Supplemental Methods and Results

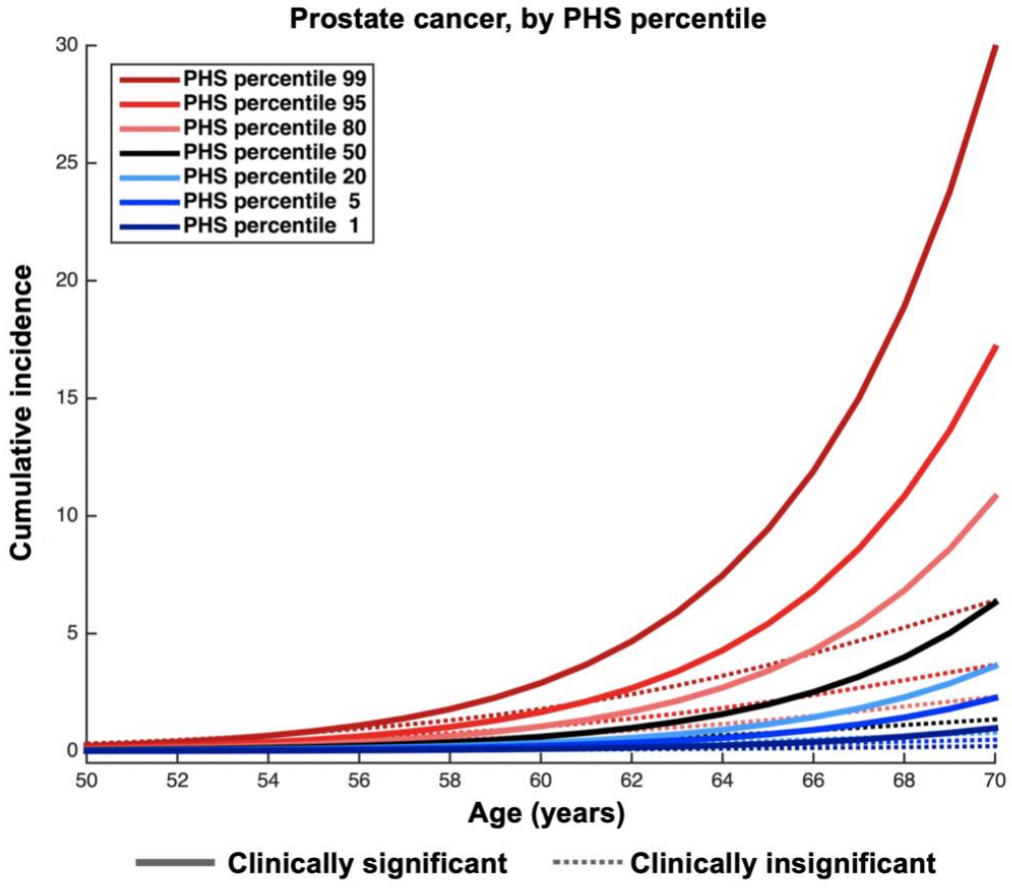
eTable 1. SNP identifier, chromosome, effect allele, reference allele, and position (based on version 37) and beta (model weight) for the 54 SNPs used in the polygenic hazard score (PHS) calculation*.

SNP ID	PHS beta	Chromosome	Position	Effect	Reference
rs6545977	-0.066	2	63301164	C	G
rs1010	0.05	2	85808982	G	A
rs16860513	0.198	2	173342367	A	G
c3_pos87230612	-0.115	3	87147922	T	A
rs6788616	-0.04	3	87205079	A	G
rs4857841	0.029	3	128046643	T	A
c3_pos171557211	0.073	3	170074517	C	G
rs6853490	-0.054	4	95544718	G	A
rs2136486	0.024	4	95571976	G	A
rs7679673 §	-0.066	4	106061534	A	G
rs7725218	-0.07	5	1282414	T	A
rs2736108	0.05	5	1297488	A	G
rs10866528	-0.045	5	1891821	A	T
rs10051795	-1.501	5	100648792	C	A
rs17596465	0.114	6	93471818	G	A
rs3910736	-0.068	6	153412476	G	A
rs651164	-0.05	6	160581374	A	G
rs7769879	0.054	6	160865645	G	A
rs6965016	-0.052	7	97807882	G	A
rs13265330	-0.06	8	23525543	A	C
rs9297746	0.055	8	127909361	A	G
rs28556804	0.077	8	128014315	G	A
c8_pos128146328	0.174	8	128077146	A	G
rs7841060	-0.082	8	128096477	C	A
rs13252265	-0.055	8	128203859	A	C
c8_pos128389706	0.066	8	128320524	C	G
rs6983267 §	-0.095	8	128413305	A	G
rs9297759	0.073	8	128519171	A	G
rs12549761	0.054	8	128540776	A	G
c10_pos8072007	-1.53	10	8032001	A	G
rs10993994 §	0.1	10	51549496	A	T
c11_pos2181240	0.068	11	2224664	G	C
rs12275055	-0.076	11	68981359	C	A
rs7929962	0.048	11	68985583	G	A

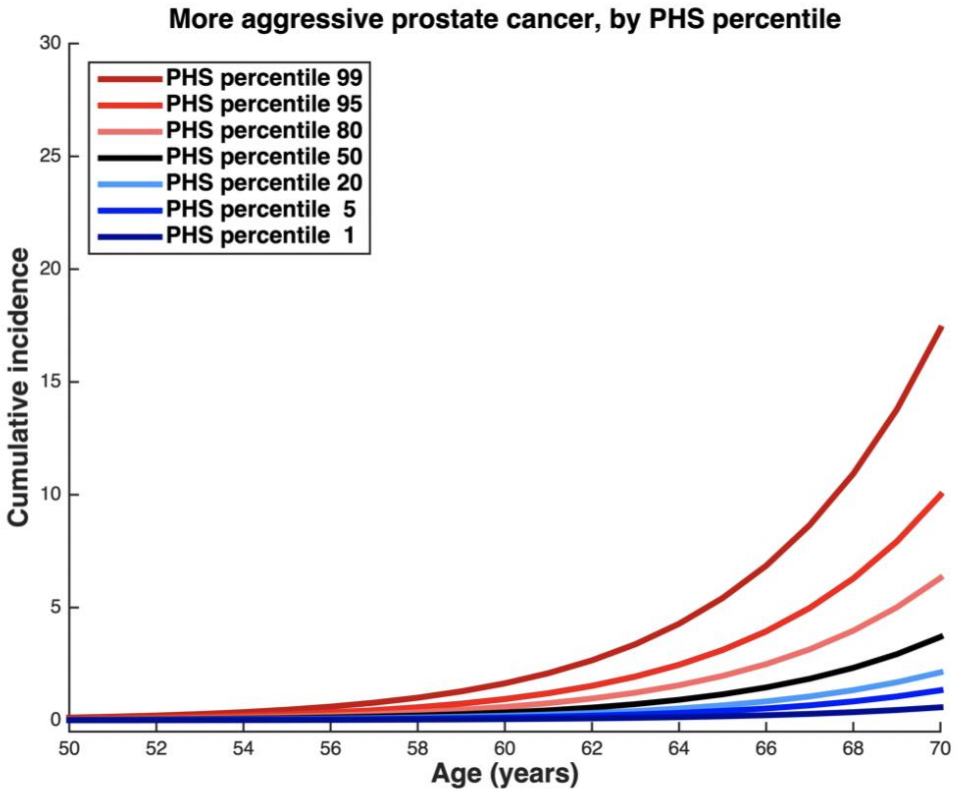
rs11568818 §	0.041	11	102401661	A	G
rs10875943 §	-0.041	12	49676010	T	A
rs4919763	-0.05	12	53279623	A	C
rs3861106	-0.914	13	63485756	A	G
rs4643253	0.052	14	69106108	G	C
rs684232 §	-0.039	17	618965	C	G
rs718961	-0.075	17	36077099	C	G
rs11651052	-0.093	17	36102381	A	G
c17_pos44175675	0.142	17	46820676	G	C
rs9889335	0.077	17	69115146	G	A
rs11672691 §	-0.059	19	41985587	A	G
rs17632542	0.14	19	51361757	G	A
rs4809311	0.049	20	62233764	A	G
c22_pos41831564	0.084	22	43501620	A	G
rs747745	0.044	22	43503547	A	G
rs4907775	0.131	23	51263200	G	A
rs5945631	-0.192	23	51268884	A	G
rs7888856	0.049	23	66751555	G	A
rs11795627	-0.042	23	69957441	A	G
rs232964	1.031	23	76136958	A	G

* Comparing the 54 SNPs included in PHS and the 147 SNPs identified in a recent meta-analysis of men with European ancestry[1], there were 7 PHS SNPs that were exact matches (§) with one of the 147 meta-analysis SNPs.

eFigure 1. Incidence of prostate cancer, stratified by clinically significant and clinically insignificant, as derived from application of polygenic hazard score (PHS) hazard ratios and population data from the United Kingdom. The overall population incidence is taken as the median risk (50th percentile); this accounts for age-specific proportions of prostate cancer that were clinically significant in the CAP trial[2]. Hazard ratios were calculated within ProtecT data for various levels of genetic risk ranges (0-2, 2-10, 10-30, 30-70, 70-90, 90-98, and 98-100) to correspond to percentiles of interest (1, 5, 20, 50, 80, 95, and 99, respectively), and used to adjust the median incidence curve. Blue lines represent genetic risk lower than the median while red lines represent genetic risk higher than the median. Solid lines represent clinically significant prostate cancer, while dashed lines represent clinically insignificant cases. The sum of clinically significant and clinically insignificant incidence would estimate the incidence of any prostate cancer.



eFigure 2. Incidence of more aggressive prostate cancer, as derived from application of polygenic hazard score (PHS) hazard ratios and population data from the United Kingdom. The stricter definition for more aggressive disease corresponds to clinical high risk or above by NCCN guidelines—i.e., any of: clinical stage T3-T4, PSA>20, Gleason score ≥8, or nodal/distant metastases[3].The overall population incidence is taken as the median risk (50th percentile); this accounts for age-specific proportions of more aggressive prostate cancer reported in the CAP trial[2]. Hazard ratios were calculated within ProtecT data for various levels of genetic risk ranges (0-2, 2-10, 10-30, 30-70, 70-90, 90-98, and 98-100) to correspond to percentiles of interest (1, 5, 20, 50, 80, 95, and 99, respectively), and used to adjust the median incidence curve. Blue lines represent genetic risk lower than the median while red lines represent genetic risk higher than the median.



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Supplemental Material

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