0.37	no
9q33.2	123643426	rs59482735	T	TAA	0.326	0.029	1.86E-09	0.250	0.038	0.14	0.296	0.073	2.22E-03	0.263	0.057	0.026	no
10p12.31	22363979	rs3011633	C	T	0.224	0.041	1.81E-19	0.061	0.018	0.65	0.212	0.016	0.52	0.198	0.033	0.18	no
10p12.2	23398448	rs1857279	C	G	0.672	0.024	1.70E-09	0.708	0.028	0.18	0.639	0.041	0.054	0.393	0.026	0.18	yes
10p12.1	28096754	rs2815506	A	G	0.823	0.036	2.13E-13	0.718	0.059	3.78E-03	0.810	0.021	0.43	0.596	0.023	0.24	no
10q11.23	51549496	rs10993994	T	C	0.391	0.085	2.66E-76	0.600	0.065	3.12E-03	0.377	0.077	6.52E-04	0.493	0.132	6.74E-09	no
10q25.2	111991733	rs562417881	G	GT	0.856	0.038	3.19E-09	0.934	0.082	0.094	0.712	-0.004	0.87	0.706	0.013	0.61	yes
10q26.12	122631067	rs9325569	A	G	0.339	0.053	4.42E-40	0.147	0.014	0.59	0.420	0.040	0.049	0.413	0.038	0.051	no
10q26.12	123049264	rs10886902	C	T	0.231	0.099	6.5E-110	0.064	0.100	9.36E-03	0.247	0.087	2.33E-04	0.264	0.109	6.06E-07	no
10q26.13	123135200	rs10788173	C	T	0.397	0.023	9.00E-09	0.580	0.017	0.43	0.407	0.003	0.88	0.391	-0.015	0.47	yes
10q26.13	123185303	rs10749415	A	G	0.944	0.104	2.93E-34	0.789	0.130	1.02E-08	0.850	0.115	6.13E-05	0.969	0.130	0.049	no
10q26.13	123349324	rs45631563	T	A	0.046	0.089	2.66E-22	0.013	0.120	0.20	0.042	0.022	0.68	0.009	0.293	0.038	no
10q26.13	126737579	rs3012065	C	T	0.321	0.022	1.28E-07	0.331	0.024	0.24	0.319	0.004	0.85	0.262	0.041	0.066	yes
11p15.5	197557	rs7103852	G	A	0.914	0.041	2.10E-08	0.597	0.043	0.029	0.912	0.022	0.56	0.959	0.093	0.22	yes
11p13	34718279	rs553481604	G	GT	0.703	0.030	1.27E-09	0.741	0.032	0.20	0.626	0.061	7.30E-03	0.612	0.022	0.35	no
11p13	34780936	rs10466455	C	T	0.400	0.040	9.24E-26	0.387	0.004	0.84	0.305	0.024	0.27	0.380	0.023	0.24	no
11q13.5	76153279	rs58015965	G	A	0.679	0.021	1.18E-07	0.785	0.011	0.61	0.771	0.036	0.15	0.871	0.005	0.85	yes
11q22.2	102396607	rs12285347	C	T	0.455	0.039	6.15E-25	0.552	-0.002	0.90	0.373	0.050	0.016	0.095	0.053	0.12	no
11q22.2	102438778	rs7129424	A	G	0.547	0.023	3.16E-09	0.735	0.031	0.13	0.560	0.050	0.015	0.779	0.046	0.043	yes
12p13.31	9222286	rs1805664	T	C	0.341	0.020	9.17E-07	0.202	0.044	0.056	0.340	0.057	7.18E-03	0.089	0.067	0.047	yes
12q14.3	66393756	rs74097857	T	C	0.870	0.033	3.59E-09	0.957	0.065	0.16	0.912	0.012	0.74	0.995	0.126	0.41	yes
12q21.31	84994000	rs61928422	T	C	0.166	0.027	1.50E-07	0.203	0.005	0.84	0.224	0.006	0.80	0.151	0.100	1.76E-04	yes
12q24.21	115099805	rs10774760	G	A	0.498	0.042	1.50E-27	0.811	0.034	0.15	0.477	0.039	0.057	0.462	0.047	0.017	no
12q24.21	115155460	rs11067251	G	T	0.573	0.022	6.83E-09	0.816	-0.019	0.43	0.565	0.019	0.37	0.864	0.074	8.65E-03	yes
12q24.23	118855432	rs1045542	G	A	0.907	0.049	7.35E-14	0.981	-0.003	0.97	0.887	0.023	0.48	0.991	-0.027	0.85	yes
13q14.3	51087443	rs202346	A	C	0.254	0.042	2.07E-22	0.296	0.070	4.36E-04	0.233	0.051	0.033	0.146	0.073	6.78E-03	no
13q14.3	51165912	rs12869529	A	G	0.961	0.065	5.11E-11	0.944	0.079	0.053	0.953	0.032	0.51	0.998	-0.110	0.67	yes
13q14.3	51445360	rs9563006	A	G	0.443	0.024	2.58E-10	0.506	0.012	0.53	0.436	0.027	0.19	0.054	0.054	0.21	no
13q22.1	74055303	rs1361057	C	T	0.254	0.022	6.42E-07	0.225	0.029	0.20	0.249	-0.003	0.89	0.430	0.052	6.87E-03	yes

13q32.1	95799006	rs61965887	A	G	0.063	0.060	1.94E-14	0.016	0.010	0.90	0.035	0.035	0.53	0.004	-0.114	0.58	yes
14q13.3	37240591	rs712329	G	A	0.444	0.020	1.69E-07	0.324	0.010	0.60	0.329	0.002	0.92	0.138	0.101	4.41E-04	yes
14q32.13	94838142	rs112635299	G	T	0.979	0.103	7.78E-15	0.997	0.423	0.076	0.990	0.211	0.056	8E-04	-	-	yes
14q32.13	95104745	rs72695000	C	T	0.821	0.054	4.10E-27	0.943	0.030	0.46	0.887	0.067	0.033	0.982	-0.011	0.89	no
15q22.31	66941399	rs8038722	G	A	0.502	0.019	3.55E-07	0.337	0.016	0.42	0.465	0.044	0.032	0.632	0.017	0.39	yes
16p13.3	4318206	rs251739	G	A	0.506	0.033	2.67E-17	0.358	0.048	0.013	0.488	0.063	1.86E-03	0.719	-0.006	0.81	no
16p13.13	11201428	rs9933507	C	T	0.431	0.022	6.58E-09	0.519	0.026	0.16	0.374	0.015	0.46	0.344	0.039	0.052	yes
16q23.1	77507275	rs7206309	C	T	0.286	0.041	5.52E-22	0.445	0.018	0.35	0.480	0.034	0.093	0.761	0.021	0.36	no
16q24.1	86554784	rs13334022	T	C	0.089	0.039	1.04E-08	0.307	0.076	2.11E-04	0.097	0.043	0.20	0.048	-0.031	0.54	yes
17p13.3	1994071	rs3760230	C	G	0.423	0.020	3.79E-07	0.518	0.021	0.27	0.363	0.012	0.56	0.725	0.047	0.030	yes
17p13.1	7571752	rs78378222	G	T	0.012	0.112	4.08E-10	0.001	-	-	0.004	0.133	0.44	8E-04	-	-	yes
17p13.1	7793367	rs34009884	C	CTG	0.106	0.038	1.49E-09	0.025	-0.056	0.37	0.057	-0.029	0.52	0.011	-0.035	0.79	yes
17p12	12320741	rs7219536	T	C	0.509	0.024	3.05E-10	0.262	0.048	0.023	0.461	0.055	7.92E-03	0.094	-0.006	0.84	yes
17p12	12556260	rs9889266	C	A	0.590	0.024	8.26E-10	0.489	0.027	0.14	0.430	0.011	0.61	0.381	0.000	0.98	yes
17q12	36099952	rs10908278	A	T	0.513	0.051	9.85E-42	0.688	0.008	0.71	0.552	0.102	8.41E-07	0.713	0.058	6.32E-03	no
18q23	76777252	rs71279357	A	T	0.729	0.035	1.31E-11	0.769	0.012	0.64	0.733	0.047	0.062	0.602	0.031	0.20	yes
19q12	32055024	rs11084590	C	T	0.682	0.036	6.87E-19	0.894	-0.013	0.68	0.775	0.020	0.41	0.926	0.020	0.60	no
19q13.32	46229711	rs6509234	G	T	0.817	0.029	1.18E-08	0.940	0.056	0.18	0.866	0.060	0.047	0.897	-0.050	0.13	yes
19q13.33	49206462	rs681343	T	C	0.488	0.019	5.94E-07	0.489	0.036	0.051	0.380	0.033	0.11	0.024	-0.008	0.90	yes
19q13.33	51225544	rs890863	G	A	0.663	0.023	3.92E-08	0.879	0.062	0.043	0.632	0.001	0.96	0.389	0.026	0.22	yes
19q13.33	51323501	rs1054713	A	G	0.330	0.040	1.38E-22	0.256	0.003	0.90	0.275	0.070	2.37E-03	0.226	-0.046	0.050	no
19q13.33	51340794	rs2659053	A	G	0.391	0.082	4.35E-92	0.449	0.042	0.026	0.547	0.049	0.018	0.615	0.046	0.049	no
19q13.33	51349841	rs113920094	C	T	0.007	0.144	1.28E-08	0.002	1.008	0.011	0.009	0.038	0.79	0.001	-	-	yes
19q13.33	51360398	rs374546878	GA	G	0.999	0.150	0.17	0.988	-0.089	0.42	0.992	0.215	0.082	0.728	0.177	1.58E-12	yes
19q13.33	51361757	rs17632542	T	C	0.923	0.366	1.1E-605	0.982	0.341	3.30E-06	0.954	0.463	3.83E-22	0.994	0.267	0.083	no
19q13.33	51365466	rs2735837	G	A	0.915	0.080	5.26E-31	0.830	0.074	3.20E-03	0.827	0.158	3.13E-09	0.579	0.227	4.73E-32	no
19q13.33	51373744	rs12983994	T	C	0.048	0.069	6.53E-15	0.071	0.015	0.68	0.046	0.030	0.54	0.056	0.216	1.39E-07	no
19q13.33	51378275	rs112103380	C	G	0.008	0.210	7.27E-18	0.002	0.244	0.49	0.005	0.299	0.10	7E-04	-	-	yes
19q13.33	51383072	rs198978	G	T	0.650	0.040	1.01E-23	0.362	0.045	0.020	0.646	0.108	4.47E-07	0.759	0.095	1.64E-05	yes
19q13.41	51421334	rs141135092	C	G	0.976	0.091	1.67E-09	0.995	-0.341	0.092	0.984	0.211	0.042	0.996	-0.013	0.95	yes
19q13.41	51441425	rs80122351	G	T	0.800	0.031	6.08E-11	0.938	0.016	0.70	0.863	-0.002	0.95	0.989	0.194	0.11	no

20q11.21	31950845	rs291671	G	A	0.100	0.049	4.46E-14	0.048	0.093	0.028	0.077	0.046	0.23	0.299	0.089	2.04E-05	yes
21q22.2	40289167	rs2836750	T	G	0.380	0.026	1.51E-10	0.524	0.053	5.27E-03	0.548	0.018	0.40	0.774	0.041	0.080	yes
22q13.31	45996298	rs13268	A	G	0.975	0.078	8.33E-10	0.992	0.173	0.13	0.986	0.158	0.099	0.999	-0.368	0.35	yes
Xp22.31	8912815	rs112062538	C	T	0.263	0.028	4.40E-17	0.271	0.034	0.041	0.185	0.052	7.38E-03	0.247	0.017	0.34	yes
Xp22.2	16844831	rs62586587	G	A	0.631	0.030	5.80E-21	0.544	0.051	7.33E-04	0.470	0.033	0.041	0.252	0.037	0.067	no
Xp22.13	17831188	rs200615037	TTG	T	0.954	0.068	3.69E-21	0.897	0.055	0.027	0.960	0.039	0.33	0.989	0.074	0.62	no
Xp22.11	24109619	rs7065158	A	G	0.318	0.037	6.75E-28	0.138	0.040	0.15	0.250	0.003	0.85	0.150	0.086	1.32E-03	no
Xp11.22	51242364	rs5987424	A	G	0.394	0.018	5.99E-09	0.287	0.010	0.54	0.267	-0.009	0.62	0.132	-0.029	0.30	yes
Xp11.21	55936822	rs10855058	A	G	0.317	0.017	7.13E-07	0.310	0.061	3.17E-04	0.448	0.028	0.071	0.304	0.004	0.83	yes
Xq13.1	68996186	rs2520386	G	A	0.730	0.022	8.09E-10	0.911	0.048	0.20	0.820	0.037	0.069	0.979	0.067	0.22	yes
Xq13.1	70125103	rs62608084	A	G	0.342	0.033	4.91E-25	0.195	0.017	0.35	0.212	0.009	0.64	0.019	0.076	0.20	yes
Xq26.2	132935739	rs4829762	T	C	0.725	0.025	1.63E-11	0.522	0.026	0.092	0.795	0.007	0.73	0.462	0.008	0.58	yes
Xq26.3	133703924	rs5930651	T	C	0.679	0.018	3.97E-08	0.292	-0.004	0.84	0.610	0.017	0.31	0.653	0.028	0.087	yes

¹ Per allele change in log(PSA)

² Variants that were independent of previously reported PSA associations at LD $r^2 < 0.01$ within ± 10 Mb were considered novel

Abbreviations:

EAF Effect allele frequency

Supplementary Table 5: Association estimates for 119 index variants associated with PSA levels detected with MR-MEGA. Genome-wide significant ($P < 5 \times 10^{-8}$) index variants were selected from the multi-ancestry meta-analysis performed with MR-MEGA using LD-based clumping at $r^2 < 0.01$ within ± 10 Mb windows. MR-MEGA is an alternative approach to cross-ancestry meta-analysis that uses meta-regression to quantify heterogeneity due to ancestry ($P_{\text{Het-Anc}}$) separately from residual heterogeneity due to other factors ($P_{\text{Het-Res}}$). All p-values are two-sided. For comparison, association p-values based on the fixed-effects multi-ancestry meta-analysis using METAL (P_{METAL}) are provided.

Region	Position (b37)	Variant ID	Effect Allele	Other Allele	Meta-Regression (MR-MEGA)							Meta-analysis
					EAF _{MEGA}	P _{MEGA}	P _{Het-Anc}	P _{Het-Res}	N	N _{study}	Direction	P _{METAL}
1p32.3	51021867	rs147696085	A	G	0.088	2.62E-09	0.51	0.16	95768	12	+++ ++++++	1.75E-11
1p32.3	51480258	rs7555006	G	A	0.439	7.11E-11	0.25	0.68	95768	12	+++++ -+++++	6.64E-13
1p22.3	88182718	rs10493801	G	A	0.511	4.41E-20	0.016	0.16	69277	11	+---? -+--+	6.11E-21
1p13.2	112264274	rs2076591	C	T	0.212	1.86E-11	0.18	0.70	95768	12	+++++ +++++ +	2.64E-13
1q32.1	205632217	rs71152447	GGCCGACAGC CCTTCTGCTG GCTCGGTGGG GCCCAGC	G	0.980	4.24E-10	0.19	0.11	44597	8	?-?-?+?-----	9.91E-12
1q32.1	205636334	rs4951018	C	A	0.227	7.05E-12	0.081	0.077	95768	12	+++++ -+++++	2.75E-13
1q41	219694903	rs12034581	A	C	0.500	1.38E-10	0.24	0.39	95768	12	+-----+--+	2.46E-12
2p24.1	20878153	rs9306895	C	T	0.353	4.15E-13	0.67	0.32	95768	12	+++++ -+++++	1.79E-15
2p23.3	25463871	rs734693	T	C	0.720	4.72E-08	0.018	0.66	95768	12	+++++ -+++++	3.88E-08
2p21	43072828	rs1123695	C	G	0.338	2.87E-13	0.95	0.73	95768	12	-----+--	3.25E-16
2p21	43618819	rs11899863	T	C	0.095	8.79E-11	0.71	0.050	95768	12	+-----++	1.72E-13
2p16.1	60759747	rs2556375	T	G	0.825	1.67E-29	0.47	0.45	95768	12	-----+--	1.75E-32
2p16.1	60790985	rs1510478	A	G	0.161	2.82E-13	0.22	0.47	95768	12	+-----+---	2.22E-15
2p15	63277843	rs58235267	G	C	0.483	2.88E-12	0.024	0.56	95768	12	-++++ -+++++	4.92E-13
3q23	141115219	rs1582874	C	T	0.444	5.11E-14	0.53	0.70	95768	12	+++++ ++++++--+	1.01E-16
3q27.3	186763665	rs59663889	A	T	0.194	4.31E-08	0.45	0.19	95768	12	+++++ ++++++--+	4.50E-10
3q28	189482770	rs6765473	C	T	0.114	1.26E-08	0.25	0.78	94949	11	+-----?	3.25E-10
3q28	191387768	rs114388981	T	A	0.983	4.40E-08	1.29E-08	0.14	38447	8	?+???+--+	0.78
4q31.22	146890261	rs9968429	G	A	0.369	2.12E-16	0.053	0.34	95768	12	+++++ ++++++--+	6.34E-18
4q32.1	157491375	rs17034927	T	C	0.356	8.03E-14	0.96	0.46	95768	12	+++++ ++++++ +	1.22E-16
5p15.33	1287194	rs2853677	A	G	0.584	2.29E-22	0.56	0.87	95768	12	-----+-----	7.91E-25

5p15.33	1322087	rs401681	T	C	0.437	1.17E-51	0.20	0.78	95768	12	-----	6.98E-54
5p15.33	1366007	rs152133	A	G	0.368	1.21E-12	0.19	0.65	95768	12	+++++--+++	8.33E-15
5q14.3	92052005	rs7732515	A	T	0.221	7.56E-12	0.56	0.62	94949	11	+++++++--+?	3.53E-14
5q15	96727294	rs291812	T	C	0.468	1.00E-08	2.24E-04	0.99	95768	12	+++++-----	9.30E-07
6p22.3	15230743	rs112266013	A	G	0.132	4.90E-10	6.20E-04	0.88	95768	12	-----	9.85E-09
6p22.3	16515154	rs236961	T	C	0.353	1.84E-10	0.12	0.43	95768	12	+++++-----	8.57E-12
6p22.1	29915061	rs2248162	C	T	0.675	2.08E-08	0.26	0.36	95768	12	-+++++--+	3.60E-10
6p21.31	34237109	rs575339229	C	G	0.976	1.64E-09	0.040	0.57	69887	7	?-?---?--?	2.79E-10
6p21.1	43710348	rs6920449	C	T	0.839	1.63E-22	1.29E-03	0.054	95768	12	-----+++-	8.05E-22
7p15.3	20909622	rs204592	G	A	0.515	3.82E-08	0.22	0.47	95768	12	+++++++-----	1.18E-09
7p15.2	27483166	rs10250340	A	G	0.321	4.66E-08	0.13	0.018	95768	12	+++++++--+	2.03E-09
7p15.2	27975919	rs67152137	C	G	0.264	8.12E-28	0.16	0.78	95768	12	-----++-	8.57E-31
8p21.2	23470583	rs7004327	A	G	0.440	1.25E-18	0.70	0.27	95768	12	-----+-----	7.77E-22
8p21.2	23529521	rs1160267	A	G	0.569	9.76E-77	0.89	0.58	95768	12	-----	6.29E-83
8q12.1	57132317	rs145612921	G	GC	0.108	1.79E-08	0.62	0.73	94949	11	-----+---	1.18E-10
8q12.1	57834357	rs4738555	T	C	0.569	9.74E-16	0.058	0.67	95768	12	-----++-	3.20E-17
8q21.13	81811566	8:81811566_ CA_C	C	CA	0.409	3.37E-09	0.16	0.44	95768	12	+-----+--	7.64E-11
8q24.21	128093297	rs1016343	T	C	0.203	1.90E-12	0.75	0.88	95768	12	+++++++ +	3.59E-15
8q24.21	128228847	rs74631227	G	A	0.040	1.87E-09	0.055	0.029	94949	11	-----+--+?	2.02E-10
8q24.21	128318755	rs10107982	C	T	0.266	1.94E-27	0.17	0.78	95768	12	-----+--	4.07E-30
8q24.21	128413305	rs6983267	T	G	0.481	5.42E-42	0.62	0.22	95768	12	-----+-----	2.55E-45
8q24.21	128455167	rs28645077	T	A	0.354	4.50E-09	0.64	0.60	95768	12	+++++++-----	1.23E-11
9q22.32	99146751	rs7020681	C	T	0.203	2.71E-09	0.012	0.68	95768	12	+++++-----	1.40E-09
9q33.1	118258187	rs9409165	G	A	0.119	1.57E-08	0.050	0.55	95768	12	+++++--+---	2.46E-09
9q33.1	120473180	rs10983756	T	C	0.057	1.46E-15	2.30E-03	0.88	94949	11	+---+---+---	3.55E-15
9q33.2	123642351	rs1609810	T	C	0.658	1.41E-10	0.10	0.24	95768	12	+--+-----+--	8.89E-12
10p12.31	21855753	rs141268071	G	T	0.019	1.97E-08	0.011	0.63	91496	9	+++++++?+--??	2.23E-08
10p12.31	22308015	rs10828285	A	G	0.713	3.76E-12	0.53	0.96	95768	12	-----+-----	2.21E-14
10p12.31	22363979	rs3011633	C	T	0.217	3.96E-17	0.43	0.80	95768	12	+++++++-----	5.92E-20
10p12.31	22590653	rs79800006	A	T	0.022	2.56E-11	2.08E-03	0.032	93960	10	+++++++?+--?	1.01E-10

10p12.1	28096754	rs2815506	A	G	0.811	8.67E-13	0.50	0.44	95768	12	+++++++--+	4.88E-15
10q11.23	51549496	rs10993994	T	C	0.402	2.31E-83	0.26	0.66	69887	7	?+?+++?+?+?	7.31E-87
10q11.23	51551900	rs57592785	C	CG	0.846	1.67E-08	0.23	0.57	69887	7	?+?+++?+?+?	5.00E-10
10q26.12	122667022	rs1530116	G	T	0.337	7.75E-38	0.47	0.65	95768	12	+++++++-----	1.07E-40
10q26.12	122926366	rs59421178	A	G	0.163	2.64E-08	3.58E-03	0.12	95768	12	+++--+-----	8.51E-08
10q26.12	122933134	rs12354663	T	C	0.098	1.00E-14	0.44	0.79	95768	12	+++++++-----	2.87E-17
10q26.12	123009023	rs144869102	A	G	0.015	1.91E-09	0.43	0.91	94014	10	++++++?---+?	1.35E-11
10q26.12	123025352	rs61872992	C	A	0.422	1.16E-21	0.93	0.51	95768	12	-----+-----	3.15E-25
10q26.12	123049264	rs10886902	C	T	0.227	5.53E-115	0.82	0.54	95768	12	+++++++ +	8.16E-118
10q26.12	123095366	rs7914065	T	C	0.253	8.09E-24	4.69E-03	0.46	95768	12	+++++++-----	5.01E-24
10q26.13	123185303	rs10749415	A	G	0.937	1.28E-41	0.87	0.32	95768	12	+++++++-----	1.83E-45
10q26.13	123349324	rs45631563	T	A	0.043	3.42E-20	0.37	0.20	94949	11	+++++++--+?	7.94E-23
11p13	34676842	rs896856	T	G	0.475	6.99E-18	0.33	0.059	95768	12	-++++-++++-	2.34E-20
11p13	34780936	rs10466455	C	T	0.396	1.10E-22	0.33	0.71	95768	12	+++++++--+--	8.02E-26
11q22.2	102396607	rs12285347	C	T	0.443	1.68E-23	0.14	1.00	95768	12	+++++++-----	2.61E-25
11q22.2	102438778	rs7129424	A	G	0.563	3.67E-09	0.50	0.54	95768	12	+++++++-----	2.50E-11
12q21.31	84994000	rs61928422	T	C	0.169	3.34E-08	0.031	0.20	95768	12	-++++-+++----	1.11E-08
12q24.21	115094260	rs11067228	G	A	0.441	2.69E-27	0.19	0.99	95768	12	-----	1.25E-29
12q24.21	115136391	rs1463888	G	T	0.337	7.38E-14	1.43E-03	0.79	95768	12	-----++----	2.66E-13
12q24.23	118601003	rs35506792	C	T	0.093	3.12E-11	0.081	0.70	94949	11	+-----+?+	2.01E-12
13q14.3	51087443	rs202346	A	C	0.251	1.37E-25	0.034	0.54	95768	12	+++++++ +	1.82E-27
13q14.3	51165912	rs12869529	G	A	0.039	3.42E-09	0.81	0.018	94949	11	---+---+---+?	9.40E-12
13q14.3	51194405	rs573666	T	C	0.340	3.17E-17	0.16	0.12	95768	12	-++++-++++-	8.44E-19
13q14.3	51446114	rs12429206	G	A	0.651	2.04E-10	1.53E-03	0.48	95768	12	-----++-+-	2.01E-09
13q32.1	95799006	rs61965887	A	G	0.059	7.89E-12	0.58	0.53	94949	11	+++++++-----?	3.69E-14
14q13.3	37240591	rs712329	A	G	0.575	4.42E-08	0.022	0.56	95768	12	---+---+---	2.01E-08
14q32.13	94838142	rs112635299	T	G	0.020	9.68E-14	0.23	0.33	90125	7	-----??-???	1.21E-15
14q32.13	95097556	rs8023057	G	A	0.166	1.00E-28	0.19	0.062	68458	10	---?--+---+?	3.23E-31
14q32.13	95138671	rs12891726	C	T	0.571	3.81E-11	0.63	0.38	95768	12	+++++++-----	9.05E-14
16p13.3	4304905	rs2386890	T	A	0.334	1.05E-10	0.52	0.59	95768	12	-++++-++++-	3.11E-13

16p13.3	4318206	rs251739	G	A	0.507	7.24E-18	0.092	0.41	95768	12	-+++++++--+	6.63E-20
16q23.1	77320605	rs12921392	G	A	0.590	1.52E-08	0.42	0.90	95768	12	-----	1.89E-10
16q23.1	77507275	rs7206309	T	C	0.685	1.44E-19	0.61	0.51	95768	12	-----+----	1.61E-22
16q24.1	86547001	rs56404456	T	C	0.350	1.43E-09	0.58	0.071	69277	11	++++?+++++--	5.93E-12
17p12	12296124	rs28444256	G	C	0.122	1.70E-08	1.42E-03	0.53	95768	12	-+++++++--+	2.10E-07
17p12	12323258	rs2721828	A	G	0.502	4.33E-11	0.017	0.74	95768	12	-----++	1.81E-11
17q12	36099840	rs11651755	C	T	0.491	6.54E-44	0.025	0.016	95768	12	-----+-----	3.94E-45
18q23	76777252	rs71279357	A	T	0.726	4.66E-10	0.71	0.94	69887	7	?+?+++?+?+?	1.83E-12
19q12	32059290	rs7252125	T	C	0.339	3.18E-13	0.013	0.79	95768	12	-----+++-	1.74E-13
19q12	32104979	rs11084596	C	T	0.386	1.14E-25	0.52	0.92	69277	11	----?-+----	4.17E-29
19q13.32	46229711	rs6509234	G	T	0.826	2.22E-08	0.030	0.79	95768	12	-++++++-+--	7.70E-09
19q13.33	51264558	rs183959820	A	C	0.021	1.13E-38	1.37E-03	1.78E-04	91442	9	-----+?-+??	1.16E-38
19q13.33	51280907	rs1122124	G	C	0.420	1.08E-11	0.24	0.057	95768	12	+++++-+---+	1.63E-13
19q13.33	51326106	rs2659058	T	C	0.681	4.63E-27	1.66E-04	0.028	95768	12	-----+-+---+	1.28E-25
19q13.33	51349090	rs266849	A	G	0.794	7.39e-316	1.44E-05	0.035	95768	12	+++++++ +	5.70e-319
19q13.33	51349781	rs112343212	T	C	0.026	2.09E-28	0.026	0.72	93960	10	+++++++?+-+?	1.07E-29
19q13.33	51356929	rs193199179	T	C	0.008	3.34E-12	0.039	0.62	92643	8	+++++++??+?-?	3.86E-13
19q13.33	51361382	rs61752561	A	G	0.037	7.51E-51	0.35	0.18	94949	11	-----+?	2.12E-54
19q13.33	51361757	rs17632542	C	T	0.072	4.1e-641	1.02E-16	1.82E-07	94949	11	-----?	3.15E-638
19q13.33	51364649	rs17632611	C	A	0.065	9.10E-63	0.59	0.88	95768	12	+++++++ +	1.05E-66
19q13.33	51383072	rs198978	T	G	0.357	2.77E-29	0.062	0.054	95768	12	-----	8.38E-31
19q13.33	51399309	rs112035754	G	A	0.103	1.26E-17	0.060	0.022	95768	12	-----+---+	3.79E-19
19q13.41	51401797	rs8104538	G	A	0.309	1.13E-08	0.16	0.84	95768	12	-----++---+	7.21E-10
19q13.41	51440765	rs2739403	A	T	0.179	1.02E-10	0.11	4.06E-03	94949	11	+-----+++?	2.53E-12
20q11.21	31950845	rs291671	A	G	0.896	2.98E-16	0.28	2.87E-03	95768	12	-----+-+--	1.19E-18
20q11.21	31966698	rs2065703	T	C	0.146	3.76E-11	0.45	0.23	95768	12	+-----+--	2.72E-13
20q11.22	32397556	rs117119427	T	C	0.078	1.12E-10	0.14	0.040	94949	11	-+++++++--+?	4.00E-12
21q22.2	40289167	rs2836750	G	T	0.595	1.73E-10	0.35	0.94	95768	12	-----	1.59E-12
22q13.31	45996298	rs13268	G	A	0.023	3.82E-08	0.74	0.37	94949	11	+-----+?	1.63E-10

Xp22.31	8912815	rs112062538	C	T	0.235	1.10E-17	0.086	0.84	95768	12	+++++++ +	4.74E-19
Xp22.2	16864303	rs5969728	A	G	0.378	1.01E-23	0.012	0.33	95768	12	-----+--	4.09E-24
Xp22.13	17831188	rs200615037	T	TTG	0.043	1.35E-19	0.47	0.012	94567	10	-----?-?	3.54E-22
Xp22.11	23996164	rs2520225	A	G	0.538	9.67E-10	0.046	0.31	95768	12	----+--+---	1.98E-10
Xp22.11	24109619	rs7065158	G	A	0.635	9.49E-27	0.18	0.18	95768	12	-----+---	1.11E-29
Xq13.1	69025920	rs2804355	T	A	0.612	1.74E-09	2.87E-03	0.52	95768	12	+++++-----	6.91E-09
Xq13.1	69767264	rs5936916	T	A	0.478	2.55E-08	0.12	0.48	95768	12	-----+--	2.75E-09
Xq13.1	70125103	rs62608084	A	G	0.293	2.84E-24	9.37E-03	0.054	94949	11	+++++++--+?	1.66E-24
Xq26.2	132942023	rs1908817	C	G	0.665	5.49E-10	0.35	0.69	95768	12	+++++++--+	6.19E-12

Abbreviations:

EAF_{MEGA} Average effect allele frequency weighted by the sample size of each input file

Supplementary Table 6: Population-specific association estimates for variants that reached genome-wide significance using MR-MEGA but not METAL. Out of the 119 independent index variants detected by MR-MEGA, four variants did not reach $P < 5 \times 10^{-8}$ in the fixed effect multi-ancestry meta-analysis using METAL. For each variant, effect sizes (β) and corresponding two-sided p-values are reported from the inverse-variance-weighted fixed-effects meta-analysis performed within each ancestry group using METAL.

Regional position	Variant ID	Effect Allele	Other Allele	EUR (N=85,824)			AFR (N=3,509)			HIS/LAT (N=3,098)			EAS (N=3,337)			New ²	
				EAF	β ¹	P _{METAL}	EAF	β ¹	P _{METAL}	EAF	β ¹	P _{METAL}	EAF	β ¹	P _{METAL}		
3q28	191387768	rs114388981	A	T	0.003	-0.031	0.62	0.126	-0.019	0.49	0.011	-0.453	3.9E-06	0.029	0.225	1.0E-04	yes
5q15	96727294	rs291812	T	C	0.486	0.016	2.3E-05	0.133	-0.026	0.35	0.474	0.010	0.64	0.350	0.097	1.2E-06	yes
10q26.12	122926366	rs59421178	A	G	0.162	0.028	1.7E-07	0.159	-0.045	0.080	0.170	0.020	0.47	0.210	0.067	5.5E-03	yes
17p12	12296124	rs28444256	C	G	0.891	-0.029	3.0E-06	0.697	-0.034	0.095	0.859	-0.108	2.4E-04	0.746	0.018	0.42	yes

¹ Per allele change in log(PSA)

² Variants that were independent of previously reported PSA associations, including those identified in the fixed-effects meta-analysis, at LD $r^2 < 0.01$ were considered novel

Abbreviations:

EAF Effect allele frequency

Supplementary Table 8: Associations with prostate cancer risk for 128 index variants associated with PSA in the multi-ancestry meta-analysis.

Odds ratios (OR) and p-values for prostate cancer were obtained from summary statistics from the PRACTICAL consortium GWAS by Conti et al³². All p-values are two-sided and derived from a meta-analysis of European ancestry studies (85,554 cases and 91,972 controls) and multi-ancestry meta-analysis (107,247 cases and 127,006). For each variant, bias-adjusted effect sizes (OR_{adj}) and p-values (P_{adj}) were calculated using the Dudbridge method³³. Two-sided bias-adjusted p-values were calculated from a chi-squared test statistic based on bias-corrected effect sizes and standard errors. For comparison, the effect of each variant on PSA levels is also presented, with two-sided p-values derived from the inverse-variance-weighted fixed-effect multi-ancestry meta-analysis of 95,768 men using METAL (P_{METAL}).

Region	Position (b37)	Variant ID	PSA-increasing Allele	P _{METAL}	Prostate Cancer (European Ancestry)				Prostate Cancer (Multi-Ancestry)			
					Original GWAS		Bias Corrected ¹		Original GWAS		Bias Corrected ²	
					OR	P	OR _{adj}	P _{adj}	OR	P	OR _{adj}	P _{adj}
1p32.3	51237409	rs12569177	C	3.2E-13	1.04	3.6E-07	1.01	0.33	1.03	4.5E-05	1.00	0.87
1p22.3	88199778	rs12131120	T	1.6E-19	1.04	1.7E-08	1.00	0.62	1.04	2.0E-09	1.01	0.49
1p13.2	112264274	rs2076591	C	2.6E-13	1.02	0.012	0.99	0.23	1.02	0.031	0.98	0.056
1q21.3	154868055	rs4845681	T	7.7E-09	1.05	2.5E-12	1.03	9.6E-04	1.05	8.5E-11	1.02	9.2E-03
1q25.3	184191716	rs12046452	C	9.0E-09	1.04	3.2E-06	1.01	0.15	1.03	9.9E-06	1.01	0.36
1q32.1	205632217	rs71152447	G	9.9E-12	1.00	0.96	0.83	6.2E-04	1.02	0.51	0.86	4.9E-04
1q32.1	205636334	rs4951018	C	2.7E-13	1.05	6.2E-07	1.01	0.40	1.05	1.1E-10	1.02	0.096
1q41	219694903	rs12034581	C	2.5E-12	1.00	0.91	0.97	1.1E-03	1.00	0.56	0.98	2.3E-03
1q41	219954267	rs6664688	G	3.9E-08	0.97	5.9E-03	0.95	5.1E-07	0.99	0.26	0.96	1.0E-04
2p24.2	18911674	rs12710685	G	2.3E-08	1.00	0.94	0.96	9.3E-03	1.01	0.39	0.97	0.025
2p24.1	20880833	rs10193919	T	1.5E-15	1.07	1.4E-19	1.04	5.8E-05	1.08	4.3E-30	1.05	2.1E-08
2p23.3	25463871	rs734693	T	3.9E-08	1.01	0.16	0.99	0.20	1.01	0.46	0.98	0.029
2p21	43072828	rs1123695	G	3.3E-16	1.04	5.3E-08	1.01	0.42	1.04	1.4E-09	1.01	0.32
2p21	43618819	rs11899863	C	1.7E-13	1.06	1.0E-05	1.01	0.72	1.05	9.9E-06	1.00	0.81
2p16.1	60759747	rs2556375	G	1.8E-32	0.98	0.079	0.92	2.3E-12	0.98	0.029	0.92	4.3E-15
2p15	63277843	rs58235267	G	4.9E-13	1.12	6.6E-54	1.09	9.8E-24	1.12	5.4E-72	1.09	8.5E-31
2p13.2	72059504	rs11679946	T	2.6E-08	1.01	0.088	0.99	0.26	1.01	0.16	0.99	0.093
2q33.1	198929083	rs34388051	A	2.2E-08	1.00	0.71	0.98	0.022	1.01	0.22	0.99	0.078
3q13.2	113290793	rs4682495	A	2.9E-09	1.09	1.7E-28	1.06	5.7E-12	1.08	2.6E-28	1.05	1.7E-10
3q21.3	128067275	rs11709611	C	2.0E-10	1.10	4.1E-18	1.06	1.2E-05	1.10	1.6E-19	1.05	1.2E-05
3q23	141115219	rs1582874	C	1.0E-16	1.05	1.8E-09	1.01	0.21	1.04	1.6E-10	1.01	0.19

3q25.33	160130592	rs10673842	TTATC	2.2E-08	1.03	9.6E-06	1.01	0.46	1.03	6.2E-05	1.00	0.83
3q27.2	185246981	rs4012714	A	1.1E-08	1.02	0.021	0.99	0.30	1.02	0.032	0.99	0.19
3q27.3	186746994	rs12629450	C	2.6E-10	1.01	0.32	0.98	0.039	1.01	0.27	0.98	0.024
3q28	189482770	rs6765473	T	3.2E-10	1.01	0.61	0.97	0.013	1.01	0.51	0.97	0.017
4p15.2	24410024	rs4276269	G	2.0E-08	0.99	0.24	0.96	3.1E-04	0.98	0.041	0.96	4.7E-06
4q31.22	146890261	rs9968429	G	6.3E-18	1.02	0.011	0.98	0.058	1.03	6.0E-05	0.99	0.28
4q32.1	157497921	rs13115840	A	4.3E-17	1.01	0.061	0.98	0.018	1.02	5.9E-03	0.98	0.056
5p15.33	1285974	rs7705526	A	1.2E-08	0.94	1.6E-12	0.92	5.3E-19	0.94	1.3E-16	0.92	1.5E-23
5p15.33	1322087	rs401681	C	7.0E-54	1.04	4.0E-06	0.97	4.2E-04	1.02	0.011	0.95	1.9E-09
5q14.3	92052005	rs7732515	A	3.5E-14	1.02	0.084	0.98	0.040	1.02	0.024	0.98	0.071
5q35.2	172945918	rs889017	C	2.6E-08	1.04	6.0E-05	1.01	0.40	1.03	1.2E-04	1.00	0.72
6p22.3	15463139	rs926309	T	1.6E-12	1.01	0.41	0.98	9.1E-03	1.01	0.13	0.98	0.024
6p22.3	16515154	rs236961	T	8.6E-12	0.97	3.0E-05	0.94	5.3E-12	0.97	5.1E-06	0.94	1.1E-13
6p22.1	29915061	rs2248162	C	3.6E-10	1.04	2.9E-06	1.01	0.35	1.03	3.9E-06	1.01	0.45
6p21.31	34212537	rs551980123	TG	1.6E-10	1.01	0.74	0.93	1.4E-03	1.01	0.68	0.93	1.6E-03
6p21.1	43711981	rs1535507	T	1.5E-22	1.05	4.8E-07	1.00	0.72	1.05	1.1E-07	0.99	0.50
6q22.33	129168057	rs73583119	A	3.5E-08	-	-	-	-	-	-	-	-
7p15.3	20909622	rs204592	G	1.2E-09	1.05	9.8E-11	1.02	6.7E-03	1.05	2.5E-13	1.02	1.9E-03
7p15.3	21839896	rs6956349	T	8.6E-09	1.03	8.9E-05	1.01	0.55	1.03	5.6E-06	1.01	0.26
7p15.2	27281792	rs17437810	A	8.0E-09	1.06	0.037	0.97	0.26	1.06	0.035	0.97	0.30
7p15.2	27483166	rs10250340	A	2.0E-09	1.02	2.9E-03	1.00	0.78	1.02	1.2E-03	1.00	0.73
7p15.2	27975919	rs67152137	G	8.6E-31	1.15	3.2E-53	1.08	8.9E-16	1.14	2.0E-63	1.08	5.5E-18
8p21.2	23437981	rs2928681	C	3.5E-18	1.05	3.2E-10	1.01	0.18	1.04	8.5E-11	1.01	0.29
8p21.2	23529521	rs1160267	G	6.3E-83	1.14	2.0E-68	1.05	1.8E-09	1.16	3.3E-112	1.07	2.1E-20
8q12.1	57138676	rs36112366	T	7.3E-11	1.02	0.045	0.98	0.18	1.02	0.074	0.98	0.099
8q12.1	57834357	rs4738555	C	3.2E-17	1.02	0.017	0.98	0.071	1.02	5.6E-03	0.99	0.072
8q21.13	81811566	8:81811566_CA_C	CA	7.6E-11	0.99	0.072	0.96	2.4E-06	0.99	0.047	0.96	6.0E-07
8q23.1	108849527	rs1494920	T	4.8E-08	1.02	0.041	0.99	0.44	1.01	0.063	0.99	0.23
8q24.21	127817460	rs7843726	G	1.7E-08	1.05	7.8E-06	1.01	0.26	1.06	1.7E-08	1.02	0.057
8q24.21	128093297	rs1016343	T	3.6E-15	1.25	2.4E-138	1.20	6.1E-72	1.25	5.9E-181	1.20	5.1E-88
8q24.21	128318755	rs10107982	T	4.1E-30	1.15	4.6E-64	1.09	1.6E-20	1.15	1.3E-69	1.09	1.7E-22

8q24.21	128413305	rs6983267	G	2.6E-45	1.23	2.8E-164	1.16	2.6E-65	1.22	2.1E-198	1.16	1.7E-77
9q22.32	99146751	rs7020681	C	1.4E-09	1.02	0.052	0.99	0.26	1.02	0.026	0.99	0.26
9q33.1	118258080	rs150402584	T	9.0E-10	1.01	0.35	0.97	0.038	1.02	0.12	0.98	0.079
9q33.1	120475302	rs4986790	A	7.1E-17	1.04	0.012	0.97	0.068	1.05	8.8E-04	0.98	0.19
9q33.2	123643426	rs59482735	T	2.9E-12	1.03	3.3E-04	0.99	0.47	1.03	1.1E-04	0.99	0.53
10p12.31	22363979	rs3011633	C	5.9E-20	1.01	0.21	0.97	9.5E-04	1.01	0.31	0.97	2.2E-04
10p12.2	23398448	rs1857279	C	3.9E-11	1.02	0.010	0.99	0.36	1.03	9.9E-05	1.00	0.92
10p12.1	28096754	rs2815506	A	4.9E-15	1.03	1.7E-03	0.99	0.32	1.03	5.8E-04	0.99	0.19
10q11.23	51549496	rs10993994	T	7.3E-87	1.23	9.1E-165	1.11	2.8E-33	1.21	8.9E-192	1.10	3.1E-34
10q25.2	111991733	rs562417881	G	5.6E-09	1.03	0.014	0.99	0.34	1.03	0.014	0.99	0.28
10q26.12	122631067	rs9325569	A	9.9E-41	1.02	0.052	0.96	1.9E-06	1.01	0.19	0.95	7.9E-09
10q26.12	123049264	rs10886902	C	8.2E-118	0.94	5.4E-11	0.84	4.9E-65	0.94	7.0E-13	0.85	4.3E-72
10q26.13	123135200	rs10788173	C	2.9E-08	1.00	0.85	0.98	5.6E-03	1.00	0.72	0.98	1.6E-03
10q26.13	123185303	rs10749415	A	1.8E-45	1.10	3.2E-08	0.97	0.14	1.11	5.2E-16	0.99	0.51
10q26.13	123349324	rs45631563	T	7.9E-23	1.06	9.4E-04	0.96	0.044	1.07	1.9E-04	0.97	0.10
10q26.13	126737579	rs3012065	C	2.2E-08	1.04	1.1E-07	1.02	0.047	1.04	1.1E-06	1.01	0.20
11p15.5	197557	rs7103852	G	1.2E-09	1.00	0.98	0.95	4.7E-03	1.00	0.70	0.95	5.0E-04
11p13	34718279	rs553481604	G	1.7E-11	1.00	0.56	0.96	6.9E-05	1.00	0.94	0.97	2.1E-04
11p13	34780936	rs10466455	C	8.0E-26	1.01	0.23	0.97	9.7E-05	1.00	0.49	0.96	1.9E-06
11q13.5	76153279	rs58015965	G	4.0E-08	1.06	8.3E-12	1.03	8.8E-04	1.05	3.6E-13	1.03	4.6E-04
11q22.2	102396607	rs12285347	C	2.6E-25	0.93	4.0E-21	0.89	3.6E-40	0.93	5.4E-25	0.89	2.1E-45
11q22.2	102438778	rs7129424	A	2.5E-11	0.98	1.8E-03	0.95	3.5E-09	0.97	2.8E-05	0.95	3.1E-12
12p13.31	9222286	rs1805664	T	9.2E-09	1.01	0.42	0.98	0.042	1.01	0.42	0.98	0.033
12q14.3	66393756	rs74097857	T	1.2E-09	1.05	2.1E-06	1.02	0.24	1.05	7.4E-06	1.01	0.35
12q21.31	84994000	rs61928422	T	1.1E-08	1.02	0.031	0.99	0.40	1.02	0.016	0.99	0.37
12q24.21	115099805	rs10774760	G	2.4E-30	1.03	8.1E-04	0.98	0.013	1.03	1.8E-04	0.98	0.012
12q24.21	115155460	rs11067251	G	1.9E-09	1.01	0.39	0.98	0.046	1.01	0.48	0.98	0.024
12q24.23	118855432	rs1045542	G	1.2E-13	1.00	0.89	0.95	2.2E-04	1.00	0.74	0.95	1.1E-04
13q14.3	51087443	rs202346	A	1.8E-27	1.04	5.3E-06	0.99	0.21	1.04	2.9E-08	0.99	0.38
13q14.3	51165912	rs12869529	A	9.4E-12	1.03	0.17	0.96	0.053	1.02	0.39	0.95	9.0E-03
13q14.3	51445360	rs9563006	A	5.6E-11	1.03	2.3E-05	1.01	0.51	1.03	2.4E-06	1.01	0.38

13q22.1	74055303	rs1361057	C	3.3E-08	1.02	0.026	0.99	0.52	1.02	0.012	0.99	0.50
13q32.1	95799006	rs61965887	A	3.7E-14	0.95	1.2E-03	0.89	1.4E-10	0.95	2.5E-03	0.89	6.3E-10
14q13.3	37240591	rs712329	G	2.0E-08	1.01	0.11	0.99	0.21	1.01	0.21	0.99	0.078
14q32.13	94838142	rs112635299	G	1.2E-15	1.14	1.7E-06	1.01	0.65	1.14	1.7E-06	1.02	0.56
14q32.13	95104745	rs72695000	C	7.4E-28	1.04	2.8E-04	0.98	0.049	1.04	8.5E-05	0.98	0.088
15q22.31	66941399	rs8038722	G	3.2E-08	1.01	0.049	0.99	0.35	1.03	4.4E-06	1.01	0.29
16p13.3	4318206	rs251739	G	6.6E-20	1.03	1.2E-05	0.99	0.55	1.03	1.4E-06	1.00	0.55
16p13.13	11201428	rs9933507	C	3.8E-10	1.00	0.54	0.97	5.1E-04	1.00	0.94	0.97	1.2E-03
16q23.1	77507275	rs7206309	C	1.6E-22	1.00	0.86	0.96	8.3E-06	1.00	0.88	0.96	1.1E-06
16q24.1	86554784	rs13334022	T	3.4E-11	1.00	0.86	0.95	2.0E-03	1.01	0.30	0.97	0.013
17p13.3	1994071	rs3760230	C	2.8E-08	1.00	0.69	0.98	0.026	1.01	0.45	0.98	0.033
17p13.1	7571752	rs78378222	G	2.8E-10	1.25	4.8E-11	1.10	0.013	1.25	4.7E-11	1.11	8.9E-03
17p13.1	7793367	rs34009884	C	1.1E-08	1.10	1.2E-12	1.06	3.2E-04	1.10	1.5E-13	1.06	1.1E-04
17p12	12320741	rs7219536	T	5.7E-12	1.01	0.24	0.98	0.035	1.01	0.090	0.98	0.072
17p12	12556260	rs9889266	C	8.9E-10	1.02	0.039	0.99	0.27	1.01	0.21	0.98	0.040
17q12	36099952	rs10908278	A	2.1E-46	1.23	2.7E-161	1.16	1.1E-63	1.22	1.1E-194	1.15	5.8E-75
18q23	76777252	rs71279357	A	1.8E-12	1.09	8.0E-21	1.04	4.3E-05	1.08	1.2E-20	1.04	1.8E-04
19q12	32055024	rs11084590	C	3.4E-18	1.00	0.69	0.96	4.7E-06	1.00	0.52	0.96	1.4E-06
19q13.32	46229711	rs6509234	G	7.7E-09	1.01	0.36	0.98	0.038	1.01	0.53	0.97	0.014
19q13.33	49206462	rs681343	T	4.4E-08	1.01	0.47	0.98	0.048	1.00	0.91	0.98	9.4E-03
19q13.33	51225544	rs890863	G	1.1E-08	1.00	0.78	0.97	2.2E-03	0.99	0.26	0.97	7.7E-05
19q13.33	51323501	rs1054713	A	4.8E-22	1.02	5.1E-03	0.98	0.026	1.02	9.2E-04	0.98	0.032
19q13.33	51340794	rs2659053	A	5.4E-94	1.06	9.8E-15	0.97	1.2E-03	1.05	2.7E-12	0.96	2.7E-06
19q13.33	51349841	rs113920094	C	6.5E-09	1.11	0.083	0.94	0.35	1.11	0.083	0.95	0.40
19q13.33	51360398	rs578067733	GA	1.7E-12	1.06	0.61	0.88	0.30	1.10	0.025	0.92	0.081
19q13.33	51361757	rs17632542	T	3.2e-638	1.35	8.3E-90	0.89	2.7E-12	1.35	3.9E-93	0.90	1.7E-10
19q13.33	51365466	rs2735837	G	7.2E-58	1.06	1.3E-04	0.94	2.1E-04	1.08	3.2E-14	0.97	0.017
19q13.33	51373744	rs12983994	T	1.1E-17	1.02	0.28	0.94	1.9E-03	1.01	0.40	0.94	1.4E-04
19q13.33	51378275	rs112103380	C	1.7E-18	1.15	3.6E-03	0.90	0.059	1.15	3.6E-03	0.91	0.080
19q13.33	51383072	rs198978	G	8.4E-31	1.00	0.55	0.95	9.1E-10	1.00	0.73	0.95	3.3E-10
19q13.41	51421334	rs141135092	C	1.2E-09	1.05	0.097	0.95	0.14	1.06	0.050	0.96	0.25

19q13.41	51441425	rs80122351	G	1.2E-10	1.01	0.33	0.97	0.019	1.00	0.60	0.97	6.2E-03
20q11.21	31950845	rs291671	G	1.2E-18	1.03	0.015	0.97	0.047	1.03	2.4E-03	0.97	0.038
21q22.2	40289167	rs2836750	T	1.6E-12	1.04	3.5E-06	1.01	0.48	1.04	6.7E-07	1.01	0.47
22q13.31	45996298	rs13268	A	1.6E-10	1.02	0.47	0.93	8.8E-03	1.02	0.48	0.93	0.010
Xp22.31	8912815	rs112062538	C	4.7E-19	1.02	2.5E-03	0.99	0.035	1.02	4.7E-03	0.98	8.8E-03
Xp22.2	16844831	rs62586587	G	3.6E-25	1.02	1.2E-03	0.98	8.0E-03	1.02	4.3E-04	0.98	6.6E-03
Xp22.13	17831188	rs200615037	TTG	3.5E-22	1.06	1.2E-04	0.98	0.26	1.06	1.9E-05	0.98	0.19
Xp22.11	24109619	rs7065158	A	1.1E-29	1.01	0.10	0.97	1.0E-05	1.01	0.15	0.97	3.4E-06
Xp11.22	51242364	rs5987424	A	2.1E-08	1.11	1.1E-78	1.09	2.4E-37	1.10	4.6E-84	1.08	4.1E-39
Xp11.21	55936822	rs10855058	A	7.6E-09	1.02	5.7E-04	1.00	1.00	1.02	8.3E-05	1.00	0.89
Xq13.1	68996186	rs2520386	G	4.2E-11	1.02	0.025	0.99	0.16	1.01	0.060	0.99	0.089
Xq13.1	70125103	rs62608084	A	1.7E-24	1.04	1.4E-14	1.01	0.37	1.04	4.6E-14	1.00	0.49
Xq26.2	132935739	rs4829762	T	5.9E-12	1.02	3.8E-03	0.99	0.23	1.01	0.012	0.99	0.056
Xq26.3	133703924	rs5930651	T	1.0E-08	1.01	0.13	0.99	0.14	1.01	0.14	0.99	0.077

¹ Bias-corrected estimated were obtained as follows: $\beta^{adj} = \beta - b * \beta_{PSA}$ and the corresponding $OR^{adj} = \exp(\beta^{adj})$

² Bias-corrected multi-ancestry effects should be interpreted with caution since the bias correction factor (b) was estimated from variants that were LD-pruned ($r^2 < 0.10$) based on 1000G EUR. The same set of pruned variants was used for European and multi-ancestry bias analyses. For the multi-ancestry analysis SNP effects on PSA and prostate cancer were obtained from multi-ancestry GWAS summary statistics.

Abbreviations:

EAF Effect allele frequency

Supplementary Table 9: Comparison of methods for quantifying index event bias. Estimates of the bias correction factor (b) derived using the Dudbridge method³³ and SlopeHunter³⁵ are presented. In each analysis PSA variation corresponds to the selection trait and prostate cancer is the outcome trait.

Method	GWAS	P_{thresh}^1	b	SE_b	(95% CI) ²
Dudbridge	EUR	-	1.1436	2.91×10^{-4}	(1.1431 – 1.1442)
	Multi-ancestry ³	-	1.1039	1.49×10^{-4}	(1.1037 – 1.1043)
		0.1	0.382	0.096	(0.195 – 0.570)
		0.05	0.368	0.036	(0.298 – 0.439)
SlopeHunter	EUR	0.01	0.322	0.157	(0.014 – 0.630)
		0.001	0.476	0.135	(0.213 – 0.740)
		0.005	0.333	0.134	(0.070 – 0.595)
		5.0×10^{-4}	0.452	0.106	(0.245 – 0.659)

¹ P-value threshold for SNP-incidence associations. Associations with p-values larger than P_{thresh} are excluded prior to fitting the main model-based clustering in SlopeHunter. The default recommended setting is 0.001. This parameter is only applicable to SlopeHunter, no thresholding or clustering is performed in the Dudbridge method.

² Bootstrapped 95% confidence intervals estimated based on 1500 replicates are expected to have better coverage than empirical 95% confidence intervals based on SE_b when the normal approximation for outcome effect sizes may be inappropriate.

³ Multi-ancestry results should be interpreted with caution because they were estimated using the same set of variants as for the European ancestry analysis, selected by LD-pruning ($r^2 < 0.10$) 1000G EUR. Effect estimates for the reference panel variants were obtained from multi-ancestry GWAS meta-analyses for PSA and prostate cancer and used as inputs to estimate the bias correction factor (b)

Supplementary Table 10: Impact of index event bias correction on 209 prostate cancer variants. Independent risk variants for prostate cancer were selected from the PRACTICAL GWAS meta-analysis by Conti et al.³² using linkage disequilibrium (LD) clumping (LD $r^2 < 0.01$, $P < 5 \times 10^{-8}$). GWAS odds ratios (OR) and two-sided p-values for prostate cancer are based on an inverse-variance-weighted fixed-effects meta-analysis of European ancestry studies (85,554 cases and 91,972 controls). Original GWAS results are compared to for associations adjusted for index event bias using the Dudbridge et al. method³³ and SlopeHunter³⁵. For each variant, bias-adjusted odds ratios (OR_{adj}) and two-sided p-values (P_{adj}) were calculated from a chi-squared test statistic derived from bias-corrected effect sizes and standard errors. For additional context, associations with PSA levels are provided. For each variant, the PSA effect size (β_{PSA}) and two-sided p-value (P_{PSA}) are based on an inverse-variance-weighted fixed-effects meta-analysis in men of European ancestry (n=85,824).

Region	Position (b37)	Index variant ID ¹	Prostate Cancer Alleles		PSA Estimates		Prostate Cancer Estimates					
			Risk	Other	β_{PSA}^2	P _{PSA}	Original GWAS		Bias Corrected ³		Bias Corrected ⁴	
							OR	P	OR _{adj}	P _{adj}	OR _{adj-S}	P _{adj-S}
1p36.22	10561604	rs6658216	T	C	0.005	0.20	1.05	4.47E-08	1.04	4.40E-05	1.04	6.21E-07
1p36.13	16380393	rs35708002	A	G	0.016	2.99E-03	1.06	3.06E-08	1.04	9.56E-04	1.05	4.81E-06
1p22.3	88224230	rs305423	T	C	0.032	1.55E-10	1.06	2.80E-09	1.02	0.062	1.04	1.02E-04
1q21.3	150609429	rs116173394	A	G	-0.002	0.83	1.10	1.72E-08	1.10	6.79E-07	1.10	3.55E-08
1q21.3	150868102	rs78132593	A	C	0.007	0.13	1.08	3.26E-16	1.07	3.58E-10	1.07	5.40E-14
1q21.3	150930926	rs114908993	C	T	-0.018	0.11	1.16	3.49E-12	1.18	1.57E-11	1.17	1.58E-12
1q21.3	153923276	rs10127983	T	C	0.013	2.38E-03	1.07	1.38E-16	1.05	2.31E-08	1.06	9.31E-13
1q21.3	154980351	rs56103503	T	C	0.026	6.27E-08	1.07	3.16E-17	1.04	2.27E-04	1.05	2.27E-09
1q22	155552910	rs61812109	G	A	0.037	3.04E-03	1.23	9.04E-12	1.18	9.09E-07	1.21	1.56E-09
1q22	155668846	rs190811727	G	A	-0.003	0.85	1.17	1.54E-08	1.18	3.25E-07	1.17	2.79E-08
1q32.1	204029748	rs4593892	T	C	0.000	0.99	1.05	5.38E-10	1.05	8.19E-08	1.05	1.74E-09
1q32.1	204518842	rs4245739	A	C	0.014	1.39E-03	1.09	2.61E-26	1.08	1.97E-14	1.09	5.04E-21
1q32.1	205738302	rs823137	G	A	0.012	1.20E-03	1.05	3.84E-09	1.03	4.87E-04	1.04	1.17E-06
2p25.1	8597123	rs62106670	T	C	-0.005	0.31	1.05	5.98E-09	1.06	8.34E-08	1.05	4.72E-09
2p25.1	10094526	rs73913932	G	A	-0.004	0.58	1.09	2.14E-09	1.09	4.52E-08	1.09	2.75E-09
2p25.1	10781975	rs1990613	T	C	0.003	0.49	1.07	1.87E-19	1.07	7.87E-14	1.07	6.89E-18
2p24.3	16024757	rs12611818	T	G	0.001	0.78	1.05	1.01E-08	1.05	8.64E-07	1.05	3.40E-08
2p24.1	20878105	rs9306894	G	A	0.030	1.53E-14	1.08	1.21E-21	1.04	1.25E-05	1.06	3.03E-11
2p21	43148487	rs4952948	G	A	0.010	0.015	1.04	2.86E-08	1.03	3.32E-04	1.04	1.94E-06
2p21	43637998	rs7591218	A	G	0.015	3.45E-04	1.08	2.54E-24	1.07	3.54E-12	1.08	2.06E-18
2p15	62792689	rs13008096	A	C	0.001	0.84	1.05	2.51E-11	1.05	1.51E-08	1.05	1.28E-10

2p15	63301164	rs6545977	G	A	0.026	4.25E-12	1.12	7.06E-50	1.08	8.93E-21	1.10	3.37E-31
2p15	63982690	rs72808211	G	A	0.016	0.11	1.15	2.85E-11	1.12	3.80E-07	1.14	1.18E-09
2p14	66652885	rs74702681	T	C	0.010	0.45	1.17	9.89E-11	1.16	2.29E-07	1.17	1.24E-09
2p11.2	85764960	rs1446668	G	T	-0.014	3.95E-04	1.09	2.51E-28	1.10	6.18E-30	1.09	1.65E-29
2q13	111893096	rs11691517	T	G	0.007	0.10	1.07	1.33E-13	1.06	2.73E-08	1.06	1.61E-11
2q13	111906762	rs1877330	A	C	0.004	0.60	1.11	6.85E-12	1.10	1.32E-08	1.11	6.30E-11
2q31.1	173287607	rs11686909	G	A	0.001	0.80	1.05	4.66E-10	1.05	1.48E-07	1.05	1.90E-09
2q31.1	173303031	rs28485589	A	G	0.019	0.020	1.27	5.01E-48	1.25	2.56E-31	1.26	1.38E-41
2q33.1	202126615	rs1861270	G	A	0.005	0.28	1.05	2.81E-09	1.05	3.53E-06	1.05	3.14E-08
2q33.3	208118301	rs12621900	C	T	0.006	0.17	1.05	3.45E-08	1.05	2.69E-05	1.05	4.02E-07
2q37.3	238440449	rs11891348	G	T	0.014	2.04E-03	1.07	2.39E-13	1.05	2.39E-06	1.06	5.85E-10
2q37.3	242135265	rs77559646	A	G	0.047	4.96E-04	1.27	1.59E-21	1.21	2.64E-10	1.25	4.32E-16
2q37.3	242139600	rs77482050	G	A	0.057	0.012	1.48	1.45E-22	1.39	6.61E-12	1.44	6.42E-18
2q37.3	242157241	rs76832527	A	G	0.007	0.16	1.10	5.00E-22	1.09	3.18E-14	1.10	2.27E-19
3p24.3	23153062	rs7618603	A	C	0.019	1.15E-04	1.06	3.08E-08	1.03	3.69E-03	1.05	1.33E-05
3p21.31	49626306	rs6446285	G	A	0.005	0.30	1.06	1.12E-08	1.05	1.06E-05	1.06	1.25E-07
3p14.1	64920084	rs55821157	G	A	0.010	0.24	1.11	6.87E-09	1.10	7.07E-06	1.11	8.75E-08
3p13	70874997	rs7622519	G	A	0.017	7.72E-06	1.04	2.46E-08	1.02	7.87E-03	1.04	2.49E-05
3p12.1	87184311	rs6770433	T	C	0.005	0.16	1.12	1.32E-50	1.11	1.94E-34	1.11	1.56E-45
3p11.2	87395326	rs114423020	G	A	0.014	0.19	1.16	4.41E-13	1.14	1.88E-08	1.15	2.05E-11
3q13.12	106962305	rs1283105	G	C	0.000	0.94	1.05	3.71E-11	1.05	1.34E-08	1.05	1.62E-10
3q13.2	113290450	rs13092681	T	C	0.023	1.15E-09	1.09	2.24E-29	1.06	2.12E-11	1.08	1.14E-18
3q21.3	127898501	rs2811476	C	A	0.024	1.79E-08	1.10	4.59E-32	1.07	4.23E-13	1.09	6.04E-21
3q21.3	128275459	rs4857906	C	T	0.010	0.036	1.06	2.74E-11	1.05	2.59E-06	1.06	3.40E-09
3q23	141140968	rs9846396	T	C	0.030	4.68E-15	1.05	2.91E-10	1.01	0.13	1.03	1.43E-04
3q25.1	152004202	rs182314334	T	C	-0.013	0.075	1.09	1.08E-11	1.11	3.05E-11	1.10	3.42E-12
3q26.2	170074517	rs78416326	G	C	0.017	4.31E-04	1.18	4.06E-68	1.16	3.40E-41	1.17	5.67E-56
4q13.3	74326647	rs113573136	T	C	0.005	0.49	1.06	2.50E-10	1.05	2.78E-05	1.05	1.77E-08
4q13.3	74442349	rs17804499	G	C	0.016	0.047	1.17	9.68E-19	1.15	4.02E-12	1.16	3.72E-16
4q22.3	95547467	rs7679542	A	G	0.006	0.11	1.09	5.03E-27	1.08	1.84E-17	1.08	1.22E-23
4q24	106065308	rs10007915	C	G	0.011	5.96E-03	1.13	5.22E-55	1.11	7.46E-34	1.12	2.28E-46

4q31.1	140915940	rs13148756	T	G	-0.006	0.35	1.05	4.50E-08	1.06	2.23E-06	1.05	6.62E-08
5p15.33	1228166	rs114674839	T	C	0.043	1.10E-05	1.12	3.78E-09	1.07	3.78E-03	1.10	6.59E-06
5p15.33	1272074	rs138895564	T	C	0.101	7.29E-06	1.27	1.75E-08	1.13	0.013	1.21	3.34E-05
5p15.33	1280028	rs2242652	G	A	0.011	0.031	1.16	5.75E-51	1.15	6.29E-33	1.16	2.78E-44
5p15.33	1292118	rs71595003	A	G	-0.023	0.059	1.19	1.73E-15	1.22	1.00E-14	1.20	6.15E-16
5p15.33	1895829	rs12653946	T	C	0.010	9.17E-03	1.08	2.57E-22	1.07	1.24E-12	1.07	3.04E-18
5q31.1	133836209	rs10793821	T	C	0.005	0.17	1.06	2.26E-14	1.05	2.54E-09	1.06	1.25E-12
5q35.2	172959030	rs9686557	C	A	0.016	2.42E-05	1.04	4.69E-09	1.03	3.03E-03	1.04	5.84E-06
5q35.3	177891551	rs2672843	G	A	0.006	0.15	1.05	4.19E-09	1.04	1.08E-05	1.04	8.87E-08
6p24.2	11217897	rs2018336	T	C	0.012	6.10E-03	1.07	1.51E-12	1.05	1.61E-06	1.06	7.66E-10
6p22.3	22314766	rs112292679	C	T	-0.001	0.93	1.11	2.02E-08	1.11	8.66E-07	1.11	4.41E-08
6p21.33	30611676	rs1140809	C	A	0.011	4.85E-03	1.05	1.01E-09	1.03	1.27E-04	1.04	2.41E-07
6p21.33	31329386	rs2596546	A	G	0.019	2.58E-06	1.07	4.71E-16	1.04	4.07E-06	1.06	1.31E-10
6p21.32	32604795	rs9272390	T	C	0.007	0.22	1.06	1.62E-11	1.06	1.27E-06	1.06	1.04E-09
6p21.31	34793124	rs9469899	A	G	0.022	1.34E-08	1.05	1.64E-09	1.02	0.017	1.04	2.31E-05
6p21.1	41538545	rs913074	C	T	0.010	0.046	1.09	3.68E-24	1.07	2.22E-12	1.08	3.17E-19
6q14.1	76479489	rs6907476	T	C	0.009	0.093	1.06	6.51E-09	1.05	3.06E-05	1.06	2.18E-07
6q21	109295293	rs2038542	C	T	0.005	0.41	1.08	5.49E-13	1.07	7.33E-09	1.08	1.06E-11
6q22.1	117200434	rs339351	C	A	0.011	7.84E-03	1.09	2.48E-27	1.08	7.00E-16	1.09	2.04E-22
6q23.2	134300641	rs6919121	T	C	0.007	0.061	1.05	4.04E-09	1.04	1.74E-05	1.05	1.33E-07
6q25.2	153430868	rs63739861	A	C	0.002	0.60	1.08	5.55E-22	1.07	4.99E-16	1.07	2.04E-20
6q25.3	160184600	rs144384356	G	A	0.018	0.071	1.13	2.31E-10	1.11	5.70E-06	1.12	1.43E-08
6q25.3	160255934	rs73030808	A	G	0.014	0.011	1.08	1.52E-12	1.06	1.42E-06	1.07	6.66E-10
6q25.3	160560845	rs628031	A	G	0.004	0.32	1.07	2.83E-19	1.07	3.20E-13	1.07	2.31E-17
6q25.3	160584693	rs7749378	A	G	0.013	0.26	1.14	4.28E-09	1.12	6.86E-06	1.13	5.98E-08
6q25.3	160584841	rs116910573	G	A	0.000	0.97	1.13	8.54E-10	1.13	9.59E-08	1.13	2.51E-09
6q25.3	160628128	rs117648937	C	T	0.000	0.99	1.29	1.47E-11	1.29	3.68E-09	1.29	5.41E-11
6q25.3	160822675	rs3105751	G	A	0.018	2.33E-05	1.11	6.02E-39	1.09	1.76E-19	1.10	6.49E-29
7p21.1	20444081	rs6973059	T	C	-0.001	0.76	1.05	8.67E-09	1.05	2.85E-07	1.05	1.74E-08
7p15.3	20999211	rs9655205	C	A	0.028	4.43E-07	1.09	2.22E-24	1.06	7.46E-08	1.08	1.15E-14
7p15.3	21800369	rs10281087	T	G	0.014	3.53E-04	1.04	2.38E-08	1.03	2.39E-03	1.04	7.89E-06

7p15.2	27220831	rs6461992	G	A	0.006	0.43	1.09	7.43E-10	1.09	9.08E-07	1.09	7.79E-09
7p15.2	27976563	rs10486567	G	A	0.049	2.42E-28	1.15	2.48E-53	1.08	4.91E-15	1.12	1.76E-23
7p14.1	40875192	rs17621345	A	C	0.021	1.91E-06	1.07	1.96E-14	1.05	1.19E-05	1.06	1.07E-09
7p12.3	47482829	rs4724578	C	A	0.002	0.61	1.06	2.40E-13	1.05	1.11E-09	1.06	2.59E-12
7p12.3	47506994	rs2964944	C	T	0.015	3.93E-04	1.05	2.61E-08	1.03	1.44E-03	1.04	6.09E-06
7p12.3	47627603	rs112289173	C	T	0.002	0.67	1.07	4.13E-08	1.07	3.19E-06	1.07	1.48E-07
7q21.3	97688440	rs4727386	A	G	0.015	1.11E-03	1.10	6.50E-40	1.09	1.10E-19	1.10	2.33E-30
8p21.3	22879734	rs4871844	T	C	0.020	5.87E-05	1.04	4.75E-08	1.02	0.029	1.04	9.38E-05
8p21.2	23443320	rs11996109	C	A	0.045	1.93E-13	1.06	1.14E-13	1.00	0.63	1.04	5.86E-04
8p21.2	23533623	rs11135766	C	T	0.069	2.27E-72	1.14	4.17E-69	1.05	1.39E-09	1.10	3.00E-16
8p21.2	25892142	rs11135910	T	C	0.006	0.24	1.08	2.23E-13	1.07	6.73E-09	1.08	8.25E-12
8q24.21	127855936	rs4870985	T	C	-0.009	0.036	1.08	1.88E-24	1.09	6.26E-22	1.08	1.12E-24
8q24.21	127906604	rs13282012	G	A	-0.004	0.27	1.10	2.92E-39	1.11	9.19E-33	1.10	1.29E-38
8q24.21	128018466	rs73351629	C	G	0.009	0.020	1.15	9.42E-69	1.14	6.91E-45	1.15	1.17E-59
8q24.21	128077146	rs77541621	A	G	0.048	2.05E-04	1.83	1.13E-174	1.73	1.16E-98	1.79	3.93E-137
8q24.21	128103979	rs5013678	T	C	0.009	0.047	1.20	1.87E-79	1.18	1.07E-54	1.19	3.71E-71
8q24.21	128108418	rs111724742	G	T	0.039	0.066	1.61	3.15E-43	1.54	6.87E-25	1.58	2.61E-36
8q24.21	128117736	rs143368544	T	C	0.050	2.51E-04	1.25	2.48E-17	1.18	5.35E-08	1.22	1.09E-12
8q24.21	128151672	rs17446776	G	C	0.007	0.58	1.25	9.43E-22	1.24	2.48E-15	1.25	6.16E-20
8q24.21	128228233	rs79125478	T	C	0.006	0.52	1.11	1.18E-11	1.10	2.66E-07	1.10	2.95E-10
8q24.21	128294091	rs283713	G	T	0.009	0.16	1.09	1.64E-12	1.08	8.84E-08	1.09	9.92E-11
8q24.21	128324147	rs382434	C	T	0.036	1.98E-14	1.15	1.80E-72	1.11	6.24E-26	1.13	5.03E-39
8q24.21	128376862	rs117627785	T	C	0.040	5.35E-03	1.23	1.36E-13	1.18	6.42E-07	1.21	1.50E-10
8q24.21	128413305	rs6983267	G	T	0.052	1.49E-42	1.23	2.84E-164	1.15	3.71E-63	1.20	8.38E-67
8q24.21	128514011	rs74592433	T	C	0.020	0.13	1.23	8.17E-10	1.20	6.44E-07	1.22	1.01E-08
8q24.21	128532137	rs10090154	T	C	0.012	0.055	1.44	4.15E-225	1.42	4.10E-146	1.43	2.00E-197
8q24.21	128582965	rs73709253	G	A	0.013	0.30	1.14	8.74E-09	1.13	8.58E-06	1.14	9.96E-08
9p22.1	18556233	rs951227	A	G	0.001	0.80	1.05	6.68E-10	1.05	1.84E-07	1.05	3.44E-09
9p22.1	19055965	rs1048169	C	T	0.007	0.085	1.06	2.81E-14	1.05	1.19E-08	1.06	4.18E-12
9p21.3	22041998	rs17694493	G	C	-0.001	0.88	1.08	3.37E-13	1.08	2.27E-10	1.08	1.44E-12
9p13.3	33935073	rs307651	A	C	0.010	0.010	1.05	3.24E-11	1.04	9.30E-06	1.05	9.01E-09

9q21.31	82087596	rs9314679	T	A	-0.011	0.052	1.07	1.02E-08	1.08	2.88E-09	1.08	2.48E-09
9q31.2	110290217	rs143655302	G	A	0.064	5.48E-06	1.27	2.29E-14	1.18	2.63E-06	1.23	3.61E-10
9q34.11	132576060	rs1182	A	C	0.006	0.23	1.06	5.65E-11	1.05	4.42E-07	1.06	1.34E-09
10p15.3	890714	rs34318754	A	G	0.014	5.99E-03	1.08	9.23E-13	1.06	1.17E-06	1.07	5.00E-10
10q11.21	45854778	rs11511618	G	A	0.023	2.58E-06	1.06	1.66E-10	1.04	1.22E-03	1.05	1.01E-06
10q11.22	47671874	rs34583261	C	T	0.019	0.11	1.09	3.52E-08	1.06	2.55E-03	1.08	6.56E-06
10q11.23	51549496	rs10993994	T	C	0.085	2.66E-76	1.23	9.11E-165	1.11	2.35E-32	1.18	1.01E-32
10q23.31	90195149	rs1935581	C	T	-0.006	0.12	1.05	6.36E-09	1.05	6.85E-09	1.05	2.52E-09
10q24.32	104408272	rs12241712	C	A	0.015	2.86E-04	1.07	5.24E-18	1.06	1.35E-08	1.07	2.32E-13
10q25.2	114715598	rs2104598	A	G	0.007	0.069	1.05	3.70E-09	1.04	2.68E-05	1.04	1.35E-07
10q26.12	122787452	rs12245671	G	A	0.001	0.81	1.06	7.05E-14	1.06	2.13E-10	1.06	5.45E-13
10q26.12	123034391	rs4468286	C	A	-0.086	1.82E-89	1.06	2.08E-10	1.17	1.02E-53	1.10	6.06E-11
10q26.13	123190200	rs17101982	C	G	0.101	1.19E-31	1.11	5.40E-09	0.99	0.48	1.05	0.018
10q26.13	126697114	rs4962419	A	G	0.021	6.08E-07	1.06	3.19E-11	1.03	1.23E-03	1.05	5.79E-07
11p15.5	1507512	rs1881502	T	C	0.003	0.54	1.06	3.04E-09	1.05	1.37E-06	1.06	2.10E-08
11p15.5	2233797	rs10840603	A	G	0.018	2.61E-04	1.18	1.04E-68	1.15	1.06E-38	1.17	3.73E-54
11p15.4	7547587	rs61890184	A	G	-0.004	0.45	1.08	2.73E-10	1.08	6.35E-09	1.08	3.59E-10
11q12.3	61908440	rs2277283	C	T	0.006	0.12	1.05	1.61E-10	1.05	1.34E-06	1.05	4.55E-09
11q13.2	66951965	rs12785905	C	G	0.015	0.075	1.12	5.10E-10	1.10	3.32E-06	1.11	1.68E-08
11q13.3	68912221	rs3018667	G	A	-0.001	0.90	1.06	5.04E-15	1.06	7.74E-12	1.06	2.36E-14
11q13.3	68981359	rs12275055	G	A	0.015	3.49E-03	1.25	2.76E-111	1.23	2.00E-70	1.24	1.06E-93
11q13.3	69071624	rs11228619	G	A	0.012	0.14	1.10	5.33E-10	1.09	5.79E-06	1.09	1.97E-08
11q13.3	69456000	rs55911137	C	G	0.030	0.014	1.20	4.32E-14	1.16	1.25E-07	1.18	3.00E-11
11q13.5	76251818	rs17749618	A	G	0.021	2.32E-07	1.06	8.08E-13	1.03	3.02E-04	1.05	5.80E-08
11q22.2	102396607	rs12285347	T	C	-0.039	6.15E-25	1.08	4.01E-21	1.12	5.79E-40	1.10	9.39E-22
11q22.3	108357137	rs74911261	A	G	0.037	1.95E-03	1.15	1.05E-08	1.11	3.98E-04	1.13	1.58E-06
11q23.2	113807181	rs11214775	G	A	0.008	0.063	1.07	1.88E-16	1.06	3.21E-10	1.07	4.68E-14
11q24.2	125144426	rs117015177	G	A	0.058	2.38E-04	1.20	1.69E-08	1.13	1.40E-03	1.17	5.11E-06
11q25	134266372	rs878987	G	A	-0.002	0.68	1.07	1.87E-10	1.07	7.37E-09	1.07	2.99E-10
12p13.1	12871099	rs2066827	T	G	0.011	0.040	1.05	4.42E-09	1.04	1.64E-04	1.05	4.48E-07
12p13.1	14416918	rs10845938	G	A	0.001	0.74	1.06	2.60E-15	1.06	2.19E-11	1.06	2.68E-14

12q13.11	48419618	rs80130819	A	C	-0.004	0.52	1.10	1.05E-11	1.10	5.71E-10	1.10	1.67E-11
12q13.12	49676010	rs10875943	C	T	0.000	0.99	1.08	1.49E-19	1.08	9.20E-15	1.08	2.20E-18
12q13.13	53312612	rs73110464	T	C	0.009	0.13	1.18	4.82E-51	1.17	3.95E-33	1.17	5.86E-45
12q14.2	65012824	rs7968403	T	C	-0.003	0.52	1.06	7.22E-14	1.06	1.05E-11	1.06	1.42E-13
12q21.33	90192866	rs4842503	G	A	0.004	0.39	1.06	3.78E-12	1.05	2.60E-08	1.06	7.56E-11
12q24.21	114666202	rs10774740	G	T	0.013	1.36E-03	1.08	3.77E-22	1.06	1.23E-11	1.07	2.69E-17
12q24.33	133067989	rs7295014	G	A	0.015	4.68E-04	1.05	1.69E-09	1.03	8.67E-04	1.04	1.44E-06
13q22.1	73719777	rs9543236	T	C	0.012	0.015	1.07	1.55E-11	1.05	2.59E-06	1.06	2.78E-09
13q22.1	73995877	rs7336001	G	C	0.038	5.88E-08	1.10	2.27E-11	1.06	1.07E-03	1.08	5.14E-07
14q11.2	23305649	rs1004030	T	C	0.006	0.15	1.05	8.17E-10	1.04	4.31E-06	1.05	2.18E-08
14q13.3	37137280	rs12893199	C	T	0.007	0.072	1.06	4.27E-13	1.05	8.33E-08	1.05	4.97E-11
14q22.1	53375302	rs7141054	A	C	0.011	0.023	1.09	6.27E-18	1.07	2.00E-10	1.08	8.59E-15
14q24.1	69027523	rs34882439	G	A	0.004	0.31	1.06	1.11E-10	1.05	3.93E-07	1.05	2.10E-09
14q24.1	69134264	rs767127	G	A	0.003	0.52	1.05	2.69E-12	1.05	1.03E-08	1.05	2.97E-11
14q24.2	71091142	rs11158871	C	T	-0.003	0.40	1.05	1.23E-08	1.05	7.15E-08	1.05	9.08E-09
15q13.3	33417586	rs1902149	G	A	-0.004	0.32	1.04	4.84E-08	1.05	1.97E-07	1.05	4.00E-08
15q15.1	40922915	rs4924487	C	G	0.015	3.18E-03	1.07	3.03E-10	1.05	7.48E-05	1.06	1.16E-07
15q21.3	56385868	rs33984059	A	G	-0.008	0.51	1.19	1.62E-09	1.20	1.16E-08	1.20	1.66E-09
15q22.31	66705043	rs80326387	A	G	0.004	0.35	1.05	2.13E-09	1.05	2.16E-06	1.05	2.10E-08
16q12.2	54473072	rs1420285	C	T	0.006	0.13	1.05	1.47E-08	1.04	2.82E-05	1.04	3.14E-07
16q21	57654576	rs11863709	C	T	-0.002	0.86	1.15	1.43E-11	1.16	2.40E-09	1.15	4.11E-11
16q21	57693055	rs16958674	C	T	0.013	0.011	1.06	2.14E-09	1.04	1.75E-04	1.05	4.11E-07
16q23.3	82166181	rs8052913	C	T	0.017	1.27E-05	1.04	3.71E-08	1.02	0.011	1.03	3.50E-05
17p13.3	618965	rs684232	C	T	0.008	0.053	1.09	1.77E-26	1.08	2.26E-16	1.08	1.10E-22
17p13.1	7571752	rs78378222	G	T	0.112	4.08E-10	1.25	4.78E-11	1.10	0.013	1.19	6.80E-06
17p13.1	7803118	rs28441558	C	T	0.042	3.34E-07	1.16	3.51E-19	1.11	1.05E-07	1.14	7.97E-13
17q11.2	30098749	rs142444269	C	T	0.010	0.096	1.07	1.45E-11	1.06	2.18E-06	1.06	1.72E-09
17q12	36047417	rs3110641	A	G	0.011	0.025	1.07	1.24E-12	1.05	8.73E-07	1.06	3.65E-10
17q12	36074979	rs11649743	G	A	0.014	3.21E-03	1.13	7.16E-38	1.11	2.58E-22	1.12	3.61E-31
17q12	36103565	rs11263763	A	G	0.049	3.13E-38	1.23	3.63E-162	1.16	5.06E-65	1.20	3.71E-70
17q12	36229129	rs8081051	A	C	0.007	0.22	1.05	1.35E-08	1.04	9.01E-05	1.05	3.84E-07

17q21.32	45993959	rs199905768	A	C	0.020	0.51	1.19	3.79E-09	1.17	8.14E-04	1.18	6.79E-07
17q21.32	46546346	rs12944450	T	C	-0.025	0.18	1.14	7.44E-09	1.17	3.14E-07	1.15	7.58E-09
17q21.32	46820676	rs117576373	T	C	0.009	0.34	1.21	4.88E-24	1.20	8.71E-17	1.20	8.32E-22
17q21.33	47451749	rs9893373	G	A	-0.003	0.58	1.05	1.93E-08	1.05	5.65E-07	1.05	3.13E-08
17q21.33	47455752	rs73324348	A	G	0.011	0.13	1.11	5.81E-14	1.10	8.02E-09	1.10	4.51E-12
17q22	56456120	rs2680708	G	A	0.014	3.57E-04	1.05	5.64E-09	1.03	1.07E-03	1.04	2.59E-06
17q24.3	69115358	rs9911515	A	G	0.002	0.53	1.17	7.26E-100	1.17	8.68E-73	1.17	3.78E-93
18q21.2	51771322	rs8089411	C	T	0.015	6.59E-05	1.04	1.98E-08	1.03	3.83E-03	1.04	1.18E-05
18q21.2	53230859	rs28607662	C	T	0.010	0.14	1.07	2.68E-08	1.06	5.14E-05	1.07	5.22E-07
18q21.32	56744666	rs12327532	G	T	0.013	1.70E-03	1.04	4.38E-08	1.03	1.66E-03	1.04	7.77E-06
18q21.33	60998567	rs2850766	C	G	-0.004	0.53	1.05	3.83E-08	1.05	6.16E-06	1.05	8.58E-08
18q22.3	73036165	rs10460109	T	C	0.001	0.78	1.04	1.56E-08	1.04	1.85E-06	1.04	5.31E-08
18q23	76770820	rs9959454	A	G	0.025	3.29E-09	1.08	7.09E-22	1.05	9.76E-08	1.07	1.74E-13
19p13.11	17214073	rs11666569	C	T	0.009	0.033	1.05	3.61E-09	1.04	4.23E-05	1.05	1.84E-07
19q13.13	38555154	rs35486025	T	C	-0.0004	0.94	1.06	8.95E-10	1.06	7.83E-08	1.06	2.61E-09
19q13.2	38744733	rs12610267	A	G	0.010	0.010	1.10	1.24E-36	1.09	5.04E-22	1.09	9.44E-31
19q13.2	41985931	rs11673591	T	A	-0.005	0.28	1.09	1.32E-23	1.10	2.88E-20	1.09	3.53E-23
19q13.33	51340794	rs2659053	A	G	0.082	4.35E-92	1.06	9.76E-15	0.97	2.37E-04	1.02	0.12
19q13.33	51362715	rs76765083	T	G	0.366	6.0E-604	1.35	4.99E-90	0.89	7.21E-12	1.14	0.013
20q11.22	34003073	rs142570322	C	T	0.023	3.49E-04	1.04	2.60E-08	1.02	0.096	1.03	2.50E-04
20q13.13	49548807	rs73909841	T	C	0.019	8.71E-03	1.11	3.28E-12	1.08	1.88E-06	1.10	1.14E-09
20q13.2	52455205	rs6091758	G	A	0.009	0.15	1.07	1.59E-17	1.06	1.09E-07	1.06	2.36E-13
20q13.33	61015240	rs34585497	A	C	0.015	4.87E-04	1.04	2.05E-08	1.03	3.30E-03	1.04	1.05E-05
20q13.33	62272248	rs2259797	T	C	0.025	5.78E-04	1.08	1.74E-08	1.05	1.77E-03	1.07	5.82E-06
20q13.33	62310240	rs62207046	C	A	0.007	0.41	1.09	3.73E-09	1.08	2.23E-05	1.08	8.80E-08
20q13.33	62374389	rs1058319	C	T	0.016	5.10E-03	1.12	1.82E-23	1.10	1.74E-13	1.11	3.44E-19
21q22.3	42866332	rs61735792	A	G	0.006	0.75	1.26	6.95E-14	1.26	9.43E-10	1.26	1.04E-12
21q22.3	42889410	rs112714648	A	G	-0.002	0.67	1.06	1.66E-13	1.07	3.41E-11	1.06	3.22E-13
22q11.21	19749525	rs1978060	G	A	0.009	0.080	1.06	1.05E-11	1.04	1.26E-05	1.05	3.73E-09
22q12.1	28888939	rs9625483	A	G	0.023	0.087	1.14	3.82E-09	1.11	7.42E-05	1.13	2.45E-07
22q13.1	40499103	rs34419824	T	A	0.001	0.80	1.08	2.54E-15	1.07	2.41E-11	1.08	3.04E-14

22q13.2	43500212	rs5759167	G	T	0.007	0.058	1.15	3.38E-78	1.14	4.15E-53	1.15	6.09E-70
22q13.2	43502152	rs2007886	T	C	0.016	0.011	1.10	2.51E-14	1.08	4.48E-08	1.09	1.21E-11

¹ Index variants were selected using LD-based clumping: $r^2 < 0.01$ within ± 10 Mb

² Per allele change in log(PSA)

³ Bias-corrected estimated were obtained as follows: $\beta^{adj} = \beta - b * \beta_{PSA}$ and the corresponding $OR^{adj} = \exp(\beta^{adj})$ where b is estimated using the Dudbridge method

⁴ Bias-corrected estimated were obtained as follows: $\beta^{adj} = \beta - b * \beta_{PSA}$ and the corresponding $OR^{adj} = \exp(\beta^{adj})$ where b is estimated using SlopeHunter

Supplementary Table 11: Development and validation of a polygenic score for PSA levels. Associations with baseline PSA in cancer-free participants from the Prostate Cancer Prevention Trial (PCPT) and Selenium and Vitamin E Cancer Prevention Trial (SELECT) were estimated using linear regression models. All p-values are two-sided. Effect estimates are presented for a 128-variant PSA polygenic score (PGS₁₂₈) developed based on clumping and thresholding (LD $r^2 < 0.01$, $P < 5 \times 10^{-8}$) and a genome-wide polygenic score with continuous shrinkage priors (PGS_{CSx}) comprised of 1,058,173 and 1,071,278 variants in PCPT and SELECT, respectively.

Study	Ancestry ¹	N	PGS ₁₂₈				PGS _{CSx}			
			β_{PGS}^2	(SE)	P	(%)	β_{PGS}^2	(SE)	P	(%)
PCPT	Pooled ³	5,883	0.168	(0.008)	1.61×10^{-98}	7.16	0.186	(0.008)	3.26×10^{-112}	8.13
	EUR	5,725	0.169	(0.008)	5.29×10^{-98}	7.33	0.194	(0.008)	1.69×10^{-115}	8.60
	AFR/EUR	103	0.088	(0.080)	0.27	-	0.029	(0.055)	0.59	-
	EAS	55	0.104	(0.126)	0.41	-	0.062	(0.109)	0.57	-
SELECT	Pooled ³	25,917	0.207	(0.004)	6.69×10^{-505}	8.00	0.258	(0.005)	1.25×10^{-619}	9.61
	EUR	22,173	0.213	(0.005)	4.24×10^{-478}	8.78	0.283	(0.005)	5.51×10^{-610}	10.94
	AFR pooled	2,936	0.154	(0.015)	1.97×10^{-24}	3.36	0.134	(0.014)	9.39×10^{-23}	3.11
	AFR/EUR	1,763	0.146	(0.018)	3.00×10^{-15}	3.32	0.157	(0.017)	4.77×10^{-19}	4.22
	AFR	1,173	0.163	(0.025)	8.22×10^{-11}	3.45	0.098	(0.022)	8.04×10^{-6}	1.64
	EAS pooled	578	0.190	(0.032)	7.24×10^{-9}	5.60	0.283	(0.033)	4.94×10^{-17}	11.39
	EAS/EUR	321	0.229	(0.042)	8.46×10^{-8}	8.45	0.315	(0.044)	5.15×10^{-12}	13.61
	EAS	257	0.136	(0.054)	0.012	2.45	0.258	(0.050)	5.94×10^{-7}	9.22

¹ Individuals were assigned to a global ancestry cluster if their ancestry score exceeded 0.80 for a single group. Individuals with ancestry scores that were >0.20 and <0.80 for at least one ancestry were designated to admixed clusters. The AFR/EUR admixed cluster includes participants with $0.20 < \text{AFR} < 0.80$ and EAS/EUR includes participants with $0.20 < \text{EAS} < 0.80$. AFR pooled combines the AFR and AFR/EUR clusters. EAS pooled combines the EAS and EAS/EUR clusters. Up to 10 genetic ancestry principal components were calculated within each global ancestry cluster.

² Effect per standard deviation increase in the standardized PGS on baseline log(PSA), derived from a linear regression model adjusted for age at PSA measurement and the top 10 population-specific genetic ancestry principal components.

³ Global genetic ancestry proportions (AFR, EAS) were included as covariates in addition to the top 10 population-specific principal components in the pooled analysis including all ancestries

Supplementary Table 12: Polygenic score associations with measures of temporal change in PSA levels.

Associations with metrics of temporal change in PSA were estimated in participants from the Prostate Cancer Prevention Trial (PCPT) and Selenium and Vitamin E Cancer Prevention Trial (SELECT) using linear regression. All p-values are two-sided. Temporal phenotypes were derived using PSA measures in men without prostate cancer or pre-diagnostic PSA values for men who were diagnosed with prostate cancer during the follow up period. Effect estimates are presented for a 128-variant PSA polygenic score (PGS₁₂₈) developed based on clumping and thresholding (LD $r^2 < 0.01$, $P < 5 \times 10^{-8}$) and a genome-wide polygenic score with continuous shrinkage priors (PGS_{CSx}) comprised of 1,058,173 and 1,071,278 variants in PCPT and SELECT, respectively. Pooled analyses included individuals of all ancestries.

Phenotype ^{1,2}		Predictor	N	SELECT			PCPT			
				β^3	(SE)	P	N	β^3	(SE)	P
PSA Increase	Velocity	PGS ₁₂₈	14908	-3.30×10 ⁻⁴	(8.6×10 ⁻⁵)	1.3×10 ⁻⁴	2933	-2.34×10 ⁻⁴	(1.2×10 ⁻⁴)	0.052
		PGS _{CSx}		-4.06×10 ⁻⁴	(9.8×10 ⁻⁵)	3.7×10 ⁻⁵		-2.65×10 ⁻⁴	(1.3×10 ⁻⁴)	0.034
	log(Velocity)	PGS ₁₂₈		-0.033	(0.007)	3.2×10 ⁻⁶		-0.039	(0.015)	6.8×10 ⁻³
		PGS _{CSx}		-0.041	(0.008)	4.4×10 ⁻⁷		-0.048	(0.015)	1.5×10 ⁻³
	Doubling time	PGS ₁₂₈		8.44	(1.62)	2.0×10 ⁻⁷		10.25	(3.14)	1.1×10 ⁻³
		PGS _{CSx}		10.37	(1.85)	2.2×10 ⁻⁸		12.88	(3.25)	7.2×10 ⁻⁵
PSA Decrease	Velocity	PGS ₁₂₈	6970	3.08×10 ⁻⁴	(2.3×10 ⁻⁴)	0.21	1728	-4.70×10 ⁻⁵	(1.5×10 ⁻⁴)	0.75
		PGS _{CSx}		5.02×10 ⁻⁴	(2.7×10 ⁻⁴)	0.067		-7.92×10 ⁻⁵	(1.5×10 ⁻⁴)	0.61
Any PSA change	Velocity	PGS ₁₂₈	21878	3.22×10 ⁻⁶	(3.7×10 ⁻⁶)	0.39	4745	-7.95×10 ⁻⁶	(4.7×10 ⁻⁵)	0.089
		PGS _{CSx}		3.50×10 ⁻⁶	(4.2×10 ⁻⁶)	0.41		-1.02×10 ⁻⁵	(4.9×10 ⁻⁶)	0.035
	Doubling time	PGS ₁₂₈		4.79	(1.92)	0.013		3.33	3.59	0.35
		PGS _{CSx}		3.65	(2.18)	0.094		3.44	3.73	0.36

¹ PSA velocity was calculated as the difference between the first and last log(PSA) values divided by the elapsed time in months: last[log(PSA)] - first[log(PSA)] / elapsed time. Due to the highly skewed velocity distribution estimates are also presented for log-transformed velocity.

² PSA doubling time calculated as: log(2)/(PSA velocity). Associations with negative doubling time are not reported, but negative values were included in the combined analysis of any (positive or negative) change in PSA levels.

³ Associations were estimated per SD increase in PGS using linear regression with adjustment for age at baseline, randomization arm, top 10 population-specific genetic ancestry principal components, and global ancestry proportions (AFR, ASN)

Supplementary Table 13: Impact of index bias correction on associations between genetics scores for PSA levels and prostate cancer. Associations between genetic scores for PSA and prostate cancer were estimated using linear regression models in men of European ancestry from the UK Biobank who were excluded from the PSA GWAS. All p-values are two-sided. For PSA, a genome-wide polygenic score with continuous shrinkage priors (PGS_{CSx}) comprised of 1,197,312 variants was used. For prostate cancer, the 269-variant polygenic risk score (PGS₂₆₉), as described in Conti et al.³² was used. Associations were compared with two versions of the bias-corrected risk scores, one with risk allele weights corrected using the Dudbridge method³³ (PGS₂₆₉^{adj}) and another version of the score with risk allele weights derived using SlopeHunter³⁵ (PGS₂₆₉^{adj-S}).

Sample size		Original (PGS ₂₆₉)			Bias-corrected (PGS ₂₆₉ ^{adj})			Bias-corrected (PGS ₂₆₉ ^{adj-S})		
		β^1	(SE)	P	β^2	(SE)	P	β^3	(SE)	P
Combined	164,452	0.241	(0.002)	2.7×10^{-2174}	0.063	(0.002)	2.1×10^{-144}	0.176	(0.002)	2.3×10^{-1128}
Cases	11,568	0.190	(0.009)	2.3×10^{-96}	0.029	(0.009)	2.7×10^{-3}	0.130	(0.009)	1.1×10^{-45}
Controls	152,884	0.236	(0.003)	6.7×10^{-1881}	0.052	(0.003)	2.2×10^{-89}	0.169	(0.003)	1.5×10^{-948}

¹ Effect estimate per standard deviation increase in PGS₂₆₉ on PGS_{PSA}, estimated using a linear regression model with adjustment genetic ancestry principal components and genotyping array

² Effect estimate per standard deviation increase in PGS₂₆₉^{adj} on PGS_{PSA}, where PGS₂₆₉^{adj} has bias-corrected risk allele weights based on the Dudbridge estimate of index event bias. Linear regression model was adjusted for the top 10 genetic ancestry principal components and genotyping array

³ Effect estimate per standard deviation increase in PGS₂₆₉^{adj-S} on PGS_{PSA}, where PGS₂₆₉^{adj} has bias-corrected risk allele weights based on the SlopeHunter estimate of index event bias. Linear regression model was adjusted for the top 10 genetic ancestry principal components and genotyping array

Supplementary Table 14: Impact of index bias corrections on associations with prostate cancer, overall and stratified by Gleason score. Associations with prostate cancer status were compared for the 269-variant genetic risk score (PGS₂₆₉), as described in Conti & Darst et al. (2021)³², and two versions of this score calculated with weights corrected for index event bias using the Dudbridge et al. method³³ (PGS₂₆₉^{adj}) and SlopeHunter³⁵ (PGS₂₆₉^{adj-S}). Associations were estimated in Genetic Epidemiology Research in Adult Health and Aging (GERA) cases (n=3673) and controls (n=2363) of European ancestry who underwent a prostate biopsy.

	Predictor	Association Estimates					
		OR ^{1,2}	(95% CI)	P	AUC ³	(95% CI)	P _{AUC} ⁴
All cases	PGS ₂₆₉	2.71	(2.28 – 3.21)	2.85×10 ⁻³⁰	0.677	(0.634 – 0.719)	-
	PGS ₂₆₉ ^{adj}	3.63	(3.01 – 4.37)	4.87×10 ⁻⁴²	0.685	(0.643 – 0.727)	3.91×10 ⁻³
	PGS ₂₆₉ ^{adj-S}	3.30	(2.76 – 3.95)	4.53×10 ⁻³⁹	0.683	(0.640 – 0.723)	9.77×10 ⁻³
Gleason score <7	PGS ₂₆₉	3.00	(2.49 – 3.61)	1.42×10 ⁻³⁰	0.680	(0.629 – 0.731)	-
	PGS ₂₆₉ ^{adj}	3.78	(3.09 – 4.63)	5.08×10 ⁻³⁸	0.686	(0.635 – 0.736)	0.064
	PGS ₂₆₉ ^{adj-S}	3.57	(2.94 – 4.34)	2.03×10 ⁻³⁷	0.686	(0.635 – 0.736)	0.151
Gleason score ≥7	PGS ₂₆₉	2.36	(1.92 – 2.91)	1.15×10 ⁻¹⁵	0.678	(0.619 – 0.736)	-
	PGS ₂₆₉ ^{adj}	3.58	(2.87 – 4.47)	8.53×10 ⁻³⁰	0.692	(0.634 – 0.750)	1.91×10 ⁻³
	PGS ₂₆₉ ^{adj-S}	3.02	(2.43 – 3.75)	1.27×10 ⁻²³	0.688	(0.629 – 0.744)	3.91×10 ⁻³

¹ Odds ratios (OR) were estimated for a dichotomized PGS comparing the top decile to the rest

² Logistic regression models were adjusted for the top 10 genetic ancestry principal components and a combined variable for genotyping array and DNA collection kit (chip-kit)

³ AUC estimates and bootstrapped confidence intervals were obtained using 10-fold cross-validation

⁴ Paired Wilcoxon rank sum test was used to compare AUC distributions across 10 folds

Supplementary Table 15: Case-only associations with prostate cancer aggressiveness. Prostate cancer patients were stratified based on disease aggressiveness as indicated by the Gleason score. Associations were estimated for a genome-wide PSA polygenic score comprised of 1,255,848 variants (PGS_{CSx}), an established 269-variant prostate cancer genetic risk score (PGS₂₆₉) as described in Conti & Darst et al. (2021), and two versions of this score calculated with weights corrected for index event bias using the Dudbridge et al. method³³ (PGS₂₆₉^{adj}) and SlopeHunter³⁵ (PGS₂₆₉^{adj-S}). Two-sided p-values, odds ratios (OR), and corresponding 95% confidence intervals were estimated using multinomial logistic regression. Analyses were performed in 4584 prostate cancer cases of European ancestry from the Genetic Epidemiology Research in Adult Health and Aging (GERA) cohort.

	N	(%)	Predictor	Continuous PGS ^{1,2}			Dichotomized PGS ^{2,3}		
				OR	(95% CI)	P	OR	(95% CI)	P
Gleason score ≤6	2798	(61.0)	-	1.00	-	-	1.00	-	-
Gleason score = 7	1366	(29.8)	PGS _{PSA}	0.79	(0.76 – 0.83)	8.48×10 ⁻⁹	0.79	(0.63 – 0.99)	0.048
			PGS ₂₆₉	0.98	(0.91 – 1.05)	0.52	0.99	(0.85 – 1.17)	0.94
			PGS ₂₆₉ ^{adj}	1.03	(0.97 – 1.11)	0.35	1.05	(0.86 – 1.23)	0.58
			PGS ₂₆₉ ^{adj-S}	1.00	(0.93 – 1.07)	0.95	1.05	(0.89 – 1.23)	0.56
Gleason score ≥8	420	(9.2)	PGS _{PSA}	0.71	(0.64 – 0.81)	1.61×10 ⁻⁷	0.73	(0.49 – 1.07)	0.11
			PGS ₂₆₉	0.87	(0.77 – 0.97)	0.011	0.72	(0.54 – 0.96)	0.024
			PGS ₂₆₉ ^{adj}	0.95	(0.85 – 1.06)	0.34	0.94	(0.75 – 1.17)	0.56
			PGS ₂₆₉ ^{adj-S}	0.90	(0.80 – 1.00)	0.053	0.93	(0.71 – 1.23)	0.62

¹ Each PGS was standardized to have a mean of 0 and standard deviation (SD) of 1 in the full GERA cohort, including cases and controls. Odds ratio (OR) were estimated per SD increase in PGS

² Associations were estimated using multinomial logistic regression with Gleason score as the outcome, operationalized as a three-level ordinal variable. Models for each PGS were adjusted for the top 10 genetic ancestry principal components and a combined variable for genotyping array and DNA collection kit

³ Odds ratios (OR) were estimated for a dichotomized PGS comparing those in the top decile to the rest of the PGS distribution

Supplementary Table 16: Impact of genetic adjustment of PSA levels on prostate biopsy referral status.

Genetic adjustment of PSA levels was implemented using a multi-ancestry genome-wide PSA polygenic score comprised of 1,255,848 variants (PGS_{PSA}). Changes in biopsy eligibility based on genetically adjusted PSA values were assessed for participants who underwent a biopsy in the Genetic Epidemiology Research in Adult Health and Aging (GERA) cohort. Reclassification was assessed with respect to age-specific PSA cut-points used to guide biopsy referral in the Kaiser Permanente health system.

Ancestry	PGS _{PSA} ¹	PSA (ng/mL) ²	Re-classification Status						Total	Net Reclassification ³	
			Eligible		Ineligible		Unchanged			%	(95% CI)
European	Mean	Mean	N	(%)	N	(%)	N	(%)	N	%	(95% CI)
Cases	0.278	5.67	138	(3.76)	453	(12.33)	3082	(83.91)	3673	-8.58	(-9.48, -7.67)
Gleason score <7	0.346	4.45	73	(3.59)	300	(14.73)	1663	(81.68)	2036	-11.15	(-12.52, -9.78)
Gleason score ≥7	0.115	6.96	51	(3.71)	117	(8.53)	1204	(87.76)	1372	-4.81	(-5.94, -3.68)
Gleason score missing	0.238	6.67	14	(5.28)	36	(13.58)	215	(81.13)	265	-8.30	(-11.62, -4.98)
Age at biopsy <65 years	0.358	4.75	22	(1.80)	179	(14.67)	1019	(83.52)	1220	-12.87	(-14.74, -10.99)
Controls	0.934	4.49	59	(2.49)	753	(31.87)	1551	(65.64)	2363	29.37	(27.53, 31.21)
Age at biopsy <65 years	1.140	4.57	8	(0.85)	349	(37.09)	584	(62.06)	941	36.23	(33.17, 39.31)
Controls without biopsy	-0.099	1.49	-	-	-	-	-	-	-	-	
African	Mean	Mean	N	(%)	N	(%)	N	(%)	N	%	(95% CI)
Cases	0.091	3.47	12	(3.06)	18	(4.59)	362	(92.35)	392	-1.53	(-2.75, -0.32)
Gleason score <7	0.117	3.40	11	(5.34)	14	(6.80)	181	(87.86)	206	-1.46	(-3.09, 0.18)
Gleason score ≥7	0.047	3.38	0	(0.0)	3	(1.79)	165	(98.21)	168	-1.79	(-3.79, 0.22)
Gleason score missing	0.096	4.82	1	(5.56)	1	(5.56)	16	(88.89)	18	0	-
Age at biopsy <65 years	0.151	3.33	3	(1.33)	13	(5.78)	209	(92.89)	225	-4.44	(-7.14, -1.75)
Controls	1.710	5.13	2	(1.85)	75	(69.44)	31	(28.70)	108	66.06	(58.77, 76.42)
Age at biopsy <65 years	2.009	4.74	0	(0.0)	39	(82.98)	8	(17.02)	47	82.98	(72.23, 93.73)
Controls without biopsy	-0.079	1.51	-	-	-	-	-	-	-	-	

¹ Mean values of the standardized PGS_{PSA} were calculated in each subset of participants. PGS_{PSA} was transformed to a z-score with mean equal to 0 and standard deviation equal to 1 based on the full GERA cohort. Therefore, a value of ~0.5 is equivalent to a PGS value approximately half SD above the mean

² For each participant who underwent a biopsy PSA values closest to the time of biopsy were selected. For controls who did not have a biopsy we first summarized all available PSA values for each participant by taking the median and then calculated the mean PSA value across participants

³ Net re-classification (NR) was tabulated separately for cases as: $NR_{case} = eligible(\%) - ineligible(\%)$ and for controls as $NR_{control} = ineligible(\%) - eligible(\%)$. Confidence intervals for each NR proportion were calculated using the normal approximation: $p \pm 1.96 \times \sqrt{p(1-p)/n}$

Supplementary Table 17: Comparison of logistic regression models for incident prostate cancer in the Prostate Cancer Prevention Trial (PCPT). Pooled analyses include 335 cases and 5548 controls of all ancestries (European ancestry: 323 cases and 5402 controls). Models are indexed from M₀ to M₈. Odds ratios (OR), corresponding 95% confidence intervals, and two-sided p-values are presented for PSA variables and polygenic scores (PGS) only. AUC is based on the full model with all covariates.

Models		Predictor	Association Estimates					
Pooled (Multi-ancestry)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.5856	(0.5542 – 0.6169)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	1.85	(1.54 – 2.24)	1.4×10 ⁻¹⁰	0.6323	(0.6029 – 0.6617)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	1.83	(1.51 – 2.21)	4.4×10 ⁻¹⁰	0.6443	(0.6142 – 0.6745)	vs M ₁ = 0.21
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	1.01	(0.90 – 1.14)	0.83	0.5950	(0.5642 – 0.6259)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.52	(1.36 – 1.70)	3.9×10 ⁻¹³	0.6528	(0.6232 – 0.6824)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.57	(1.40 – 1.76)	7.8×10 ⁻¹⁵	0.6561	(0.6262 – 0.6859)	vs M ₄ = 0.52
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	1.47	(1.31 – 1.65)	3.6×10 ⁻¹¹	0.6800	(0.6519 – 0.7082)	vs M ₂ = 2.9×10 ⁻³ vs M ₄ = 1.1×10 ⁻³
		log(PSA)	1.72	(1.42 – 2.09)	3.7×10 ⁻⁸			
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	1.52	(1.36 – 1.70)	4.3×10 ⁻¹³	0.6848	(0.6566 – 0.7130)	vs M ₄ = 5.5×10 ⁻⁴ vs M ₆ = 0.24
		log(PSA ^G)	1.85	(1.52 – 2.24)	4.8×10 ⁻¹⁰			
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	1.55	(1.39 – 1.74)	3.0×10 ⁻¹⁴	0.6855	(0.6570 – 0.7139)	vs M ₅ = 7.5×10 ⁻⁴ vs M ₇ = 0.87
		log(PSA ^G)	1.81	(1.49 – 2.19)	1.6×10 ⁻⁹			
European ancestry			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.5895	(0.5576 – 0.6213)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	1.88	(1.55 – 2.29)	1.8×10 ⁻¹⁰	0.6391	(0.6094 – 0.6688)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	1.90	(1.56 – 2.31)	1.3×10 ⁻¹⁰	0.6486	(0.6187 – 0.6786)	vs M ₁ = 0.24
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	1.01	(0.90 – 1.14)	0.86	0.6054	(0.5744 – 0.6364)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.53	(1.36 – 1.72)	4.6×10 ⁻¹³	0.6550	(0.6251 – 0.6848)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.57	(1.40 – 1.76)	1.9×10 ⁻¹⁴	0.6584	(0.6282 – 0.6885)	vs M ₄ = 0.49
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	1.48	(1.32 – 1.66)	4.2×10 ⁻¹¹	0.6817	(0.6531 – 0.7104)	vs M ₂ = 5.2×10 ⁻³ vs M ₄ = 1.9×10 ⁻³
		log(PSA)	1.77	(1.45 – 2.15)	1.6×10 ⁻⁸			
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	1.53	(1.37 – 1.73)	4.5×10 ⁻¹³	0.6870	(0.6586 – 0.7155)	vs M ₄ = 8.2×10 ⁻⁴ vs M ₆ = 0.19
		log(PSA ^G)	1.92	(1.57 – 2.34)	1.2×10 ⁻¹⁰			
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	1.55	(1.38 – 1.74)	7.2×10 ⁻¹⁴	0.6875	(0.6589 – 0.7162)	vs M ₅ = 1.4×10 ⁻³ vs M ₇ = 0.90
		log(PSA ^G)	1.88	(1.55 – 2.29)	4.3×10 ⁻¹⁰			

¹ Odds ratios were estimated per standard deviation increase in standardized PGS₂₆₉ and PGS_{PSA}. Models with genetic predictors (PSA^G, PGS₂₆₉, PGS₂₆₉^{adj}, and PGS_{PSA}) were adjusted for the top 10 genetic ancestry principal components and global ancestry proportions in the pooled analysis.

² Two-sided p-values based on De Long's test for two correlated ROC curves.

Supplementary Table 18: Comparison of logistic regression models for incident aggressive prostate cancer in the Prostate Cancer Prevention Trial (PCPT). Pooled, multi-ancestry analyses include 75 cases and 5548 controls (European ancestry: 71 cases, 5402 controls). Models are indexed from M₀ to M₈. Odds ratios (OR), corresponding 95% confidence intervals, and two-sided p-values are presented for PSA variables and polygenic scores (PGS) only. AUC is based on the full model with all covariates.

Models		Predictor	Association Estimates					
Pooled (Multi-ancestry)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.5647	(0.5007 – 0.6287)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	2.84	(1.86 – 4.31)	1.2×10 ⁻⁶	0.6781	(0.6190 – 0.7371)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	2.87	(1.98 – 4.65)	6.9×10 ⁻⁷	0.7055	(0.6451 – 0.7649)	vs M ₁ = 0.23
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	0.98	(0.77 – 1.25)	0.89	0.5925	(0.5271 – 0.6579)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.46	(1.16 – 1.84)	1.5×10 ⁻³	0.6409	(0.5740 – 0.7077)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.55	(1.23 – 1.95)	2.4×10 ⁻⁴	0.6509	(0.5836 – 0.7183)	vs M ₄ = 0.21
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	1.37	(1.08 – 1.73)	8.7×10 ⁻³	0.7113	(0.6518 – 0.7708)	vs M ₂ = 0.035
		log(PSA)	2.67	(1.74 – 4.11)	8.0×10 ⁻⁵			vs M ₄ = 2.2×10 ⁻³
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	1.45	(1.15 – 1.83)	1.6×10 ⁻³	0.7238	(0.6632 – 0.7844)	vs M ₄ = 4.7×10 ⁻⁴
		log(PSA ^G)	2.91	(1.91 – 4.44)	7.4×10 ⁻⁷			vs M ₆ = 0.18
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	1.52	(1.20 – 1.92)	4.3×10 ⁻⁴	0.7264	(0.6653 – 0.7876)	vs M ₅ = 8.1×10 ⁻⁴
		log(PSA ^G)	2.84	(1.86 – 4.31)	1.1×10 ⁻⁶			vs M ₇ = 0.58
European ancestry			OR ²	(95% CI)	P	AUC	(95% CI)	P _{AUC} ³
0	Baseline age + RCT arm	-	-	-	-	0.5807	(0.5156 – 0.6458)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	2.80	(1.81 – 4.31)	3.2×10 ⁻⁶	0.6842	(0.6234 – 0.7450)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	2.99	(1.95 – 4.59)	4.8×10 ⁻⁷	0.7108	(0.6519 – 0.7697)	vs M ₁ = 0.061
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	0.94	(0.73 – 1.20)	0.63	0.6139	(0.5579 – 0.6698)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.45	(1.14 – 1.83)	2.3×10 ⁻³	0.6453	(0.5819 – 0.7087)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.55	(1.22 – 1.96)	3.0×10 ⁻⁴	0.6572	(0.5941 – 0.7203)	vs M ₄ = 0.22
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	1.36	(1.08 – 1.73)	0.010	0.7093	(0.6471 – 0.7715)	vs M ₂ = 0.92
		log(PSA)	2.66	(1.72 – 4.13)	1.1×10 ⁻⁵			vs M ₄ = 6.3×10 ⁻³
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	1.45	(1.15 – 1.84)	2.0×10 ⁻³	0.7273	(0.6659 – 0.7887)	vs M ₄ = 1.5×10 ⁻³
		log(PSA ^G)	3.05	(1.98 – 4.71)	4.5×10 ⁻⁷			vs M ₆ = 0.073
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	1.53	(1.21 – 1.93)	4.6×10 ⁻⁴	0.7335	(0.6722 – 0.7948)	vs M ₅ = 1.5×10 ⁻³
		log(PSA ^G)	2.97	(1.93 – 4.57)	6.8×10 ⁻⁷			vs M ₇ = 0.26

¹ Odds ratios were estimated per standard deviation increase in standardized PGS₂₆₉ and PGS_{PSA}. Models with genetic predictors (PSA^G, PGS₂₆₉, PGS₂₆₉^{adj}, and PGS_{PSA}) were adjusted for the top 10 genetic ancestry principal components and global ancestry proportions in the pooled analysis.

² P-values based on De Long's test for two correlated ROC curves.

Supplementary Table 19: Comparison of logistic regression models for incident non-aggressive prostate cancer in the Prostate Cancer Prevention Trial (PCPT). Pooled, multi-ancestry analyses include 260 cases and 5548 controls (European ancestry: 252 cases, 5402 controls). Models are indexed from M₀ to M₈. Odds ratios (OR), corresponding 95% confidence intervals, and two-sided p-values are presented for PSA variables and polygenic scores (PGS) only. AUC is based on the full model with all covariates.

Models		Predictor	Association Estimates					
Pooled (Multi-ancestry)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.5915	(0.5560 – 0.6270)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	1.66	(1.34 – 2.04)	2.2×10 ⁻⁶	0.6228	(0.5895 – 0.6561)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	1.63	(1.32 – 2.01)	5.6×10 ⁻⁶	0.6341	(0.6000 – 0.6682)	vs M ₁ = 0.24
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	1.02	(0.90 – 1.16)	0.77	0.6060	(0.5711 – 0.6408)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.54	(1.36 – 1.75)	3.1×10 ⁻¹¹	0.6599	(0.6274 – 0.6924)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.58	(1.39 – 1.79)	2.8×10 ⁻¹²	0.6614	(0.6285 – 0.6924)	vs M ₄ = 0.79
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	1.50	(1.32 – 1.70)	5.7×10 ⁻¹⁰	0.6786	(0.6473 – 0.7100)	vs M ₂ = 2.3×10 ⁻³ vs M ₄ = 0.014
		log(PSA)	1.54	(1.24 – 1.91)	7.8×10 ⁻⁵			
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	1.54	(1.36 – 1.75)	2.8×10 ⁻¹¹	0.6822	(0.6510 – 0.7134)	vs M ₄ = 0.010 vs M ₆ = 0.35
		log(PSA ^G)	1.65	(1.33 – 2.04)	5.2×10 ⁻⁶			
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	1.56	(1.38 – 1.78)	5.8×10 ⁻¹²	0.6814	(0.6500 – 0.7128)	vs M ₅ = 0.015 vs M ₇ = 0.87
		log(PSA ^G)	1.61	(1.30 – 2.00)	1.2×10 ⁻⁵			
European ancestry			OR ²	(95% CI)	P	AUC	(95% CI)	P _{AUC} ³
0	Baseline age + RCT arm	-	-	-	-	0.5919	(0.5558 – 0.6280)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	1.70	(1.37 – 2.10)	1.5×10 ⁻⁶	0.6275	(0.5939 – 0.6610)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	1.68	(1.35 – 2.09)	2.6×10 ⁻⁶	0.6376	(0.6033 – 0.6719)	vs M ₁ = 0.28
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	1.03	(0.90 – 1.18)	0.65	0.6082	(0.5727 – 0.6437)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.55	(1.36 – 1.77)	2.5×10 ⁻¹¹	0.6597	(0.6264 – 0.6930)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.57	(1.38 – 1.79)	6.0×10 ⁻¹²	0.6606	(0.6268 – 0.6945)	vs M ₄ = 0.87
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	1.51	(1.33 – 1.72)	5.2×10 ⁻¹⁰	0.6788	(0.6467 – 0.7110)	vs M ₂ = 4.5×10 ⁻³ vs M ₄ = 0.019
		log(PSA)	1.59	(1.28 – 1.98)	3.2×10 ⁻⁵			
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	1.55	(1.37 – 1.77)	2.2×10 ⁻¹¹	0.6821	(0.6503 – 0.7139)	vs M ₄ = 0.013 vs M ₆ = 0.40
		log(PSA ^G)	1.70	(1.37 – 2.12)	2.3×10 ⁻⁶			
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	1.56	(1.37 – 1.78)	1.3×10 ⁻¹²	0.6810	(0.6490 – 0.7130)	vs M ₅ = 0.019 vs M ₇ = 0.82
		log(PSA ^G)	1.66	(1.34 – 2.07)	5.4×10 ⁻⁶			

¹ Odds ratios were estimated per standard deviation increase in standardized PGS₂₆₉ and PGS_{PSA}. Models with genetic predictors (PSA^G, PGS₂₆₉, PGS₂₆₉^{adj}, and PGS_{PSA}) were adjusted for the top 10 genetic ancestry principal components and global ancestry proportions in the pooled analysis.

² Two-sided p-values based on De Long's test for two correlated ROC curves.

Supplementary Table 20: Case-only analyses of prostate cancer aggressiveness in the Prostate Cancer Prevention Trial (PCPT). Comparison of logistic regression models for distinguishing aggressive (Pooled: n=75; European ancestry: n=71) from non-aggressive (Pooled: n=260; European ancestry: n=252) disease. Models are indexed from M₀ to M₈. Odds ratios (OR), corresponding 95% confidence intervals, and two-sided p-values are presented for PSA variables and polygenic scores (PGS) only. AUC is based on the full model with all covariates.

Models		Predictor	Association Estimates					
Pooled (Multi-ancestry)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.5124	(0.4360 – 0.5888)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	1.86	(1.12 – 3.10)	0.017	0.6033	(0.5286 – 0.6781)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	2.06	(1.23 – 3.45)	5.9×10 ⁻³	0.6456	(0.5716 – 0.7197)	vs M ₁ = 0.19
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	0.88	(0.66 – 1.19)	0.41	0.6055	(0.5285 – 0.6825)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	0.91	(0.68 – 1.22)	0.54	0.6029	(0.5259 – 0.6799)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	0.97	(0.73 – 1.29)	0.85	0.5944	(0.5157 – 0.6730)	vs M ₄ = 0.17
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	0.88	(0.65 – 1.18)	0.39	0.6396	(0.5656 – 0.7137)	vs M ₂ = 0.69
		log(PSA)	1.94	(1.14 – 3.28)	0.014			vs M ₄ = 0.23
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	0.93	(0.69 – 1.25)	0.63	0.6476	(0.5748 – 0.7205)	vs M ₄ = 0.16
		log(PSA ^G)	2.04	(1.22 – 3.42)	6.4×10 ⁻³			vs M ₆ = 0.55
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	0.98	(0.73 – 1.31)	0.88	0.6457	(0.5720 – 0.7195)	vs M ₅ = 0.11
		log(PSA ^G)	2.06	(1.23 – 3.44)	5.9×10 ⁻³			vs M ₇ = 0.62
European ancestry			OR ²	(95% CI)	P	AUC	(95% CI)	P _{AUC} ³
0	Baseline age + RCT arm	-	-	-	-	0.5142	(0.4380 – 0.5904)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	1.81	(1.07 – 3.05)	0.026	0.5924	(0.5156 – 0.6692)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	2.02	(1.20 – 3.38)	7.8×10 ⁻³	0.6254	(0.5505 – 0.7003)	vs M ₁ = 0.24
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	0.87	(0.64 – 1.17)	0.34	0.5822	(0.5068 – 0.6575)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	0.90	(0.67 – 1.21)	0.50	0.5787	(0.5016 – 0.6558)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	0.97	(0.73 – 1.29)	0.84	0.5740	(0.4954 – 0.6526)	vs M ₄ = 0.63
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	0.87	(0.65 – 1.18)	0.38	0.6159	(0.5397 – 0.6920)	vs M ₂ = 0.60
		log(PSA)	1.87	(1.10 – 3.17)	0.020			vs M ₄ = 0.29
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	0.92	(0.68 – 1.24)	0.59	0.6249	(0.5520 – 0.6977)	vs M ₄ = 0.22
		log(PSA ^G)	2.00	(1.19 – 3.35)	8.4×10 ⁻³			vs M ₆ = 0.57
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	0.97	(0.73 – 1.30)	0.86	0.6245	(0.5500 – 0.6989)	vs M ₅ = 0.19
		log(PSA ^G)	2.02	(1.20 – 3.38)	7.8×10 ⁻³			vs M ₇ = 0.94

¹ Odds ratios were estimated per standard deviation increase in standardized PGS₂₆₉ and PGS_{PSA}. Models with genetic predictors (PSA^G, PGS₂₆₉, PGS₂₆₉^{adj}, and PGS_{PSA}) were adjusted for the top 10 genetic ancestry principal components and global ancestry proportions in the pooled analysis.

² Two-sided p-values based on De Long's test for two correlated ROC curves.

Supplementary Table 21: Comparison of logistic regression models for incident prostate cancer in the Selenium and Vitamin E Cancer Prevention Trial (SELECT). Pooled analysis includes 572 cases and 23,667 cancer-free controls of all ancestries. Ancestry-stratified analyses were also performed. Models are indexed from M₀ to M₈. Odds ratios (OR), corresponding 95% confidence intervals, and two-sided p-values are presented for PSA variables and polygenic scores (PGS) only. AUC is based on the full model with all covariates.

Models		Predictor	Association Estimates					
Pooled (Multi-ancestry)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.5082	(0.4844 – 0.5321)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	3.88	(3.35 – 4.50)	4.1×10 ⁻⁷³	0.7365	(0.7176 – 0.7555)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	3.53	(3.07 – 4.07)	5.3×10 ⁻⁶⁸	0.7278	(0.7080 – 0.7476)	vs M ₁ = 0.096
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	1.23	(1.12 – 1.35)	2.4×10 ⁻⁵	0.5682	(0.5446 – 0.5917)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.74	(1.59 – 1.90)	2.9×10 ⁻³⁵	0.6587	(0.6361 – 0.6813)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.65	(1.51 – 1.79)	3.8×10 ⁻³⁰	0.6496	(0.6269 – 0.6724)	vs M ₄ = 0.019
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉ log(PSA)	1.58 3.68	(1.44 – 1.73) (3.17 – 4.28)	1.0×10 ⁻²³ 3.8×10 ⁻⁶⁵	0.7634	(0.7447 – 0.7820)	vs M ₂ = 2.7×10 ⁻⁷ vs M ₄ = 1.5×10 ⁻²⁵
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉ log(PSA ^G)	1.70 3.53	(1.55 – 1.85) (3.05 – 4.08)	1.1×10 ⁻³¹ 5.3×10 ⁻⁶⁵	0.7606	(0.7415 – 0.7797)	vs M ₄ = 4.2×10 ⁻²⁴ vs M ₆ = 0.48
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj} log(PSA ^G)	1.60 3.47	(1.46 – 1.74) (3.01 – 4.01)	2.6×10 ⁻²⁶ 7.8×10 ⁻⁶⁵	0.7561	(0.7370 – 0.7752)	vs M ₅ = 2.3×10 ⁻²⁴ vs M ₇ = 0.011
European (467 cases 20,173 controls)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.5035	(0.4788 – 0.5281)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	3.98	(3.38 – 4.69)	7.9×10 ⁻⁶¹	0.7382	(0.7175 – 0.7588)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	3.85	(3.27 – 4.53)	2.1×10 ⁻⁵⁹	0.7346	(0.7132 – 0.7561)	vs M ₁ = 0.55
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	1.21	(1.09 – 1.35)	5.9×10 ⁻⁴	0.5702	(0.5450 – 0.5953)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.81	(1.64 – 2.00)	8.8×10 ⁻³³	0.6670	(0.6428 – 0.6912)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.70	(1.55 – 1.87)	7.9×10 ⁻²⁸	0.6562	(0.6319 – 0.6804)	vs M ₄ = 0.015
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉ log(PSA)	1.63 3.70	(1.47 – 1.80) (3.13 – 4.37)	6.8×10 ⁻²² 5.7×10 ⁻⁵³	0.7671	(0.7470 – 0.7872)	vs M ₂ = 1.9×10 ⁻⁵ vs M ₄ = 2.7×10 ⁻²²
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉ log(PSA ^G)	1.76 3.85	(1.59 – 1.94) (3.26 – 4.55)	3.1×10 ⁻²⁹ 1.8×10 ⁻⁵⁶	0.7681	(0.7471 – 0.7891)	vs M ₄ = 1.3×10 ⁻²¹ vs M ₆ = 0.81
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj} log(PSA ^G)	1.64 3.46	(1.49 – 1.80) (3.19 – 4.43)	7.7×10 ⁻²⁴ 3.6×10 ⁻⁵⁶	0.7629	(0.7419 – 0.7839)	vs M ₅ = 5.9×10 ⁻²² vs M ₇ = 9.2×10 ⁻³
African ³ (88 cases 2733 controls)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.5808	(0.5175 – 0.6441)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	3.63	(2.54 – 5.20)	2.0×10 ⁻¹²	0.7423	(0.6925 – 0.7921)	-

2	Baseline age + RCT arm + baseline PSA ^G [PGS _{CSx}]	log(PSA ^G)	2.68	(1.94 – 3.69)	1.7×10 ⁻⁹	0.7266	(0.6760 – 0.7772)	vs M ₁ = 0.35
	Baseline age + RCT arm + baseline PSA ^G [PGS ₁₂₈]	log(PSA ^G)	3.37	(2.38 – 4.78)	7.6×10 ⁻¹²	0.7500	(0.7003 – 0.7998)	vs M ₁ = 0.56
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	1.30	(1.05 – 1.62)	0.018	0.6383	(0.5784 – 0.6981)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.43	(1.15 – 1.78)	1.3×10 ⁻³	0.6573	(0.5950 – 0.7196)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.42	(1.15 – 1.75)	1.3×10 ⁻³	0.6638	(0.6026 – 0.7250)	vs M ₄ = 0.22
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	1.34	(1.07 – 1.68)	0.012	0.7689	(0.7202 – 0.8176)	vs M ₂ = 4.4×10 ⁻³
		log(PSA)	3.63	(2.52 – 5.25)	5.7×10 ⁻¹²			vs M ₄ = 3.4×10 ⁻⁵
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G [PGS _{CSx}]	PGS ₂₆₉	1.42	(1.13 – 1.77)	2.3×10 ⁻³	0.7432	(0.6934 – 0.7930)	vs M ₄ = 4.7×10 ⁻⁴
		log(PSA ^G)	2.66	(1.93 – 3.68)	3.1×10 ⁻⁹			vs M ₆ = 0.016
	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G [PGS ₁₂₈]	PGS ₂₆₉	1.43	(1.14 – 1.78)	1.8×10 ⁻³	0.7636	(0.7134 – 0.8138)	vs M ₄ = 8.1×10 ⁻⁵
		log(PSA ^G)	3.42	(2.40 – 4.87)	1.2×10 ⁻¹¹			vs M ₆ = 0.54
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	1.41	(1.13 – 1.76)	2.0×10 ⁻³	0.7460	(0.6969 – 0.7951)	vs M ₅ = 7.4×10 ⁻⁴
		log(PSA ^G)	2.66	(1.93 – 3.68)	2.7×10 ⁻⁹			vs M ₇ = 0.33
East Asian⁴ (13 cases 544 controls)			OR¹	(95% CI)	P	AUC	(95% CI)	P_{AUC}²
0	Baseline age + RCT arm	-	-	-	-	0.6361	(0.4532 – 0.8190)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	2.60	(1.03 – 6.54)	0.043	0.7039	(0.5673 – 0.8405)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	2.15	(0.82 – 5.62)	0.12	0.8271	(0.7104 – 0.9438)	vs M ₁ = 0.011
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	1.54	(0.76 – 3.12)	0.23	0.8183	(0.6961 – 0.9405)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	2.07	(0.97 – 4.41)	0.059	0.8334	(0.7120 – 0.9548)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.62	(0.81 – 3.24)	0.17	0.8262	(0.7046 – 0.9478)	vs M ₄ = 0.49
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	2.07	(0.97 – 4.38)	0.059	0.8501	(0.7453 – 0.9550)	vs M ₂ = 0.099
		log(PSA)	2.91	(1.01 – 8.42)	0.049			vs M ₄ = 0.62
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	2.02	(0.96 – 4.24)	0.063	0.8484	(0.7399 – 0.9569)	vs M ₄ = 0.54
		log(PSA ^G)	2.17	(0.80 – 5.87)	0.13			vs M ₆ = 0.91
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	1.59	(0.81 – 3.14)	0.18	0.8391	(0.7248 – 0.9533)	vs M ₅ = 0.59
		log(PSA ^G)	2.14	(0.81 – 5.65)	0.13			vs M ₇ = 0.28

¹ Odds ratios were estimated per standard deviation increase in standardized PGS₂₆₉ and PGS_{PSA}. Models with genetic predictors (PSA^G, PGS₂₆₉, PGS₂₆₉^{adj}, and PGS_{PSA}) were adjusted for the top 10 genetic ancestry principal components and global ancestry proportions in the pooled analysis.

² Two-sided p-values based on De Long's test for two correlated ROC curves.

³ African ancestry group includes men of African (AFR≥0.80) and admixed African and European (0.20<AFR/EUR<0.80) ancestry.

⁴ East Asian group includes men of East Asian (AFR≥0.80) and admixed East Asian and European (0.20<EAS/EUR<0.80) ancestry.

Supplementary Table 22: Comparison of logistic regression models for incident aggressive prostate cancer in the Selenium and Vitamin E Cancer Prevention Trial (SELECT). Pooled analysis includes 106 cases and 23,667 cancer-free controls of all ancestries. Ancestry-stratified analyses were also performed. Models are indexed from M₀ to M₈. Odds ratios (OR), corresponding 95% confidence intervals, and two-sided p-values are presented for PSA variables and polygenic scores (PGS) only. AUC is based on the full model with all covariates.

Models		Predictor	Association Estimates					
Pooled (Multi-ancestry)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.6090	(0.5553 – 0.6628)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	3.31	(2.38 – 4.60)	1.1×10 ⁻¹²	0.7375	(0.6919 – 0.7831)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	3.44	(2.49 – 4.75)	6.2×10 ⁻¹⁴	0.7549	(0.7091 – 0.8008)	vs M ₁ = 0.12
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	1.02	(0.82 – 1.27)	0.86	0.6579	(0.5952 – 0.7006)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.73	(1.42 – 2.11)	8.5×10 ⁻⁸	0.7120	(0.6638 – 0.7077)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.76	(1.44 – 2.14)	1.7×10 ⁻⁸	0.7198	(0.6718 – 0.7677)	vs M ₄ = 5.9×10 ⁻³
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	1.59	(1.30 – 1.95)	6.3×10 ⁻⁶	0.7810	(0.7392 – 0.8228)	vs M ₂ = 0.056
		log(PSA)	3.16	(2.26 – 4.42)	1.7×10 ⁻¹¹			vs M ₄ = 3.1×10 ⁻⁴
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	1.70	(1.39 – 2.07)	2.2×10 ⁻⁷	0.7861	(0.7413 – 0.8309)	vs M ₄ = 7.2×10 ⁻⁴
		log(PSA ^G)	3.46	(2.49 – 4.81)	1.5×10 ⁻¹³			vs M ₆ = 0.51
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	1.71	(1.40 – 2.08)	8.0×10 ⁻⁸	0.7875	(0.7436 – 0.8314)	vs M ₅ = 1.3×10 ⁻³
		log(PSA ^G)	3.38	(2.44 – 4.67)	2.4×10 ⁻¹³			vs M ₇ = 0.71
European (85 cases 20,173 controls)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.6045	(0.5443 – 0.6648)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	3.40	(2.34 – 4.93)	1.1×10 ⁻¹⁰	0.7420	(0.6938 – 0.7901)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	3.81	(2.62 – 5.54)	2.5×10 ⁻¹²	0.7766	(0.7291 – 0.8242)	vs M ₁ = 0.026
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	0.98	(0.76 – 1.26)	0.87	0.6768	(0.6196 – 0.7339)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.76	(1.41 – 2.21)	7.4×10 ⁻⁷	0.7264	(0.6709 – 0.7819)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.81	(1.45 – 2.25)	1.3×10 ⁻⁷	0.7301	(0.6753 – 0.7849)	vs M ₄ = 0.58
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	1.61	(1.28 – 2.02)	3.7×10 ⁻⁵	0.7956	(0.7501 – 0.8410)	vs M ₂ = 0.13
		log(PSA)	3.20	(2.19 – 4.67)	1.5×10 ⁻⁹			vs M ₄ = 3.4×10 ⁻⁴
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	1.72	(1.38 – 2.15)	2.0×10 ⁻⁶	0.8026	(0.7545 – 0.8506)	vs M ₄ = 6.8×10 ⁻⁴
		log(PSA ^G)	3.82	(2.61 – 5.60)	6.1×10 ⁻¹²			vs M ₆ = 0.29
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	1.74	(1.40 – 2.16)	7.3×10 ⁻⁷	0.8039	(0.7568 – 0.8510)	vs M ₅ = 5.4×10 ⁻⁴
		log(PSA ^G)	3.69	(2.53 – 5.38)	1.0×10 ⁻¹¹			vs M ₇ = 0.26
African ³ (18 cases 2733 controls)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.7201	(0.6015 – 0.8387)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	2.82	(1.33 – 5.99)	6.8×10 ⁻³	0.7541	(0.6219 – 0.8862)	-

2	Baseline age + RCT arm + baseline PSA ^G [PGS _{CSx}]	log(PSA ^G)	2.48	(1.24 – 4.97)	0.011	0.8066	(0.6954 – 0.9178)	vs M ₁ = 0.076
	Baseline age + RCT arm + baseline PSA ^G [PGS ₁₂₈]	log(PSA ^G)	2.96	(1.43 – 6.12)	3.5×10 ⁻³	0.8079	(0.6991 – 0.9167)	vs M ₁ = 0.051
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	1.09	(0.67 – 1.79)	0.72	0.7875	(0.6998 – 0.8752)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.63	(1.01 – 2.64)	0.045	0.8030	(0.7219 – 0.8841)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.62	(1.02 – 2.59)	0.042	0.8070	(0.7243 – 0.8897)	vs M ₄ = 0.54
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	1.54	(0.95 – 2.51)	0.081	0.8277	(0.7392 – 0.9162)	vs M ₂ = 0.40
		log(PSA)	2.75	(1.28 – 5.90)	9.5×10 ⁻³			vs M ₄ = 0.36
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G [PGS _{CSx}]	PGS ₂₆₉	1.62	(0.99 – 2.62)	0.053	0.8246	(0.7284 – 0.9207)	vs M ₄ = 0.49
		log(PSA ^G)	2.47	(1.22 – 5.00)	0.012			vs M ₆ = 0.83
	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G [PGS ₁₂₈]	PGS ₂₆₉	1.61	(0.99 – 2.60)	0.052	0.8234	(0.7239 – 0.9228)	vs M ₄ = 0.50
		log(PSA ^G)	2.97	(1.41 – 6.27)	4.1×10 ⁻³			vs M ₆ = 0.68
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	1.61	(1.00 – 2.57)	0.048	0.8268	(0.7304 – 0.9231)	vs M ₅ = 0.52
		log(PSA ^G)	2.46	(1.22 – 4.98)	0.012			vs M ₇ = 0.65

¹ Odds ratios were estimated per standard deviation increase in standardized PGS₂₆₉ and PGSPSA. Models with genetic predictors (PSA^G, PGS₂₆₉, PGS₂₆₉^{adj}, and PGS_{PSA}) were adjusted for the top 10 genetic ancestry principal components and global ancestry proportions in the pooled analysis.

² Two-sided p-values based on De Long's test for two correlated ROC curves.

³ African ancestry group includes men of African (AFR≥0.80) and admixed African and European (0.20<AFR/EUR<0.80) ancestry.

Supplementary Table 23: Comparison of logistic regression models for incident non-aggressive prostate cancer in the Selenium and Vitamin E Cancer Prevention Trial (SELECT). Pooled analysis includes 466 cases and 23,667 cancer-free controls of all ancestries. Ancestry-stratified analyses were also performed. Models are indexed from M₀ to M₈. Odds ratios (OR), corresponding 95% confidence intervals, and two-sided p-values are presented for PSA variables and polygenic scores (PGS) only. AUC is based on the full model with all covariates.

Models		Predictor	Association Estimates					
Pooled (Multi-ancestry)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.5254	(0.5000 – 0.5507)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	4.03	(3.42 – 4.74)	6.3×10 ⁻⁶³	0.7428	(0.7220 – 0.7636)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	3.56	(3.04 – 4.16)	1.2×10 ⁻⁵⁶	0.7290	(0.7071 – 0.7509)	vs M ₁ = 0.017
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	1.28	(1.15 – 1.42)	4.0×10 ⁻⁶	0.5776	(0.5510 – 0.6043)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.74	(1.58 – 1.92)	2.5×10 ⁻²⁹	0.6569	(0.6318 – 0.6821)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.62	(1.47 – 1.78)	1.3×10 ⁻²³	0.6445	(0.6192 – 0.6698)	vs M ₄ = 3.2×10 ⁻³
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉ log(PSA)	1.57 3.82	(1.43 – 1.74) (3.23 – 4.51)	1.3×10 ⁻¹⁹ 3.7×10 ⁻⁵⁶	0.7657	(0.7450 – 0.7865)	vs M ₂ = 1.5×10 ⁻⁶ vs M ₄ = 9.1×10 ⁻²³
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉ log(PSA ^G)	1.69 3.55	(1.54 – 1.87) (3.02 – 4.17)	2.7×10 ⁻²⁶ 3.8×10 ⁻⁵⁴	0.7606	(0.7395 – 0.7817)	vs M ₄ = 1.8×10 ⁻²¹ vs M ₆ = 0.24
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj} log(PSA ^G)	1.57 3.49	(1.43 – 1.73) (2.98 – 4.09)	1.4×10 ⁻²⁰ 3.6×10 ⁻⁵⁴	0.7551	(0.7340 – 0.7762)	vs M ₅ = 4.6×10 ⁻²² vs M ₇ = 5.9×10 ⁻³
European (382 cases 20,173 controls)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.5209	(0.4928 – 0.5491)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	4.12	(3.43 – 4.94)	2.2×10 ⁻⁵²	0.7430	(0.7202 – 0.7658)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	3.86	(3.23 – 4.62)	2.1×10 ⁻⁴⁹	0.7357	(0.7119 – 0.7594)	vs M ₁ = 0.26
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	1.27	(1.13 – 1.44)	1.0×10 ⁻⁴	0.5792	(0.5511 – 0.6073)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.82	(1.63 – 2.03)	1.0×10 ⁻²⁷	0.6669	(0.6396 – 0.6942)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.68	(1.51 – 1.86)	5.0×10 ⁻²³	0.6522	(0.6248 – 0.6796)	vs M ₄ = 2.1×10 ⁻³
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉ log(PSA)	1.63 3.82	(1.46 – 1.82) (3.17 – 4.60)	2.0×10 ⁻¹⁹ 1.2×10 ⁻⁴⁵	0.7694	(0.7470 – 0.7918)	vs M ₂ = 7.1×10 ⁻⁵ vs M ₄ = 2.9×10 ⁻¹⁹
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉ log(PSA ^G)	1.76 3.86	(1.58 – 1.96) (3.21 – 4.63)	1.0×10 ⁻²⁴ 5.6×10 ⁻⁴⁷	0.7684	(0.7452 – 0.7916)	vs M ₄ = 7.7×10 ⁻¹⁹ vs M ₆ = 0.83
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj} log(PSA ^G)	1.61 3.77	(1.45 – 1.79) (3.15 – 4.52)	7.3×10 ⁻¹⁹ 7.2×10 ⁻⁴⁷	0.7620	(0.7386 – 0.7853)	vs M ₅ = 4.6×10 ⁻²² vs M ₇ = 5.9×10 ⁻³
African ³ (70 cases 2733 controls)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.5602	(0.4964 – 0.6240)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	3.90	(2.60 – 5.86)	5.5×10 ⁻¹¹	0.7565	(0.7030 – 0.8099)	-

2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	2.75	(1.92 – 3.94)	3.6×10 ⁻⁸	0.7385	(0.6838 – 0.7931)	vs M ₁ = 0.054
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	1.36	(1.07 – 1.74)	0.012	0.6634	(0.5978 – 0.7290)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.39	(1.09 – 1.77)	7.9×10 ⁻³	0.6630	(0.5964 – 0.7295)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.37	(1.08 – 1.74)	8.6×10 ⁻³	0.6666	(0.6006 – 0.7324)	vs M ₄ = 0.47
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉ log(PSA)	1.29 3.97	(1.01 – 1.66) (2.62 – 6.03)	0.046 8.9×10 ⁻¹¹	0.7835	(0.7288 – 0.8382)	vs M ₂ = 1.6×10 ⁻³ vs M ₄ = 2.3×10 ⁻⁵
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉ log(PSA ^G)	1.37 2.73	(1.07 – 1.75) (1.90 – 3.92)	0.014 6.0×10 ⁻⁸	0.7499	(0.6946 – 0.8051)	vs M ₄ = 5.3×10 ⁻⁴ vs M ₆ = 2.6×10 ⁻³
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj} log(PSA ^G)	1.36 2.73	(1.06 – 1.73) (1.90 – 3.92)	0.014 5.4×10 ⁻⁸	0.7520	(0.6977 – 0.8062)	vs M ₅ = 8.2×10 ⁻⁴ vs M ₇ = 0.47

¹ Odds ratios were estimated per standard deviation increase in standardized PGS₂₆₉ and PGS_{PSA}. Models with genetic predictors (PSA^G, PGS₂₆₉, PGS₂₆₉^{adj}, and PGS_{PSA}) were adjusted for the top 10 genetic ancestry principal components and global ancestry proportions in the pooled analysis.

² Two-sided p-values based on De Long's test for two correlated ROC curves.

³ African ancestry group includes men of African (AFR≥0.80) and admixed African and European (0.20<AFR/EUR<0.80) ancestry.

Supplementary Table 24: Case-only analyses of prostate cancer aggressiveness in the Selenium and Vitamin E Cancer Prevention Trial (SELECT). Pooled analysis includes 106 aggressive cases and 466 non-aggressive cases of all ancestries. Stratified analyses were performed in participants of European ancestry (85 aggressive, 382 non-aggressive) and African ancestry (18 aggressive, 70 non-aggressive). Models are indexed from M₀ to M₈. Odds ratios (OR), corresponding 95% confidence intervals, and two-sided p-values are presented for PSA variables and polygenic scores (PGS) only. AUC is based on the full model with all covariates.

Models		Predictor	Association Estimates					
Pooled (Multi-ancestry)			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.6383	(0.5790 – 0.6975)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	0.89	(0.61 – 1.30)	0.54	0.6375	(0.5790 – 0.6960)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	1.07	(0.72 – 1.59)	0.75	0.6565	(0.5975 - 0.7156)	-
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	0.79	(0.61 – 1.03)	0.078	0.6697	(0.6118 - 0.7276)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.01	(0.80 – 1.27)	0.96	0.6554	(0.5961 – 0.7147)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.10	(0.87 – 1.39)	0.42	0.6585	(0.5990 – 0.7180)	-
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	1.02	(0.80 – 1.29)	0.90	0.6549	(0.5956 – 0.7143)	-
		log(PSA)	0.89	(0.60 – 1.31)	0.55			-
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	1.00	(0.79 – 1.27)	0.98	0.6564	(0.5973 – 0.7155)	-
		log(PSA ^G)	1.07	(0.72 – 1.59)	0.75			-
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	1.10	(0.87 – 1.39)	0.43	0.6600	(0.6006 – 0.7194)	-
		log(PSA ^G)	1.06	(0.71 – 1.57)	0.78			-
European ancestry			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.6302	(0.5641 – 0.6962)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	0.92	(0.62 – 1.42)	0.71	0.6313	(0.5654 – 0.6972)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	1.13	(0.71 – 1.78)	0.61	0.7015	(0.6380 – 0.7650)	-
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	0.75	(0.55 – 1.02)	0.065	0.7068	(0.6447 – 0.7688)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	1.05	(0.81 – 1.36)	0.72	0.6983	(0.6346 – 0.7621)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	1.17	(0.90 – 1.51)	0.24	0.7017	(0.6369 – 0.7664)	-
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	0.89	(0.56 – 1.41)	0.62	0.6975	(0.6339 – 0.7611)	-
		log(PSA)	1.06	(0.81 – 1.38)	0.67			-
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	1.12	(0.71 – 1.78)	0.63	0.7013	(0.6373 – 0.7652)	-
		log(PSA ^G)	1.04	(0.80 – 1.35)	0.76			-
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	1.10	(0.70 – 1.75)	0.67	0.7039	(0.6391 – 0.7687)	-
		log(PSA ^G)	1.16	(0.90 – 1.50)	0.26			-

African ancestry			OR ¹	(95% CI)	P	AUC	(95% CI)	P _{AUC} ²
0	Baseline age + RCT arm	-	-	-	-	0.7201	(0.5840 – 0.8580)	-
1	Baseline age + RCT arm + baseline PSA	log(PSA)	0.66	(0.27 – 1.61)	0.37	0.7298	(0.6036 – 0.8559)	-
2	Baseline age + RCT arm + baseline PSA ^G	log(PSA ^G)	0.83	(0.29 – 2.38)	0.73	0.8254	(0.7260 – 0.9248)	-
3	Baseline age + RCT arm + PGS _{PSA}	PGS _{PSA}	0.64	(0.31 – 1.33)	0.23	0.8294	(0.7241 – 0.9346)	-
4	Baseline age + RCT arm + PGS ₂₆₉	PGS ₂₆₉	0.99	(0.42 – 2.35)	0.98	0.8222	(0.7212 – 0.9233)	-
5	Baseline age + RCT arm + PGS ₂₆₉ ^{adj}	PGS ₂₆₉ ^{adj}	0.98	(0.40 – 2.40)	0.97	0.8222	(0.7210 – 0.9234)	-
6	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA	PGS ₂₆₉	0.94	(0.39 – 2.23)	0.88	0.8437	(0.7491 – 0.9382)	-
		log(PSA)	0.55	(0.19 – 1.61)	0.27			-
7	Baseline age + RCT arm + PGS ₂₆₉ + baseline PSA ^G	PGS ₂₆₉	0.95	(0.39 – 2.30)	0.92	0.8270	(0.7291 – 0.9249)	-
		log(PSA ^G)	0.82	(0.28 – 2.40)	0.71			-
8	Baseline age + RCT arm + PGS ₂₆₉ ^{adj} + baseline PSA ^G	PGS ₂₆₉ ^{adj}	0.93	(0.37 – 2.36)	0.89	0.8278	(0.7301 – 0.9255)	-
		log(PSA ^G)	0.81	(0.27 – 2.42)	0.70			-

¹ Odds ratios were estimated per standard deviation increase in standardized PGS₂₆₉ and PGS_{PSA}. Models with genetic predictors (PSA^G, PGS₂₆₉, PGS₂₆₉^{adj}, and PGS_{PSA}) were adjusted for the top 10 genetic ancestry principal components and global ancestry proportions in the pooled analysis.

² Two-sided p-values based on De Long's test for two correlated ROC curves.

³ African ancestry group includes men of African (AFR≥0.80) and admixed African and European (0.20<AFR/EUR<0.80) ancestry.

Supplementary Table 25: Field codes used to extract PSA values from linked GP records in the UK Biobank

HES Field code	Description
X80QD	Prostate specific antigen
XE25C	Prostate-specific antigen level
XabAM	Serum prostate specific antigen level
XaPqN	Total prostate specific antigen level
XaQ9n	Ultra-sensitive prostate specific antigen level

Supplementary Table 26: Study-specific GWAS approach and adjustment covariates

Study	GWAS Phenotype	Analysis	Covariates
UKB	Median log(PSA)	Linear regression	Age at PSA measurement, baseline BMI, baseline smoking status (never, current, former smokers), diagnosed with benign prostatic hyperplasia (BPH) or prostatitis (1=ever, 0=never), time between median PSA and BPH or prostatitis diagnosis (coded as 0 for those without a corresponding diagnosis), finasteride use (1=ever, 0=never), genotyping array (UK BiLEVE vs. UKB Affymetrix Axiom), PC1-PC15
	Random Intercept	Linear mixed model	Age at each observation, baseline BMI, baseline smoking status (never, current, former smokers), diagnosed with benign prostatic hyperplasia (BPH) or prostatitis (1=ever, 0=never), finasteride use (1=ever, 0=never), genotyping array (UK BiLEVE vs. UKB Affymetrix Axiom), PC1-PC15
GERA	Random Intercept	Linear mixed model	Age at each observation, composite variable for DNA collection kit and genotyping array (chip-kit), PC1-PC10
PLCO	Baseline log(PSA)	Linear mixed model	Age at PSA measurement, baseline BMI, baseline smoking status (never, current, former smokers), benign prostatic hyperplasia (surgically-treated BPH, BPH without surgery, none) and ancestry-specific PC1-PC10. Residuals and models were created and run separately by ancestry, genotype array, and imputation batch.
BioVU	Median log(PSA)	Linear regression	Median age of PSA measurements, median BMI, diagnosed with BPH (1=ever, 0=never), testosterone use (1=ever, 0=never), finasteride use (1=ever, 0=never), PC1-PC10
MDCS	Baseline log(PSA)	Linear regression	Age at blood draw for PSA measurement, genotyping batch, PC1-PC10