Table W1. Selected Characteristics of Participants in REDUCE and CAPS.

Characteristic*	REDUCE†			CAPS	
	All [N = 3239 (%)]	Non-cases in Placebo [N = 1244 (%)]	Cases in Placebo [N = 410 (%)]	Controls [N = 1722 (%)]	Cases [N = 2899 (%)]
Age (years)					
Mean ± SD	62.76 ± 6.00	62.22 ± 6.01	63.52 ± 5.98	67.14 ± 7.39	66.37 ± 7.14
Range	49–76	49–76	50–76	45–80	45–82
<63	1561 (48.19)	639 (51.37)	185 (45.12)	547 (31.77)	998 (34.43)
≥63	1678 (51.81)	605 (48.63)	225 (54.88)	1175 (68.23)	1901 (65.57)
tPSA level (ng/ml)					
Median (Q1–Q3)	5.7 (4.4–7.2)	5.7 (4.3–7.2)	5.7 (4.7–7.4)	1.45 (0.78–2.92)	12.0 (7.0–34.0)
<2.5	8 (0.25)	4 (0.32)	0	1204 (69.96)	57 (2.03)
2.5–3.9	529 (16.37)	220 (17.74)	50 (12.22)	234 (13.60)	91 (3.23)
4.0–10.0	2677 (82.85)	1011 (81.53)	358 (87.53)	230 (13.36)	1082 (38.45)
>10.0	17 (0.53)	5 (0.40)	1 (0.24)	53 (3.08)	1584 (56.29)
Missing	8	4	1	1	79
fPSA level (ng/ml)					
Median (Q1–Q3)	0.9 (0.7–1.2)	0.9 (0.7–1.2)	0.9 (0.6–1.2)	0.45 (0.27–0.79)	0.31 (0.03–1.21)
<0.70	799 (24.74)	302 (24.37)	103 (25.18)	1222 (71.01)	1828 (63.19)
0.70–0.89	718 (22.23)	296 (23.89)	93 (22.74)	147 (8.54)	135 (4.67)
0.90–1.20	1043 (32.29)	398 (32.12)	134 (32.76)	131 (7.61)	203 (7.02)
>1.20	670 (20.74)	243 (19.613)	79 (19.32)	221 (12.84)	727 (25.13)
Missing	9	5	1	1	6
%fPSA (%)					
Median (Q1–Q3)	16.0 (12.5–20.0)	16.0 (12.5–19.79)	15.52 (11.63–18.87)	31.1 (23.4–40.3)	15.5 (10.85–23.2)
<10.0	330 (10.22)	109 (8.80)	65 (15.89)	27 (1.55)	460 (20.68)
10.0–25.0	2679 (82.94)	1044 (84.26)	320 (78.24)	496 (28.49)	1291 (58.05)
>25.0	221 (6.84)	86 (6.94)	24 (5.87)	1218 (69.96)	473 (21.27)
Missing	9	5	1	5	651
Prostate cancer‡					
Nonaggressive (%)	286 (69.76)	1619 (56.81)			
Aggressive (%)			124 (30.24)		1231 (43.19)

*Age, tPSA and fPSA levels, and %fPSA were measured at baseline for REDUCE, at recruitment for CAPS controls, and at diagnosis for CAPS cases.

†Cases were prostate cancer patients newly diagnosed in the placebo group during a 4-year follow-up.

‡For REDUCE, those who developed a prostate tumor with a Gleason score of 7 or higher, stage T3b or higher, and/or lymph node or metastasis positive (N+ or M+, respectively) were defined as having an aggressive disease; for CAPS, patients were classified as having aggressive disease if their tumors had a clinical stage of T3/T4, N+, M+, Gleason score of 8 or higher, or a serum PSA level of >50 ng/ml; otherwise, the patients were classified as nonaggressive cases.

Table W2. Summary Results for Selected SNPs Associated with %fPSA in REDUCE GWAS and Replication in CAPS Controls with Intermediate tPSA Levels (2.5–10 ng/ml).

Chromosome	SNP	Position	Major/Minor Allele	GWAS in REDUCE (N = 3192)				Replication in CAPS (N = 464)				P_{combined}*
				MAF	Mean†	β	P‡	MAF	Mean†	β	P‡	
2	rs1432302	122669620	C/T	0.298	16.13/16.83/17.19	0.042	6.42E–06	0.302	26.12/25.86/24.73	−0.015	0.581	3.96E–05
7	rs7456553	1210051	T/C	0.380	17.04/16.29/15.84	−0.043	1.15E–06	0.384	26.27/25.11/27.17	−0.010	0.697	2.10E–06
7	rs10238880	26441399	T/C	0.182	16.85/15.94/15.06	−0.052	4.06E–06	0.212	25.18/27.27/24.09	0.039	0.217	8.82E–05
12	rs3213764	14478568	A/G	0.467	15.73/16.61/17.34	0.049	1.85E–08	0.504	23.85/26.22/27.15	0.065	9.65E–03	6.45E–10
19	rs1354774	56084930	A/G	0.343	15.64/17.14/17.45	0.058	7.39E–11	0.309	23.98/27.82/27.05	0.075	4.71E–03	1.25E–12

*P_{combined} values were estimated using inverse variance–weighted meta-analyses according to regression coefficients (β) and corresponding SEs.

†Mean levels of %fPSA (%) by genotypes (major homozygote/heterozygote/minor homozygote).

‡P values were from linear regression models adjusted for age.

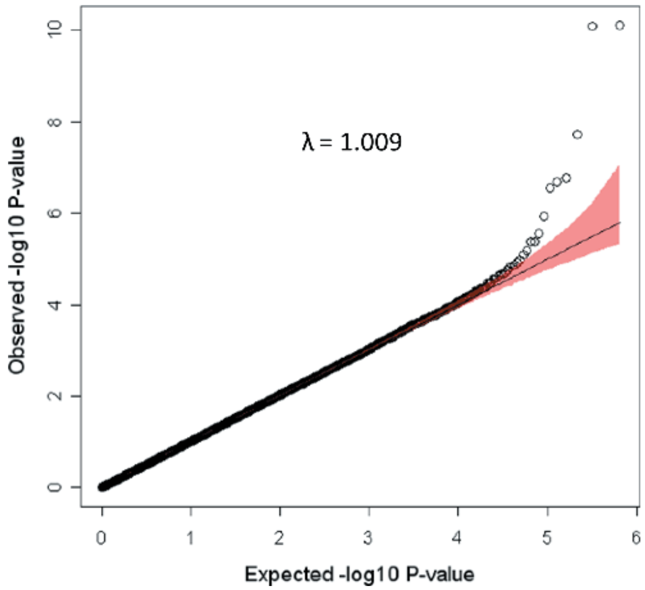

Figure W1. Q-Q plots and genomic inflation factors (λ) for the associations with %fPSA, with observed *P* values plotted as a function of expected *P* values; red areas indicate the 90% confidence region from a null distribution of *P* values (generated from 100 simulations).

Table W3. Summary Results for Selected SNPs Associated with %fPSA in REDUCE GWAS and Replication in All of the CAPS Controls.

Chromosome	SNP	Position	Major/Minor Allele	GWAS in REDUCE (N = 3192)				Replication in CAPS (N = 1722)				P_{combined}*
				MAF	Mean[†]	β	P[‡]	MAF	Mean[†]	β	P[‡]	
2	rs1432302	122669620	C/T	0.298	16.13/16.83/17.19	0.042	6.42E−06	0.297	32.37/32.62/32.58	0.005	0.730	4.99E−05
7	rs7456553	1210051	T/C	0.380	17.04/16.29/15.84	−0.043	1.15E−06	0.378	32.61/32.27/32.74	0.001	0.936	3.65E−05
7	rs10238880	26441399	T/C	0.182	16.85/15.94/15.06	−0.052	4.06E−06	0.213	32.43/32.69/31.48	0.007	0.691	2.56E−04
12	rs3213764	14478568	A/G	0.467	15.73/16.61/17.34	0.049	1.85E−08	0.499	31.21/32.85/33.02	0.032	0.023	1.97E−09
19	rs1354774	56084930	A/G	0.343	15.64/17.14/17.45	0.058	7.39E−11	0.335	29.77/34.50/35.34	0.101	1.05E−11	6.48E−20

*P_{combined} values were estimated using inverse variance–weighted meta-analyses according to regression coefficients (β) and corresponding SEs.

[†] Mean levels of %fPSA (%) by genotypes (major homozygote/heterozygote/minor homozygote).

[‡] *P* values were from linear regression models adjusted for age.

Table W4. SNPs at 12p13 and 19q13 Associated with %fPSA with a *P* Value Less than 1 × 10^{-5}.

Chromosome	SNP	Position	Status	Major/Minor Allele	MAF	Mean*	β	SE	*P*†	LD with Lead SNP‡	*P* Conditioned by Lead SNP§
SNPs at 12p13 associated with %fPSA											
12	rs6488674	14380181	Genotyped	G/T	0.459	15.92/16.49/17.36	0.041	0.009	2.70E–06	0.822	0.534
12	rs6488679	14412643	Imputed	T/G	0.493	15.84/16.50/17.34	0.043	0.009	9.73E–07	0.745	0.881
12	rs7137532	14415239	Imputed	T/G	0.493	15.85/16.51/17.35	0.043	0.009	1.02E–06	0.745	0.871
12	rs7312042	14424757	Imputed	A/G	0.490	15.85/16.46/17.34	0.043	0.009	9.38E–07	0.747	0.826
12	rs11055956	14425693	Imputed	A/G	0.490	15.83/16.48/17.35	0.044	0.009	5.72E–07	0.746	0.696
12	rs11055960	14427933	Imputed	T/G	0.447	15.92/16.56/17.41	0.042	0.009	1.93E–06	0.905	0.149
12	rs10734875	14433808	Imputed	G/A	0.489	15.85/16.48/17.35	0.043	0.009	6.29E–07	0.747	0.708
12	rs7954210	14439581	Imputed	C/A	0.487	15.81/16.49/17.38	0.045	0.009	1.80E–07	0.773	0.297
12	rs7966054	14442292	Imputed	C/T	0.445	15.92/16.56/17.42	0.043	0.009	1.12E–06	0.907	0.155
12	rs7970587	14466726	Genotyped	G/A	0.486	15.82/16.49/17.37	0.045	0.009	2.05E–07	0.746	0.496
12	rs2417349	14472716	Imputed	C/T	0.411	17.20/16.28/15.61	–0.047	0.009	1.06E–07	0.617	0.126
12	rs3213764	14478568	Genotyped	A/G	0.467	15.73/16.61/17.34	0.049	0.009	1.85E–08	–	–
12	rs10772782	14484110	Imputed	A/G	0.383	17.16/16.31/15.53	–0.046	0.009	3.96E–07	0.564	0.118
12	rs7310929	14485169	Genotyped	T/C	0.375	17.14/16.31/15.48	–0.046	0.009	1.69E–07	0.527	0.087
12	rs7964899	14487023	Imputed	G/A	0.446	15.93/16.56/17.42	0.042	0.009	1.47E–06	0.908	0.154
12	rs7298685	14498988	Genotyped	C/A	0.433	17.25/16.27/15.89	–0.040	0.009	4.09E–06	0.520	0.406
12	rs12366507	14500066	Imputed	G/A	0.438	17.26/16.30/15.87	–0.039	0.009	6.31E–06	0.531	0.434
12	rs962504	14501706	Imputed	G/A	0.448	15.91/16.54/17.42	0.043	0.009	1.03E–06	0.926	0.278
12	rs11055980	14502789	Imputed	C/T	0.450	15.86/16.54/17.42	0.045	0.009	4.52E–07	0.937	0.575
12	rs4764090	14503590	Imputed	A/G	0.450	15.86/16.54/17.42	0.045	0.009	4.38E–07	0.939	0.548
12	rs4237951	14515841	Imputed	A/C	0.413	17.21/16.31/15.63	–0.046	0.009	2.15E–07	0.621	0.128
12	rs2900333	14545134	Imputed	C/T	0.372	17.16/16.27/15.44	–0.049	0.009	6.51E–08	0.538	0.048
SNPs at 19q13 associated with %fPSA											
19	rs198972	56071705	Genotyped	G/A	0.296	15.84/17.25/16.97	0.048	0.009	2.78E–07	0.519	0.499
19	rs16987929	56077065	Genotyped	A/G	0.240	15.92/17.29/17.70	0.065	0.010	7.90E–11	0.591	0.020
19	rs8103659	56077214	Imputed	A/G	0.235	15.92/17.30/17.74	0.065	0.010	1.35E–10	0.593	0.040
19	rs198957	56081372	Imputed	C/T	0.341	15.63/17.19/17.36	0.057	0.009	1.81E–10	1.000	–
19	rs198956	56082165	Imputed	A/G	0.342	15.63/17.18/17.36	0.057	0.009	1.83E–10	1.000	–
19	rs7256586	56082621	Imputed	C/A	0.238	15.93/17.28/17.77	0.066	0.010	6.51E–11	0.614	0.018
19	rs1354774	56084930	Genotyped	A/G	0.343	15.64/17.14/17.45	0.058	0.009	7.39E–11	–	–
19	rs2739482	56086098	Imputed	C/T	0.343	15.64/17.14/17.39	0.057	0.009	2.28E–10	1.000	–
19	rs61044983	56088734	Imputed	G/T	0.238	15.93/17.27/17.77	0.065	0.010	7.77E–11	0.617	0.019
19	rs8105985	56089883	Imputed	C/A	0.238	15.93/17.27/17.77	0.065	0.010	7.77E–11	0.617	0.019
19	rs1629856	56090700	Imputed	A/C	0.343	15.64/17.14/17.41	0.057	0.009	1.68E–10	1.000	–

*Mean levels of %fPSA (%) by genotypes (major homozygote/heterozygote/minor homozygote).

†*P* values were from linear regression models adjusted for age.

‡The r^2 values were presented as a measure of LD for each SNP at 12p13 or 19q13 with rs3213764 or rs1354774, respectively.

§*P* values were from linear regression models adjusted for age and conditioned by rs3213764 at 12p13 or rs154774 at 19q13.

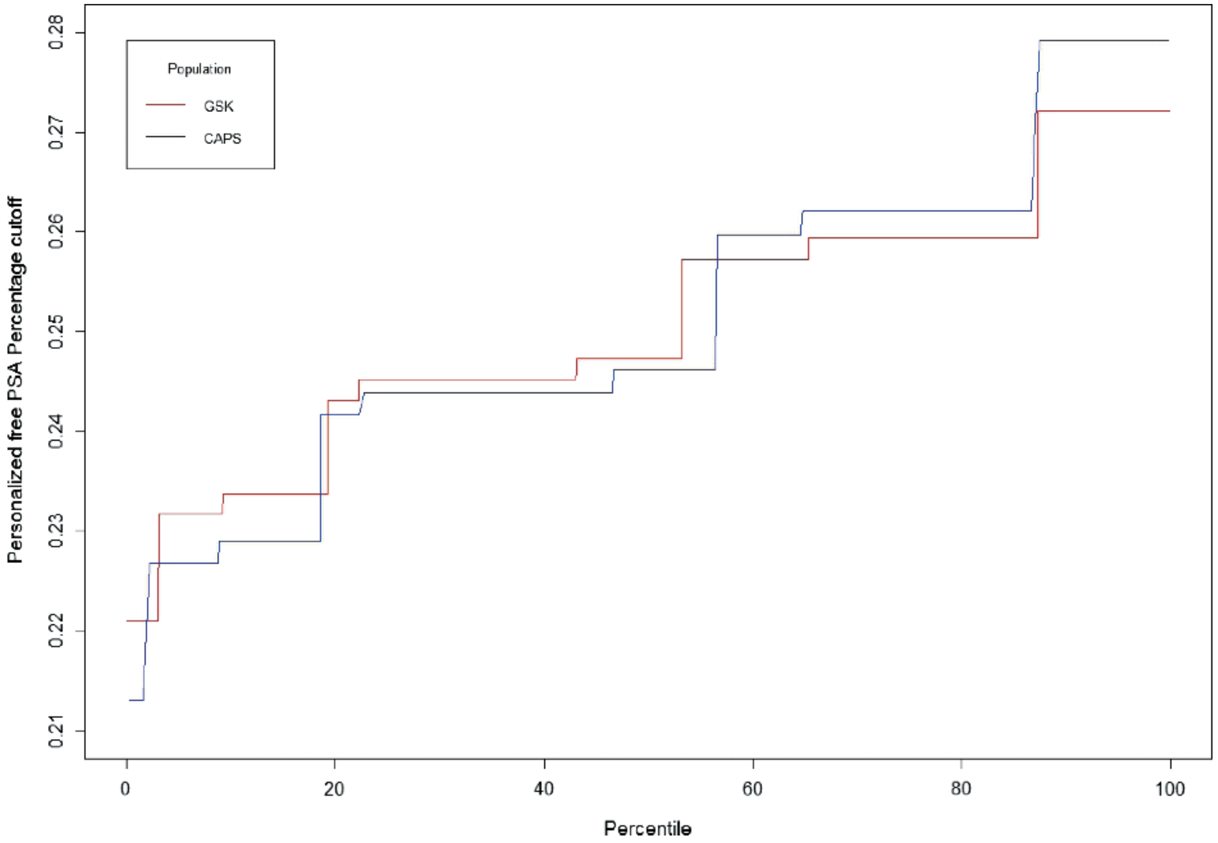

Figure W2. Cumulative distribution of the personalized %fPSA cutoff values after genetic correction. Personalized %fPSA cutoff values (shown on the *Y*-axis) were estimated by using a genetic correction for the two %fPSA-associated SNPs (rs3213764 and rs1354774) to the commonly used %fPSA cutoff value of 0.25 in the GSK (red line) and CAPS (blue line) study populations. The *X*-axis represents the percentile of the population.