

Supplementary Information

Supplementary Table 1. SNP identifier, chromosome, effect allele, reference allele, and position (based on version 37), and beta (model weight) for the 290 SNPs used in the calculation of PHS290. The effect-allele-frequency (EAF) was estimated from controls in the training dataset with age less than 70 years. The HGNC identifier and Variant Consequence for each SNP were extracted from dbSNP.

SNP ID	Chr	Effect	Ref	Position	beta	EAF	HGNC	Variant Consequence
rs12262998	10	C	T	104428716	0.0254	0.6792		
rs10885396	10	T	C	114711755	0.0095	0.5434	TCF7L2	intron_variant
rs4558107	10	A	G	122794926	0.0227	0.3932		
rs140783917	10	C	T	122834482	0.1275	0.9989		
rs10788167	10	T	A	123054018	0.0249	0.7674		
rs10749415	10	A	G	123185303	0.0602	0.9469		
rs12769682	10	C	G	126697494	0.0358	0.2720	CTBP2	intron_variant;non_coding_transcript_variant
rs7075427	10	A	C	46104943	0.0069	0.9209		
rs11599847	10	T	C	47599029	-0.0171	0.9629		
rs10993994	10	T	C	51549496	0.1176	0.3906		
rs11817544	10	C	A	80236999	0.0338	0.9413	LINC00856	non_coding_transcript_variant;intron_variant
rs12412705	10	C	T	80835998	0.0180	0.0692	ZMIZ1	intron_variant
rs12781100	10	T	C	838636	0.0543	0.1600		
rs1935581	10	C	T	90195149	0.0323	0.6297	RNLS	intron_variant;non_coding_transcript_variant
rs11568818	11	T	C	102401661	0.0333	0.5494		
rs74911261	11	A	G	108357137	0.0598	0.0245	KDELC2	missense_variant;NMD_transcript_variant;non_coding_transcript_exon_variant
rs138466039	11	T	C	125054793	0.0801	0.0103	PKNOX2	intron_variant;non_coding_transcript_variant;NMD_transcript_variant
rs878987	11	G	A	134266372	0.0241	0.1460	B3GAT1	intron_variant;non_coding_transcript_variant
rs1881502	11	T	C	1507512	0.0107	0.1903	MOB2	intron_variant;non_coding_transcript_variant
rs72853963	11	A	G	2224664	0.0190	0.1822		
rs11043143	11	T	C	2234093	0.0735	0.1948		
rs68010938	11	T	TA	47428209	0.0186	0.3047		non_coding_transcript_variant;intron_variant
rs1048374	11	G	A	58902679	-0.0747	0.0037		non_coding_transcript_exon_variant
rs2277283	11	C	T	61908440	0.0356	0.3045	INCENP	missense_variant;non_coding_transcript_exon_variant
rs12785905	11	C	G	66951965	0.0247	0.0389	KDM2A	intron_variant
rs3018690	11	T	C	68882926	0.0297	0.4431		
rs11825796	11	A	G	68980788	-0.0164	0.2625		
rs12275055	11	G	A	68981359	0.0453	0.1652		
chr11_68985583	11	C	T	68985583	-0.0531	0.4928		

rs11228580	11	C	T	69002342	0.0094	0.1655		
rs3918298	11	A	G	69463273	0.0824	0.0274	CCND1	intron_variant;non_coding_transcript_variant
rs61890184	11	A	G	7547587	0.0334	0.1179	PPFIBP2	intron_variant
rs56159348	11	T	G	76267331	0.0259	0.6783		
rs77121786	12	G	T	102446675	0.0341	0.1981	CCDC53	NMD_transcript_variant;intron_variant;non_coding_transcript_variant
rs1270884	12	A	G	114685571	0.0239	0.4816		
rs2066827	12	T	G	12871099	0.0348	0.7603	CDKN1B	non_coding_transcript_variant;intron_variant;misseuse_variant;non_coding_transcript_variant;intron_variant;coding_sequence_variant
rs77216612	12	A	G	12877983	0.0030	0.7240		
rs7295014	12	G	A	133067989	0.0243	0.3349	FBRSL1	intron_variant
rs10845938	12	G	A	14416918	0.0315	0.5489		
rs80130819	12	A	C	48419618	0.0519	0.9104		
rs56222401	12	G	A	49672714	0.0180	0.2499		
rs10875943	12	C	T	49676010	0.0178	0.2810		
rs113925811	12	A	C	53308932	0.0789	0.1267	KRT8	intron_variant
rs187809440	12	T	C	53329231	0.2268	0.0003	KRT8	intron_variant
rs7968403	12	T	C	65012824	0.0265	0.6390	RASSF3	intron_variant;NMD_transcript_variant;intron_variant;NMD_transcript_variant
rs4842687	12	A	G	90156377	0.0303	0.7122		;
rs1327653	13	T	C	51076440	0.0295	0.2546	DLEU1	non_coding_transcript_variant;intron_variant
rs7489409	13	C	T	73716861	0.0414	0.1847		
rs7336001	13	G	C	73995877	0.0554	0.9055	LINC00393	intron_variant;non_coding_transcript_variant
rs1004030	14	T	C	23305649	0.0146	0.5830		;
rs6571758	14	G	A	37136194	0.0324	0.6195	PAX9	intron_variant;non_coding_transcript_variant
rs11849126	14	G	A	38144592	0.0026	0.6944	TTC6	intron_variant;NMD_transcript_variant
rs4901313	14	G	T	53387109	0.0401	0.8151	FERMT2	intron_variant;NMD_transcript_variant
rs8005621	14	G	A	61106699	0.0385	0.0947		
rs79133931	14	T	C	64687926	-0.1985	0.0010	SYNE2	intron_variant;NMD_transcript_variant;non_coding_transcript_variant;intron_variant
rs2093202	14	A	G	68923908	0.0160	0.6143	RAD51B	intron_variant;NMD_transcript_variant;non_coding_transcript_variant
rs767127	14	G	A	69134264	0.0238	0.4978	RAD51B	intron_variant;non_coding_transcript_variant
rs17565772	14	G	A	70756333	0.0246	0.4595		non_coding_transcript_variant;intron_variant
rs11561564	15	G	A	40965044	0.0262	0.8413		
rs33984059	15	A	G	56385868	0.0808	0.9754	RFX7	missense_variant;NMD_transcript_variant
rs74634457	15	G	A	66835704	0.0380	0.2563	ZWILCH	intron_variant

rs12913603	15	A	C	70668824	0.0195	0.4757		
rs7188897	16	T	C	54469331	0.0145	0.3503		
rs13380763	16	C	T	54678305	0.0265	0.8116		
rs11863709	16	C	T	57654576	0.0594	0.9647	GPR56	intron_variant;non_coding_transcript_variant;NMD_transcript_variant
rs28709974	16	C	T	79847632	0.0517	0.0528		non_coding_transcript_variant;intron_variant
rs8052913	16	C	T	82166181	0.0315	0.3854		non_coding_transcript_variant;intron_variant
rs72811270	17	A	G	12585459	0.0382	0.1155		intron_variant;non_coding_transcript_variant;NMD_transcript_variant;intron_variant
rs4795646	17	G	A	30092898	0.0294	0.7781		non_coding_transcript_variant;intron_variant
rs3110641	17	A	G	36047417	0.0120	0.2274	HNF1B	intron_variant;intron_variant
rs11649743	17	G	A	36074979	0.0482	0.8100	HNF1B	intron_variant
rs718961	17	A	G	36077099	-0.0171	0.2301	HNF1B	intron_variant
rs11651052	17	A	G	36102381	-0.0153	0.4697	HNF1B	intron_variant
rs11263763	17	A	G	36103565	0.0816	0.5295	HNF1B	intron_variant;intron_variant
chr17_46820676	17	T	C	46820676	0.0944	0.0410		
rs2960158	17	T	C	47380305	0.0114	0.7714	ZNF652	intron_variant;NMD_transcript_variant
rs565189650	17	T	C	47398245	0.0493	0.0755	ZNF652	intron_variant;NMD_transcript_variant;intron_variant;NMD_transcript_variant
rs12938538	17	T	C	56426027	0.0172	0.5631	BZRAP1-AS1	non_coding_transcript_variant;intron_variant;NMD_transcript_variant;intron_variant
rs684232	17	C	T	618965	0.0538	0.3546	VPS53	intron_variant
rs9889335	17	T	G	69115146	0.0288	0.4817	CASC17	non_coding_transcript_variant;intron_variant
rs148511027	17	G	GTT AT	69117532	0.0585	0.4745	CASC17	non_coding_transcript_variant;intron_variant
rs78378222	17	G	T	7571752	0.1025	0.0107	TP53	intron_variant;non_coding_transcript_exon_variant;3_prime_UTR_variant;3_prime_UTR_variant;intron_variant;non_coding_transcript_exon_variant;3_prime_UTR_variant;3_prime_UTR_variant
rs28441558	17	C	T	7803118	0.0623	0.0568	CHD3	intron_variant
rs8089411	18	C	T	51771322	0.0161	0.4421		
rs35283980	18	G	C	56745999	0.0131	0.3023		
rs533722308	18	CT	C	60961193	0.0244	0.3634	BCL2	intron_variant;intron_variant
rs11876000	18	T	G	73035513	0.0228	0.4137		
rs9959454	18	A	G	76770820	0.0489	0.7318		
rs10412482	19	C	T	17228554	0.0338	0.7162	MYO9B	intron_variant
rs17501397	19	C	T	32168343	0.0217	0.9097		

rs59710626	19	G	T	38548094	0.0094	0.8637	SIPA1L3	intron_variant;non_coding_transcript_variant
rs4802297	19	G	C	38738130	0.0368	0.4976	SPINT2	intron_variant
chr19_41985587	19	A	G	41985587	-0.0470	0.2589		intron_variant;non_coding_transcript_variant
rs11673591	19	T	A	41985931	0.0036	0.7391		intron_variant;non_coding_transcript_variant
rs2659051	19	G	C	51345568	0.0421	0.7945		intron_variant;non_coding_transcript_variant
rs61752561	19	G	A	51361382	0.1099	0.9565	KLK3	missense_variant;3_prime_UTR_variant;NMD_transcript_variant;intron_variant;non_coding_transcript_exon_variant;coding_sequence_variant;3_prime_UTR_variant;NMD_transcript_variant;intron_variant;non_coding_transcript_exon_variant
chr19_51361757	19	C	T	51361757	-0.1912	0.0735	KLK3	missense_variant;3_prime_UTR_variant;NMD_transcript_variant;non_coding_transcript_exon_variant;coding_sequence_variant;3_prime_UTR_variant;NMD_transcript_variant;non_coding_transcript_exon_variant
rs2847344	1	A	G	10564675	0.0167	0.6902	PEX14	non_coding_transcript_variant;intron_variant
rs1811698	1	C	T	150772613	0.0468	0.8913	CTSK	intron_variant
rs607518	1	A	G	150954671	0.0242	0.2100	ANXA9	5_prime_UTR_variant
rs10127983	1	T	C	153923276	0.0390	0.3115	CRTC2	intron_variant;NMD_transcript_variant;non_coding_transcript_variant
rs56103503	1	T	C	154980351	0.0347	0.3841	ZBTB7B	intron_variant;non_coding_transcript_variant
rs147847496	1	C	T	155118588	0.0829	0.9783		
rs184104770	1	A	C	155690186	-0.0083	0.0100	MSTO1	intron_variant;intron_variant;non_coding_transcript_variant
rs80237341	1	C	G	157119915	0.0593	0.0127		
rs6660538	1	A	C	163295678	0.0168	0.3681	NUF2	intron_variant;non_coding_transcript_variant;NMD_transcript_variant
rs10803412	1	C	T	16376831	0.0133	0.1711	CLCNKB	intron_variant
rs4075646	1	T	A	167135941	0.0405	0.0372		
rs507603	1	A	C	179897070	0.0044	0.1580		intron_variant;non_coding_transcript_variant
rs34295433	1	CTAAG	C	183032447	0.0250	0.5325	LAMC1	intron_variant
rs138638958	1	TTTTG	T	204030362	0.0173	0.5364		
rs4245739	1	A	C	204518842	0.0379	0.7297	MDM4	3_prime_UTR_variant;non_coding_transcript_exon_variant;intron_variant;3_prime_UTR_variant;non_coding_transcript_exon_variant;intron_variant

rs708723	1	C	T	205739266	0.0268	0.4366	RAB7L1	3_prime_UTR_variant;NMD_transcript_variant
rs544780844	1	T	C	46251655	0.0301	0.1424		
rs7542260	1	T	C	5743196	-0.0044	0.0533		
rs56391074	1	AT	A	88210715	0.0170	0.3664		
rs11480453	20	C	CA	31347512	0.0280	0.6164		
rs6141551	20	C	T	34006970	0.0111	0.6137		
rs73909841	20	T	C	49548807	0.0352	0.9278		intron_variant;non_coding_transcript_variant
rs6126986	20	C	T	52464719	0.0388	0.4825		
rs381331	20	A	G	62229989	0.0178	0.6224	GMEB2	intron_variant
chr20_62233638	20	G	A	62233638	-0.0118	0.4016	GMEB2	intron_variant
rs3787099	20	A	G	62307517	0.0800	0.9156	RTEL1	intron_variant;NMD_transcript_variant;intron_variant
rs1058319	20	C	T	62374389	0.0392	0.8611	SLC2A4RG	3_prime_UTR_variant;non_coding_transcript_exon_variant
rs11701433	21	C	T	40296411	0.0187	0.3265		intron_variant;non_coding_transcript_variant
rs61735792	21	A	G	42866332	0.1249	0.0139	TMPRSS2	synonymous_variant;intron_variant;non_coding_transcript_variant
rs9978557	21	C	T	42882462	0.0600	0.9001	TMPRSS2	intron_variant
rs1978060	22	G	A	19749525	0.0290	0.6086	TBX1	intron_variant;non_coding_transcript_variant;intron_variant
rs9625483	22	A	G	28888939	0.0625	0.0247	TTC28	intron_variant
rs138708	22	G	A	39138332	0.0418	0.9795		intron_variant;non_coding_transcript_variant;misense_variant;non_coding_transcript_exon_variant
rs34584683	22	T	A	40499107	0.0246	0.2073	TNRC6B	intron_variant
rs6003062	22	G	A	43499741	0.0026	0.9308		
rs5759167	22	G	T	43500212	0.0631	0.5003		
chr22_43501620	22	C	T	43501620	-0.0779	0.0736		
chr22_43503547	22	C	T	43503547	-0.0108	0.4232		
rs9615099	22	T	A	45698149	0.0191	0.7483		
rs17321482	23	C	T	11482634	0.0249	0.8710	ARHGAP6	intron_variant;NMD_transcript_variant;non_coding_transcript_variant
rs5972255	23	T	C	30896320	0.0085	0.2403	TAB3	intron_variant
rs4907775	23	G	A	51263200	0.0484	0.3575		
rs5943724	23	G	A	52695895	0.0081	0.6578		
rs4826594	23	A	G	54454406	-0.0046	0.0586		
chrX_66751555	23	G	A	66751555	-0.0288	0.1555		
rs5919393	23	T	C	66825357	0.0141	0.8457	AR	intron_variant;non_coding_transcript_variant;NMD_transcript_variant
rs11795627	23	T	C	69957441	-0.0138	0.4819	TEX11	intron_variant
rs371707439	23	A	G	70139908	0.0217	0.1969		

rs960417	23	A	G	9811095	0.0214	0.7182	SHROOM2	intron_variant
rs73913932	2	G	A	10094526	0.0591	0.0742	GRHL1	NMD_transcript_variant;intron_variant;non_coding_transcript_variant
rs1990613	2	T	C	10781975	0.0401	0.5153	NOL10	intron_variant
rs2165108	2	A	T	111861993	0.0385	0.0420		intron_variant;non_coding_transcript_variant;intron_variant
rs11691517	2	T	G	111893096	0.0336	0.7489	BCL2L11	intron_variant;NMD_transcript_variant
rs111595856	2	T	C	121103598	0.0639	0.0676		
rs10206072	2	G	A	121373466	0.0457	0.9009		
rs7602028	2	C	A	16016503	0.0135	0.7221		
rs16854905	2	C	T	169012955	0.0126	0.9021	STK39	intron_variant
rs77167534	2	C	T	173319930	0.1191	0.9411	ITGA6	intron_variant
rs34925593	2	C	T	174234547	0.0205	0.4899		
rs1861270	2	G	A	202126615	0.0202	0.7350	CASP8	intron_variant;non_coding_transcript_variant;NMD_transcript_variant;intron_variant
rs12621900	2	C	T	208118301	0.0236	0.7631		non_coding_transcript_variant;intron_variant
rs9306894	2	G	A	20878105	0.0148	0.3690		non_coding_transcript_exon_variant;non_coding_transcript_exon_variant
rs74001374	2	C	T	238411293	0.1019	0.9926	MLPH	intron_variant;non_coding_transcript_variant;intron_variant
rs2292884	2	G	A	238443226	0.0354	0.2415	MLPH	intron_variant;missense_variant;non_coding_transcript_variant;non_coding_transcript_exon_variant;missense_variant;intron_variant;coding_sequence_variant;non_coding_transcript_variant;non_coding_transcript_exon_variant;coding_sequence_variant
rs77559646	2	A	G	242135265	0.1676	0.0227	ANO7	missense_variant;splice_region_variant;intron_variant
rs77482050	2	G	A	242139600	0.2496	0.9892	ANO7	missense_variant;stop_gained
rs2074840	2	C	T	242141719	0.0210	0.3041	ANO7	splice_region_variant;synonymous_variant
rs76832527	2	A	G	242157241	0.0458	0.1740	ANO7	missense_variant
rs6738169	2	C	G	43064555	0.0286	0.7073		
rs7591218	2	A	G	43637998	0.0307	0.3130	THADA	intron_variant;NMD_transcript_variant;non_coding_transcript_variant
rs28514770	2	C	G	43851282	0.0139	0.7124		
rs11125927	2	G	A	62752975	0.0327	0.1139		
rs58235267	2	G	C	63277843	0.0203	0.4733	OTX1	intron_variant
chr2_63301164	2	A	G	63301164	-0.0327	0.4982		
rs139283528	2	G	A	63938756	0.1070	0.9882	WDPCP	non_coding_transcript_variant;intron_variant

rs74702681	2	T	C	66652885	0.0564	0.0225		
rs2028900	2	C	T	85767735	0.0384	0.5539	MAT2A	intron_variant;non_coding_transcript_variant
rs11686272	2	T	G	8598444	0.0180	0.4473		
rs1283104	3	G	C	106962521	0.0154	0.3755	LINC00883	intron_variant;non_coding_transcript_variant
rs151038334	3	C	T	107193337	0.0431	0.9157		
rs2271494	3	A	T	113300183	0.0474	0.5699	SIDT1	intron_variant;non_coding_transcript_variant
rs2811476	3	C	A	127898501	0.0096	0.2660	EEFSEC	intron_variant;non_coding_transcript_variant
rs4857841	3	A	G	128046643	0.0427	0.2779	EEFSEC	intron_variant;non_coding_transcript_variant
rs35006112	3	G	A	128213994	0.0296	0.8415		intron_variant;non_coding_transcript_variant
rs1457063	3	A	G	137562823	0.0182	0.6146		
rs7650602	3	C	T	141147414	0.0135	0.4413	ZBTB38	intron_variant
rs2293607	3	T	C	169482335	0.0284	0.7525	TERC	non_coding_transcript_exon_variant;non_coding_transcript_exon_variant
rs78416326	3	G	C	170074517	0.1039	0.7929		;
rs577952184	3	C	CTT TTT	170083540	0.0331	0.8809	SKIL	intron_variant;NMD_transcript_variant
rs6550597	3	A	G	18738940	0.0135	0.7138		non_coding_transcript_variant;intron_variant
rs7618603	3	A	C	23153062	0.0205	0.1704		
rs34680713	3	A	AT	49621718	0.0300	0.1756	BSN	intron_variant
rs13091518	3	T	C	70796696	0.0264	0.5766		
rs143745027	3	G	A	87144017	0.0597	0.0650		
chr3_87147922	3	T	A	87147922	-0.0020	0.9268		
rs7628934	3	C	T	87175984	0.0189	0.5055		
rs6788616	3	G	A	87205079	0.0301	0.4599		
rs114810266	3	A	G	87399362	0.0438	0.9775		
rs7679673	4	C	A	106061534	0.0668	0.5983		non_coding_transcript_variant;intron_variant
rs17035310	4	C	T	106064754	0.0243	0.8683		
rs77821238	4	C	T	140948835	0.0156	0.8315	MAML3	intron_variant
rs72725734	4	G	A	146879237	0.0102	0.1402		
rs147762399	4	T	C	152030340	0.0429	0.0363	SH3D19	non_coding_transcript_variant;intron_variant
rs17804499	4	G	C	74442349	0.0502	0.9437	RASSF6	missense_variant
rs13142786	4	T	A	74477135	0.0275	0.4797	RASSF6	intron_variant;non_coding_transcript_variant
rs6853490	4	G	A	95544718	0.0218	0.4364	PDLIM5	intron_variant;non_coding_transcript_variant;NMD_transcript_variant
chr4_95562877	4	T	C	95562877	-0.0317	0.3507	PDLIM5	intron_variant;non_coding_transcript_variant;NMD_transcript_variant
rs2242652	5	G	A	1280028	0.0198	0.8007	TERT	non_coding_transcript_variant;intron_variant;NMD_transcript_variant;intron_variant;non_coding_transcript_variant;intron_variant

									;NMD_transcript_variant; intron_variant
rs7725218	5	A	G	1282414	-0.0393	0.3501	TERT		non_coding_transcript_va riant;intron_variant;NMD_ transcript_variant;intron_v ariant
rs71595003	5	A	G	1292118	0.0815	0.0285	TERT		intron_variant;NMD_trans cript_variant;intron_varian t
rs2736098	5	T	C	1294086	0.0348	0.2626	TERT		synonymous_variant;NM D_transcript_variant;syno nymous_variant
rs2736108	5	T	C	1297488	0.0173	0.2944			;
rs10793821	5	T	C	133836209	0.0195	0.5760			
rs71599622	5	T	TG A	14372362	0.0136	0.2826	TRIO		intron_variant;NMD_trans cript_variant;non_coding_ transcript_variant
rs76551843	5	A	G	169172133	0.1520	0.9913	DOCK2		intron_variant;NMD_trans cript_variant;non_coding_ transcript_variant
rs9686557	5	C	A	172959030	0.0216	0.4429			
rs61739424	5	G	A	177683905	0.0495	0.9624	COL23A1		missense_variant
rs2672843	5	G	A	177891551	0.0207	0.4090	COL23A1		intron_variant
rs4975758	5	G	C	1891174	0.0254	0.4757			non_coding_transcript_va riant;intron_variant
rs10941370	5	T	C	37833419	0.0081	0.4452	GDNF		intron_variant
rs1482675	5	T	C	44368506	0.0054	0.3113	FGF10		intron_variant
rs9292122	5	A	G	56087910	0.0181	0.7106			
rs2038542	6	C	T	109295293	0.0352	0.1455			
rs2018336	6	T	C	11217897	0.0415	0.7696			intron_variant;non_coding _transcript_variant;intron _variant;NMD_transcript_ variant
rs339351	6	C	A	117200434	0.0409	0.6990	RFX6		non_coding_transcript_va riant;intron_variant
rs3910736	6	T	C	153412476	-0.0212	0.3242	RGS17		intron_variant
rs13215045	6	C	T	153447516	0.0202	0.6868	RGS17		intron_variant
rs963800	6	C	T	160150279	0.0285	0.7868	SOD2		intron_variant;intron_vari ant;non_coding_transcript _variant
rs4646284	6	TG	T	160581543	0.0942	0.2974			
rs7769879	6	C	G	160865645	0.0325	0.3645	SLC22A3		intron_variant
rs2814811	6	A	G	1670985	0.0187	0.4043	GMDS		intron_variant;non_coding transcript_variant
rs6927369	6	C	T	21330689	0.0333	0.8084			
rs4269363	6	G	A	21471490	0.0167	0.5721			
rs12665509	6	A	C	21878849	0.0150	0.4603	CASC15		intron_variant;non_coding transcript_variant
rs62407547	6	C	T	30216712	0.0212	0.2467	HCG17		intron_variant;non_coding transcript_variant
rs9275160	6	A	G	32652620	0.0371	0.3525			
rs9469899	6	A	G	34793124	0.0333	0.3648	UHRF1BP 1		intron_variant
rs4714485	6	G	T	41536587	0.0384	0.2754	FOXP4		intron_variant
rs9472120	6	C	T	43709785	0.0173	0.4902			

rs9443189	6	A	G	76495882	0.0116	0.8596	MYO6	intron_variant
rs4513875	7	T	C	1928159	0.0240	0.3860	MAD1L1	intron_variant
rs11452686	7	T	TA	20414110	0.0005	0.5922	ITGB8	intron_variant;non_coding_transcript_variant
rs9655205	7	C	A	20999211	0.0448	0.2274	LINC01162	intron_variant;non_coding_transcript_variant
rs35389879	7	T	G	21812043	0.0238	0.4149	DNAH11	intron_variant
rs6956484	7	A	C	27564862	0.0335	0.6145		
rs10486567	7	G	A	27976563	0.0460	0.7708	JAZF1	intron_variant;NMD_transcript_variant
rs12701838	7	A	G	40877473	0.0275	0.7309	SUGCT	intron_variant;non_coding_transcript_variant
rs834608	7	A	T	47451918	0.0243	0.5760	TNS3	intron_variant
rs6955627	7	C	T	92577760	0.0216	0.9154		
rs4727386	7	A	G	97688440	0.0188	0.4545		;
rs6965016	7	C	A	97807882	0.0337	0.4591	LMTK2	intron_variant
rs73700335	8	G	A	108923107	0.0308	0.8343	RSPO2	intron_variant
rs2572375	8	C	T	11217455	0.0152	0.7046	TDH	non_coding_transcript_variant;intron_variant
rs6984837	8	G	A	127901649	0.0026	0.3184	PCAT1	intron_variant;non_coding_transcript_variant
rs9297746	8	C	T	127909361	-0.0391	0.5029	PCAT1	intron_variant;non_coding_transcript_variant
rs7011138	8	A	T	127922200	-0.0162	0.8196	PCAT1	intron_variant;non_coding_transcript_variant
rs28556804	8	G	A	128014315	-0.0592	0.2627	PCAT1	intron_variant;non_coding_transcript_variant
rs7463326	8	G	A	128027954	0.0069	0.7470	PCAT1	intron_variant;non_coding_transcript_variant
rs77541621	8	A	G	128077146	0.2435	0.0251		
rs1016343	8	T	C	128093297	-0.0015	0.2058	PCAT2	non_coding_transcript_variant;intron_variant
rs72725879	8	T	C	128103969	0.0994	0.1849		
rs183373024	8	G	A	128104117	0.3390	0.0063		
rs78809737	8	G	A	128104218	0.0370	0.9540		
rs60163266	8	A	G	128323157	0.0184	0.1382	CASC8	intron_variant;non_coding_transcript_variant
rs201057014	8	T	C	128325355	0.0110	0.1109	CASC8	intron_variant;non_coding_transcript_variant
rs17464492	8	A	G	128342866	0.0642	0.7142	CASC8	intron_variant;non_coding_transcript_variant
rs6983267	8	G	T	128413305	0.0832	0.5138	CASC8	intron_variant;non_coding_transcript_variant;intron_variant;non_coding_transcript_variant
rs7812894	8	T	A	128520479	-0.0862	0.8998		
rs10090154	8	T	C	128532137	0.0492	0.0997		
rs34265760	8	T	C	128535543	0.0466	0.9806		
rs12549761	8	C	G	128540776	0.0899	0.8769		
rs6557704	8	A	G	23470785	0.0285	0.2839		
chr8_23525358	8	C	T	23525358	0.0519	0.4314		
rs12677206	8	A	C	26063165	0.0152	0.3396		

rs11467	8	A	G	38644914	0.0178	0.6294	TACC1	intron_variant;non_coding_transcript_variant;5_prime_UTR_variant
rs870167	8	G	A	8498803	0.0256	0.0648		
rs4451364	9	A	G	109532734	0.0281	0.7642		
rs817872	9	C	T	110144887	0.0298	0.2772		
rs143655302	9	G	A	110290217	0.1524	0.9855		
rs2241167	9	A	G	130430116	0.0244	0.5134	STXBP1	intron_variant
rs12634	9	T	G	132573536	0.0342	0.2361	TOR1B	3_prime_UTR_variant
rs34540271	9	C	T	18554773	0.0132	0.6956	ADAMTSL1	intron_variant
rs10122990	9	C	A	19072246	0.0190	0.3753	HAUS6	intron_variant
rs17694493	9	G	C	22041998	0.0260	0.1366	CDKN2B-AS1	non_coding_transcript_variant;intron_variant
rs10122495	9	T	A	34049779	0.0032	0.2858		
rs139135938	20	TGGCA GTGG CAGC	T	61001061	0.0250	0.6818	RBBP8NL	intron_variant
rs555607708	22	A	AG	29091856	0.1694	0.0024	CHEK2	frameshift_variant;intron_variant;3_prime_UTR_variant;NMD_transcript_variant
rs145053401	3	C	CAT	152011745	0.0435	0.8924	MBNL1	non_coding_transcript_variant;intron_variant
rs150184171	6	G	GT GTT GT	134292717	0.0231	0.5643	TBPL1	intron_variant
rs57588856	8	C	CA A	127836925	0.0221	0.6435		
rs142727307	9	T	TG	82090723	0.0178	0.1115		
rs11338635	23	GA	G	51245276	0.0032	0.3563		intron_variant;non_coding_transcript_variant
rs141811748	8	C	CC AAA	25894201	0.0487	0.1442		

Harrell's concordance index

Conventional area under the curve (AUC) and optimal operating points are appropriate for analyses of binary discrimination. The present study used a survival analysis approach to evaluate association with age at diagnosis of clinically significant prostate cancer. Moreover, the survival analysis includes censoring, which conventional AUC cannot account for.

One proposed metric for survival analyses is the Harrell's concordance index¹. Briefly, individuals in the dataset are compared in pairs, and the concordance is the percentage of pairs for which the earlier time to event (in this study, age at diagnosis of clinically significant prostate cancer) occurs in the individual with higher score (in this study, PHS46 or PHS290). Where censoring in one or both individuals in a given pair interferes with assessing concordance, that pair is excluded from the index. There are limitations to the interpretation of the Harrell's concordance index^{2,3}, and it may not be ideal for situations like polygenic risk, where the extremes of genetic risk are of more clinical interest than the scores of individuals within, say, the 30th-70th percentiles.

Nevertheless, we calculated the Harrell's concordance index for PHS46 and PHS290 in each testing dataset to evaluate whether PHS290 represented an improvement in concordance index for the endpoint of age at diagnosis of clinically significant prostate cancer. As before, 1,000 bootstrap samples were generated to yield 95% confidence intervals.

The concordance index improved in each testing dataset. In the ProtecT dataset, concordance index was 0.63 [95% CI: 0.60-0.65] for PHS46 and 0.67 [0.64-0.69] for PHS290. Corresponding concordance index results for the other datasets were as follows. African dataset: 0.62 [0.58-0.65] for PHS46 and 0.69 [0.63-0.74] for PHS290. Asian dataset: 0.62 [0.58-0.65] for PHS46 and 0.66 [0.63-0.69] for PHS290. COSM dataset: 0.58 [0.57-0.60] for PHS46 and 0.63 [0.62-0.65] for PHS290.

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