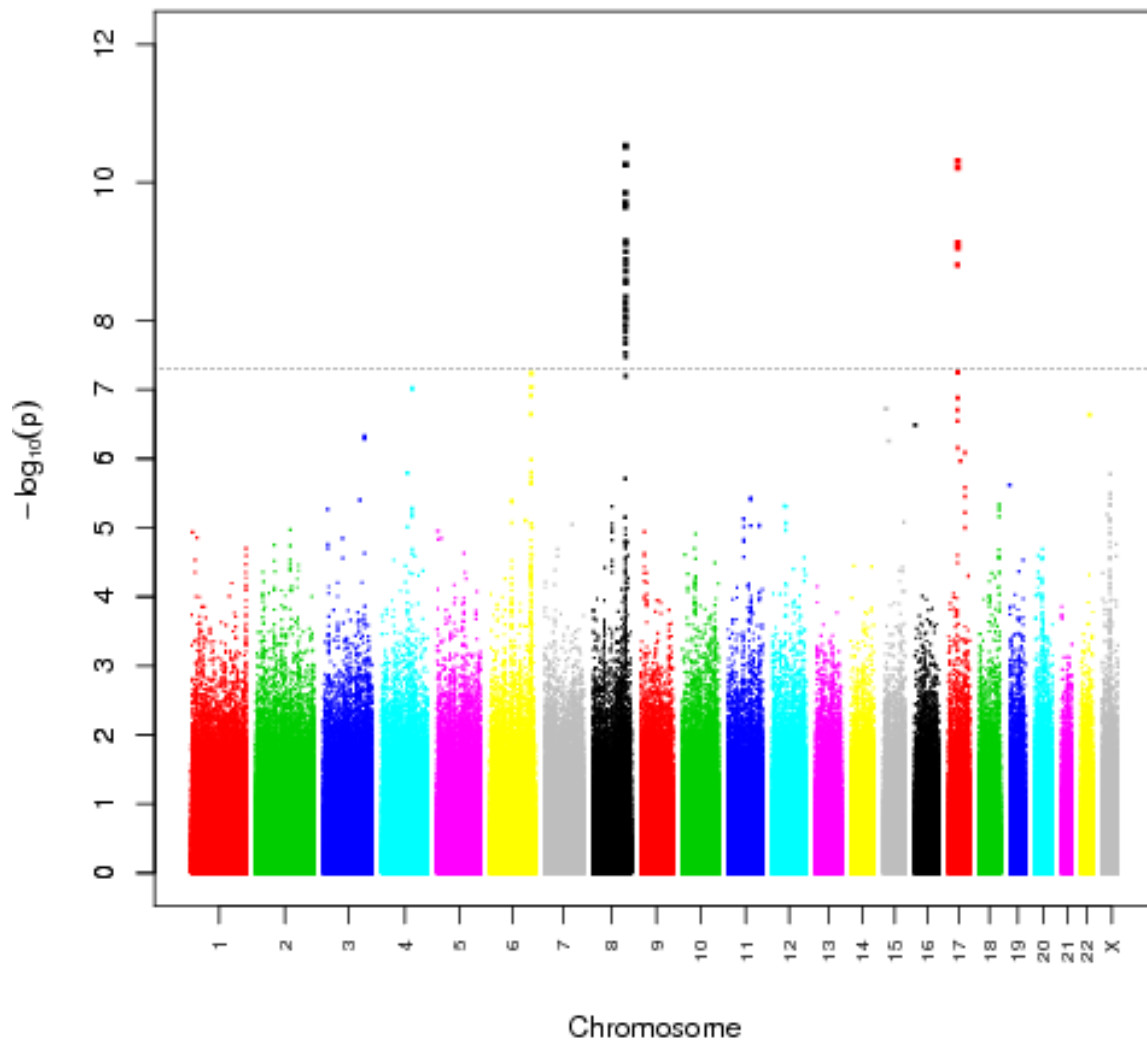
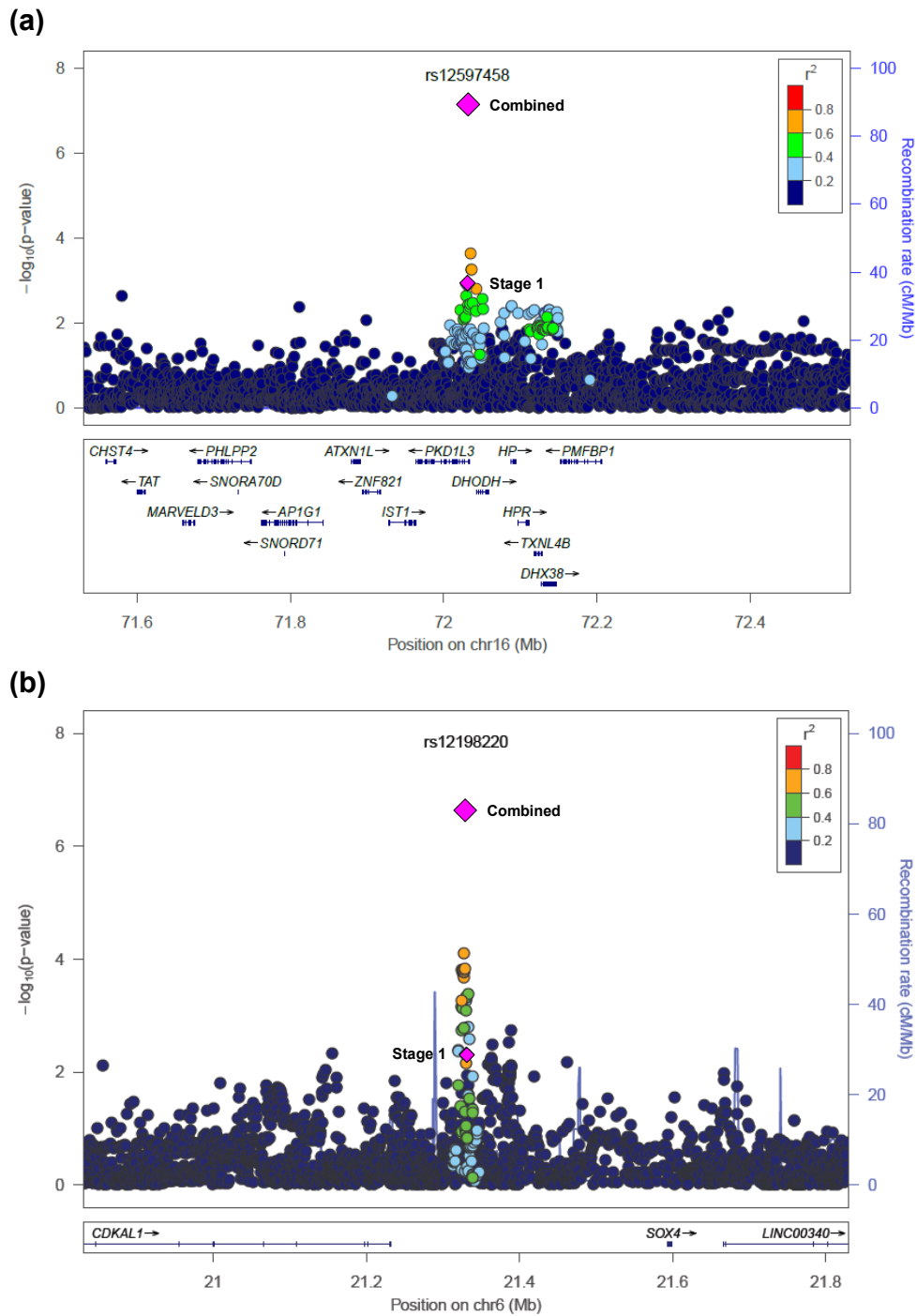


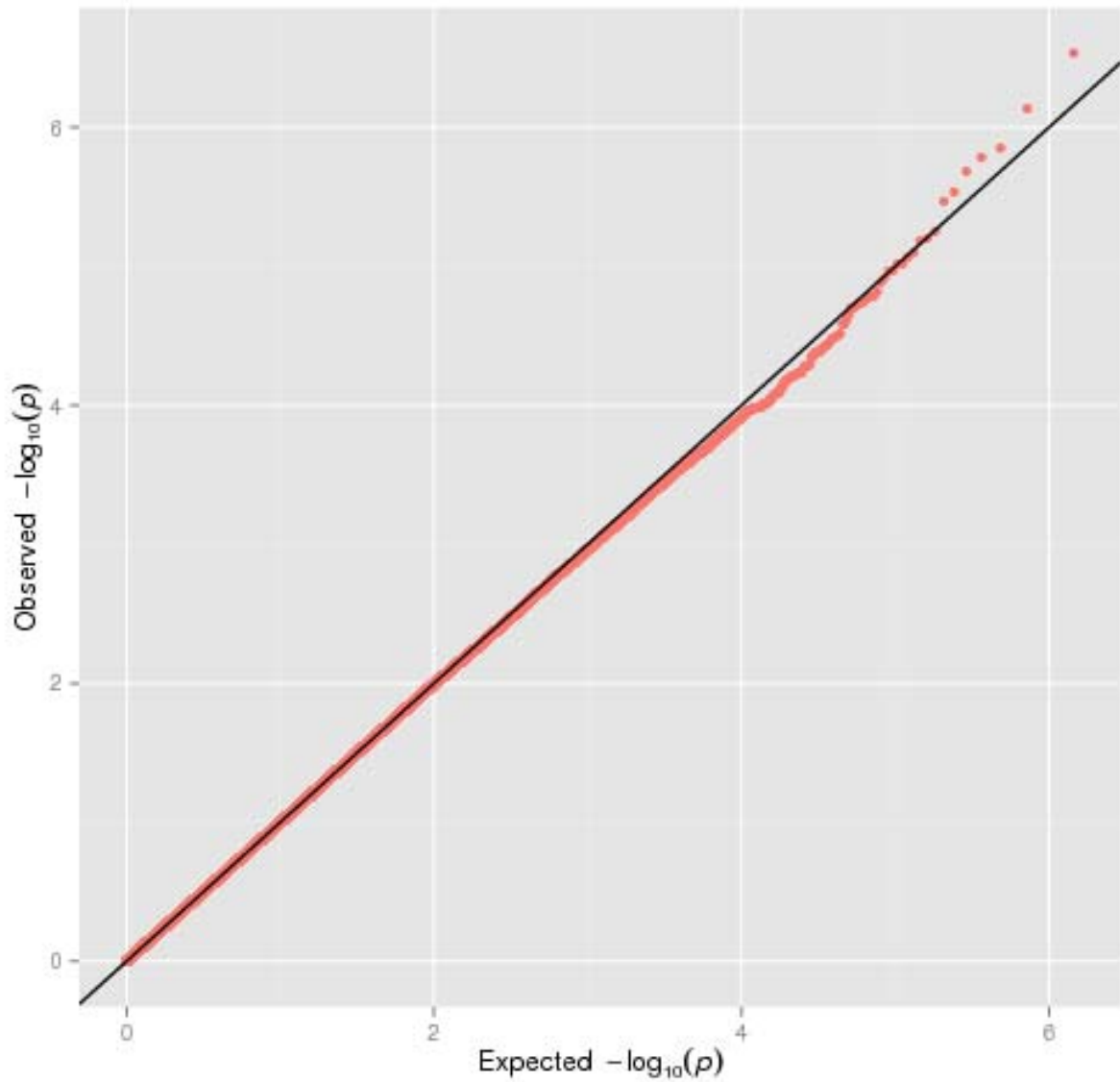
Supplementary Figure 1. Quantile-quantile (Q-Q) plot of the $-\log_{10}$ p-value association results from logistic regression models for prostate cancer risk in stage 1 (red) and after removing any SNPs within 500 kb of a previously established locus (green).



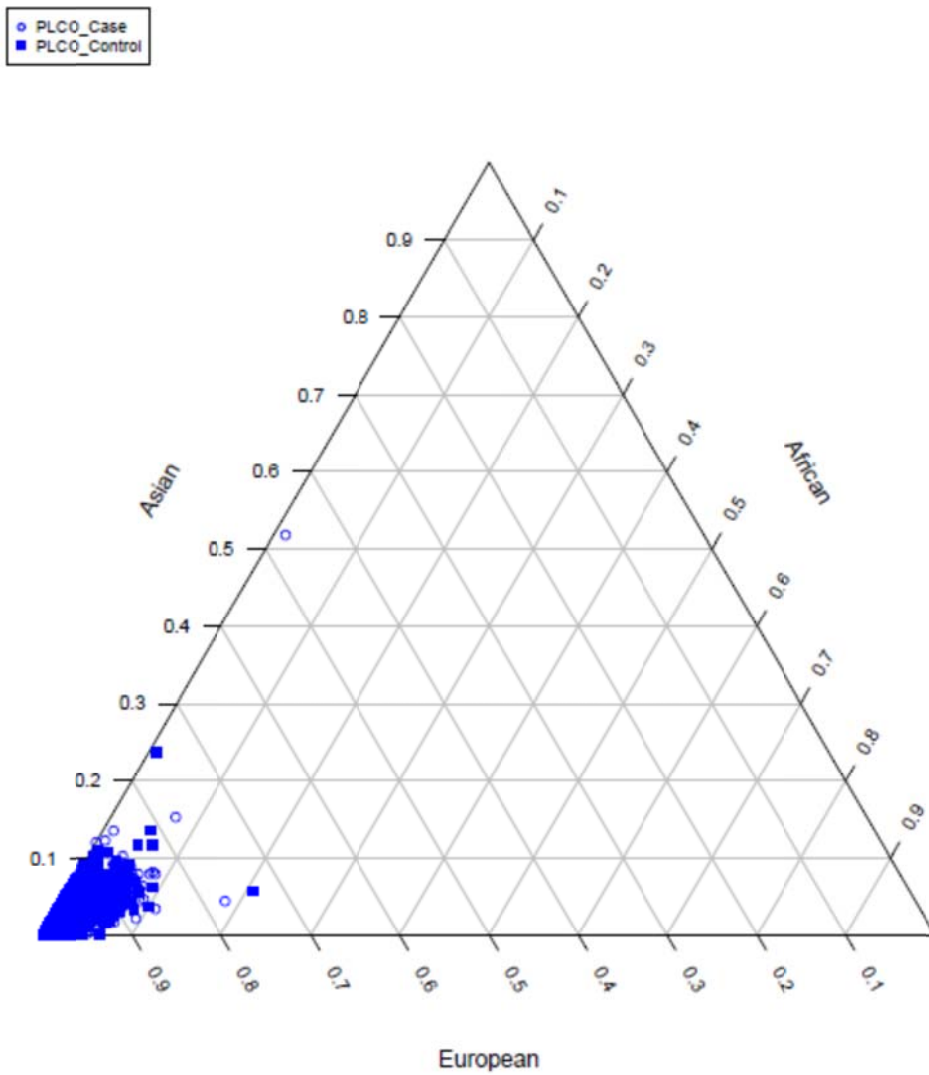
Supplementary Figure 2. Manhattan plot showing the statistical significance of the association for all genotyped SNPs in the stage 1 analysis. SNPs are plotted on the x-axis according to their position on each chromosome against the significance of the association on the y-axis (shown as $-\log_{10}$ P-value). P-values are based on logistic regression models for prostate cancer risk. Red line denotes $P=5 \times 10^{-8}$ statistical significance.



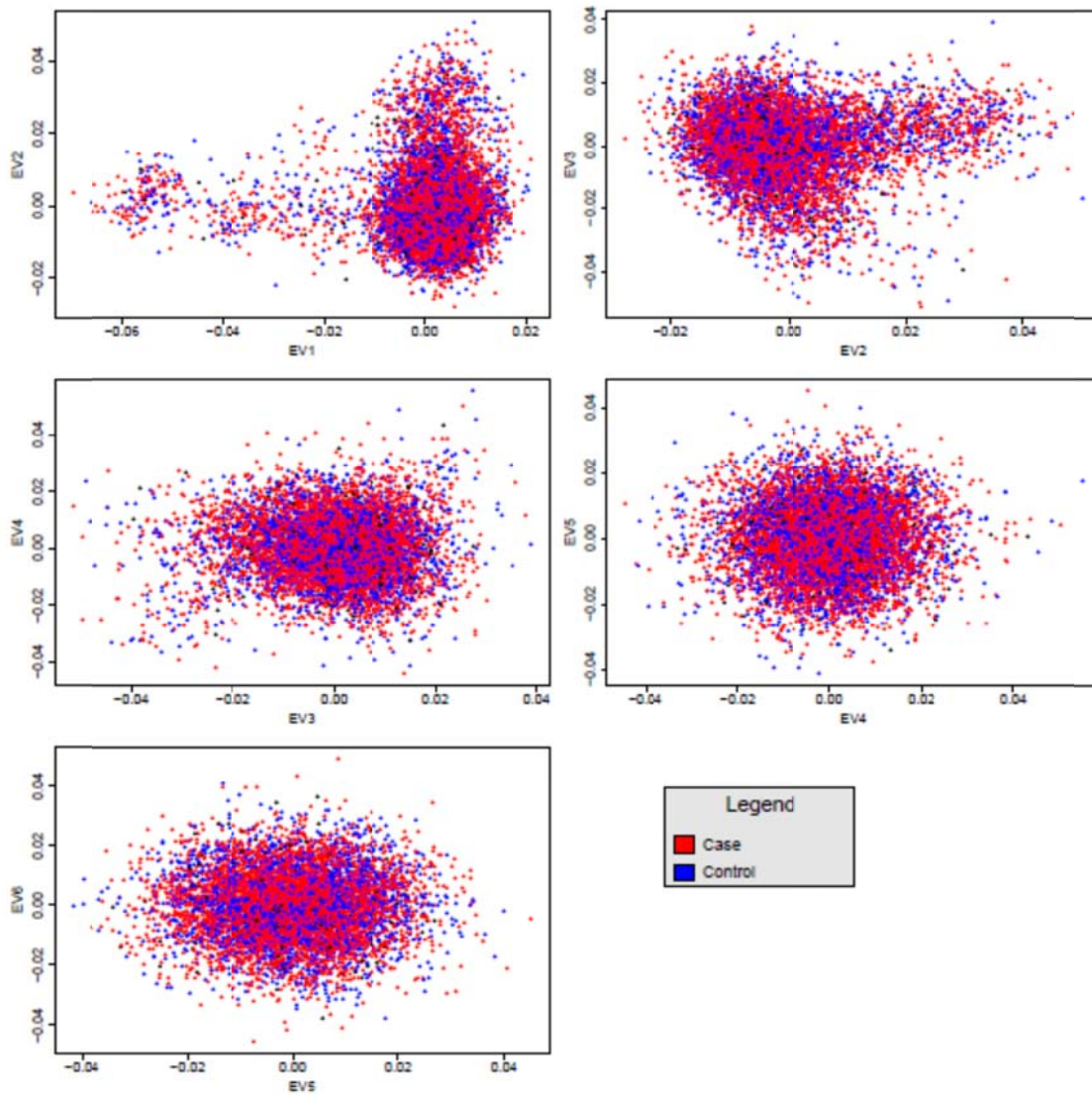
Supplementary Figure 3. Regional association plots of the two suggestive loci associated with prostate cancer risk: (a) chromosome 16q22.2 (rs12597458) and (b) chromosome 6p22.3 (rs12198220). Shown are the $-\log_{10}$ association p-values for stage 1 (dots and lower pink diamond) and $-\log_{10}$ p-value for the combined stage 1-3 analysis (upper diamond) based on logistic regression models.



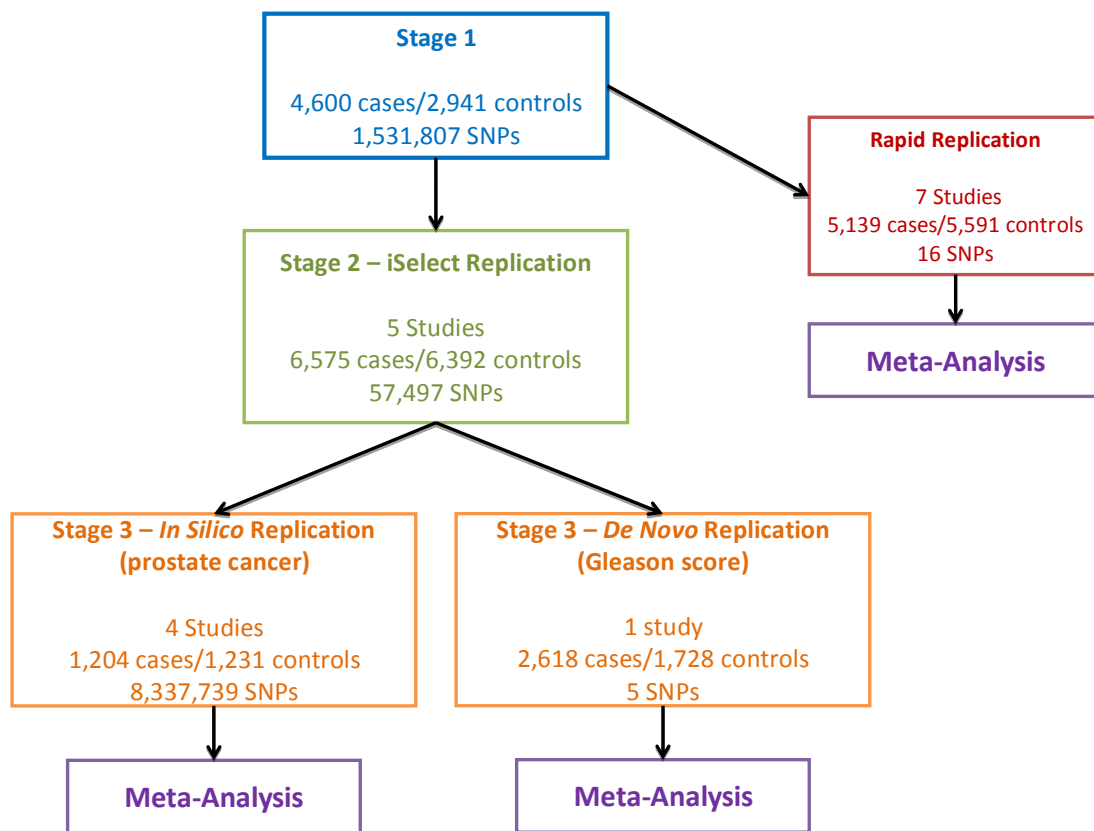
Supplementary Figure 4. Quantile-quantile (Q-Q) plot of the association results ($-\log_{10}$ p-values) for Gleason score as a quantitative trait among prostate cancer cases in stage 1 (red). P-values were calculated from linear regression models.



Supplementary Figure 5. Plot of estimated admixture for individuals in stage 1. Individuals with <80% European ancestry were excluded.



Supplementary Figure 6. Plot of top eigenvectors from stage 1 data based on principal components analysis.



Supplementary Figure 7. Flowchart describing the multistage study design

Supplementary Table 1. Baseline characteristics of the subjects included in stage 1 and stage 2

| | Stage 1 | Stage 2 Studies | | | | |
|----------------------------|---|--------------------------------------|---|--|--------------------------------------|--------------------------------------|
| | Pegasus (4600 cases, 2941 controls) | ATBC (979 cases, 942 controls) | CPSII (2714 cases, 2440 controls) | CeRePP (1338 cases, 1340 controls) | HPFS (885 cases, 893 controls) | PLCO (659 cases, 777 controls) |
| Mean age (\pm SD) | | | | | | |
| Cases | 68.8 \pm 5.8 | 69.8 \pm 5.8 | 70.2 \pm 5.7 | 65.5 \pm 8.3 | 69.8 \pm 7.4 | 72.4 \pm 5.4 |
| Controls | 67.9 \pm 5.8 | 69.3 \pm 6.1 | 70.3 \pm 5.7 | 65.3 \pm 8.2 | 67.2 \pm 7.8 | 70.4 \pm 5.7 |
| Gleason score | | | | | | |
| \leq 6 | 2693 (58.5%) | 196 (20.0%) | 1389 (51.2%) | 420 (31.4%) | 418 (47.2%) | 274 (41.6%) |
| 7 | 1429 (31.1%) | 80 (8.2%) | 661 (24.4%) | 668 (49.9%) | 238 (26.9%) | 267 (40.5%) |
| \geq 8 | 423 (9.2%) | 52 (5.3%) | 271 (10.0%) | 246 (18.4%) | 64 (7.2%) | 111 (16.8%) |
| Unknown | 55 (1.2%) | 651 (66.5%) | 356 (13.1%) | 0 | 154 (17.4%) | 7 (1.1%) |
| Disease aggressiveness | | | | | | |
| Stage I/II and Gleason <8 | 3729 (81.1%) | 163 (16.6%) | 1858 (68.5%) | 844 (63.1%) | 590 (66.7%) | 503 (76.3%) |
| Stage III/IV or Gleason 8+ | 815 (17.7%) | 112 (11.4%) | 458 (16.9%) | 490 (36.6%) | 119 (13.4%) | 149 (22.6%) |
| Unknown | 56 (1.2%) | 704 (71.9%) | 398 (14.7%) | 4 (0.3%) | 176 (19.9%) | 7 (1.1%) |

Supplementary Table 2. Stage 1 association results for risk of prostate cancer with previously reported loci

| SNP | Chr | Position | Effect allele | Other allele | Info | EAF | No. cases/ No. controls | OR | Lower CI | Upper CI | P | Reference | PUBMED ID |
|--------------------------------|---------|-----------|---------------|--------------|-------|-------|-------------------------|------|----------|----------|----------|---------------|-----------|
| Discovered in Europeans | | | | | | | | | | | | | |
| rs636291 | 1p35 | 10556097 | A | G | 0.983 | 0.674 | 4,599/2,940 | 1.04 | 0.97 | 1.12 | 0.24 | Al Olama A | 25217961 |
| rs17599629 | 1q21 | 150658287 | G | A | 1 | 0.212 | 4,600/2,941 | 1.11 | 1.03 | 1.21 | 0.007 | Al Olama A | 25217961 |
| rs1218582 | 1q21.3 | 154834183 | A | G | 0.994 | 0.554 | 4,600/2,941 | 0.95 | 0.89 | 1.01 | 0.12 | Eeles RA | 23535732 |
| rs1775148 | 1q32 | 205757824 | T | C | 0.953 | 0.625 | 4,599/2,940 | 0.96 | 0.89 | 1.02 | 0.21 | Al Olama A | 25217961 |
| rs4245739 | 1q32.1 | 204518842 | A | C | 1 | 0.729 | 4,600/2,941 | 1.07 | 1.00 | 1.16 | 0.06 | Eeles RA | 23535732 |
| rs10187424 | 2p11.2 | 85794297 | C | T | 1 | 0.418 | 4,600/2,941 | 0.98 | 0.92 | 1.05 | 0.60 | Kote-Jarai Z | 21743467 |
| rs721048 | 2p15 | 63131731 | A | G | 1 | 0.187 | 4,600/2,941 | 1.04 | 0.95 | 1.13 | 0.38 | Gudmundsson J | 18264098 |
| rs1465618 | 2p21 | 43553949 | C | T | 0.995 | 0.791 | 4,600/2,940 | 0.96 | 0.89 | 1.04 | 0.31 | Eeles RA | 19767753 |
| rs9287719 | 2p25 | 10710730 | T | C | 0.998 | 0.533 | 4,600/2,941 | 0.94 | 0.88 | 1.00 | 0.06 | Al Olama A | 25217961 |
| rs11902236 | 2p25.1 | 10117868 | T | C | 1 | 0.279 | 4,600/2,941 | 1.02 | 0.95 | 1.10 | 0.54 | Eeles RA | 23535732 |
| rs12621278 | 2q31.1 | 173311553 | G | A | 0.998 | 0.060 | 4,600/2,940 | 0.90 | 0.78 | 1.04 | 0.15 | Eeles RA | 19767753 |
| rs7584330 | 2q37.3 | 238387228 | G | A | 1 | 0.229 | 4,600/2,941 | 1.11 | 1.03 | 1.20 | 0.008 | Kote-Jarai Z | 21743467 |
| rs2292884 | 2q37.3 | 238443226 | G | A | 1 | 0.242 | 4,600/2,941 | 1.07 | 0.99 | 1.16 | 0.08 | Schumacher FR | 21743057 |
| rs3771570 | 2q37.3 | 242382864 | T | C | 0.985 | 0.153 | 4,600/2,941 | 1.02 | 0.93 | 1.11 | 0.69 | Eeles RA | 23535732 |
| rs2660753 | 3p12.1 | 87110674 | C | T | 1 | 0.889 | 4,600/2,941 | 0.91 | 0.82 | 1.01 | 0.07 | Eeles RA | 18264097 |
| rs17181170 | 3p12.1 | 87173324 | A | G | 1 | 0.492 | 4,600/2,941 | 0.95 | 0.89 | 1.01 | 0.12 | Eeles RA | 19767753 |
| rs7611694 | 3q13.2 | 113275624 | C | A | 1 | 0.415 | 4,600/2,941 | 0.92 | 0.86 | 0.99 | 0.02 | Eeles RA | 23535732 |
| rs10934853 | 3q21.3 | 128038373 | A | C | 1 | 0.268 | 4,600/2,941 | 1.13 | 1.05 | 1.21 | 0.001 | Gudmundsson J | 19767754 |
| rs6763931 | 3q23 | 141102833 | A | G | 1 | 0.434 | 4,600/2,941 | 1.06 | 0.99 | 1.13 | 0.09 | Kote-Jarai Z | 21743467 |
| rs10936632 | 3q26.2 | 170130102 | A | C | 0.987 | 0.501 | 4,599/2,940 | 1.15 | 1.08 | 1.23 | 2.05E-05 | Kote-Jarai Z | 21743467 |
| rs10009409 | 4q13 | 73855253 | T | C | 1 | 0.300 | 4,600/2,941 | 1.11 | 1.03 | 1.19 | 0.004 | Al Olama A | 25217961 |
| rs1894292 | 4q13.3 | 74349158 | A | G | 1 | 0.482 | 4,600/2,941 | 0.95 | 0.89 | 1.01 | 0.12 | Eeles RA | 23535732 |
| rs17021918 | 4q22.3 | 95562877 | T | C | 0.999 | 0.353 | 4,599/2,940 | 0.95 | 0.89 | 1.02 | 0.17 | Eeles RA | 19767753 |
| rs12500426 | 4q22.3 | 95514609 | C | A | 0.984 | 0.545 | 4,600/2,940 | 0.94 | 0.88 | 1.00 | 0.06 | Eeles RA | 19767753 |
| rs7679673 | 4q24 | 106061534 | A | C | 1 | 0.416 | 4,600/2,941 | 0.86 | 0.81 | 0.92 | 1.06E-05 | Eeles RA | 19767753 |
| rs2121875 | 5p12 | 44365545 | A | C | 1 | 0.675 | 4,600/2,941 | 0.94 | 0.88 | 1.01 | 0.10 | Kote-Jarai Z | 21743467 |
| rs2242652 | 5p15.33 | 1280028 | A | G | 0.949 | 0.198 | 4,600/2,941 | 0.88 | 0.81 | 0.96 | 0.004 | Kote-Jarai Z | 21743467 |
| rs6869841 | 5q35.2 | 172939426 | T | C | 1 | 0.215 | 4,600/2,941 | 0.99 | 0.91 | 1.07 | 0.72 | Eeles RA | 23535732 |

| SNP | Chr | Position | Effect allele | Other allele | Info | EAF | No. cases/ No. controls | OR | Lower CI | Upper CI | P | Reference | PUBMED ID |
|-------------|----------|-----------|---------------|--------------|-------|-------|-------------------------|------|----------|----------|----------|---------------------------------|------------------------------------|
| rs115306967 | 6p21 | 32400939 | C | G | 0.997 | 0.334 | 4,599/2,941 | 0.90 | 0.84 | 0.97 | 0.003 | Al Olama A | 25217961 |
| rs3096702 | 6p21.32 | 32192331 | G | A | 1 | 0.638 | 4,600/2,941 | 0.95 | 0.88 | 1.01 | 0.11 | Eeles RA | 23535732 |
| rs130067 | 6p21.33 | 31118511 | G | T | 1 | 0.194 | 4,600/2,941 | 1.06 | 0.98 | 1.15 | 0.13 | Kote-Jarai Z | 21743467 |
| rs115457135 | 6p22 | 30073776 | A | G | 0.966 | 0.201 | 4,599/2,941 | 1.06 | 0.97 | 1.15 | 0.20 | Al Olama A | 25217961 |
| rs4713266 | 6p24 | 11219030 | T | C | 0.996 | 0.495 | 4,599/2,941 | 0.92 | 0.86 | 0.98 | 0.01 | Al Olama A | 25217961 |
| rs9443189 | 6q14 | 76495882 | G | A | 0.997 | 0.152 | 4,599/2,940 | 0.83 | 0.76 | 0.92 | 0.0001 | Al Olama A | 25217961 |
| rs2273669 | 6q21 | 109285189 | G | A | 1 | 0.144 | 4,600/2,941 | 1.10 | 1.01 | 1.21 | 0.04 | Eeles RA | 23535732 |
| rs1933488 | 6q25.2 | 153441079 | G | A | 1 | 0.416 | 4,600/2,941 | 0.98 | 0.92 | 1.05 | 0.51 | Eeles RA | 23535732 |
| rs651164 | 6q25.3 | 160581374 | G | A | 1 | 0.682 | 4,600/2,941 | 1.10 | 1.03 | 1.19 | 0.007 | Eeles RA, Schumacher FR | 19767753, 21743057 |
| rs9364554 | 6q25.3 | 160833664 | T | C | 1 | 0.270 | 4,600/2,941 | 1.22 | 1.13 | 1.31 | 9.35E-08 | Eeles RA | 18264097 |
| rs56232506 | 7p12 | 47437244 | A | G | 0.993 | 0.452 | 4,600/2,941 | 1.09 | 1.02 | 1.17 | 0.008 | Al Olama A | 25217961 |
| rs12155172 | 7p15.3 | 20994491 | G | A | 1 | 0.785 | 4,600/2,941 | 0.88 | 0.82 | 0.96 | 0.002 | Eeles RA | 23535732 |
| rs6465657 | 7q21.3 | 97816327 | T | C | 1 | 0.542 | 4,600/2,941 | 0.93 | 0.88 | 1.00 | 0.04 | Eeles RA | 18264097 |
| rs1512268 | 8p21.2 | 23526463 | C | T | 1 | 0.576 | 4,600/2,941 | 0.89 | 0.84 | 0.96 | 0.0010 | Eeles RA | 19767753 |
| rs11135910 | 8p21.2 | 25892142 | T | C | 1 | 0.151 | 4,600/2,941 | 1.14 | 1.04 | 1.25 | 0.004 | Eeles RA | 23535732 |
| rs16902094 | 8q24.21 | 128320346 | G | A | 0.986 | 0.139 | 4,599/2,941 | 1.08 | 0.98 | 1.19 | 0.11 | Gudmundsson J | 19767754 |
| rs1016343 | 8q24.21 | 128093297 | T | C | 1 | 0.198 | 4,600/2,941 | 1.28 | 1.18 | 1.38 | 1.23E-09 | Schumacher FR | 21743057 |
| rs16901979 | 8q24.21 | 128124916 | A | C | 1.000 | 0.029 | 4,600/2,941 | 1.65 | 1.39 | 1.95 | 5.45E-09 | Gudmundsson J | 17401366 |
| rs445114 | 8q24.21 | 128323181 | C | T | 1 | 0.374 | 4,600/2,941 | 0.86 | 0.81 | 0.93 | 3.09E-05 | Gudmundsson J | 19767754 |
| rs6983267 | 8q24.21 | 128413305 | T | G | 1 | 0.501 | 4,600/2,941 | 0.81 | 0.76 | 0.87 | 4.37E-10 | Yeager M, Thomas G, Eeles RA | 17401363, 18264096, 18264097 |
| rs1447295 | 8q24.21 | 128485038 | C | A | 0.996 | 0.899 | 4,600/2,941 | 0.74 | 0.67 | 0.82 | 7.57E-09 | Gudmundsson J, Yeager M | 17401366, 17401363 |
| rs4242382 | 8q24.21 | 128517573 | G | A | 1 | 0.901 | 4,600/2,941 | 0.73 | 0.66 | 0.80 | 5.03E-10 | Thomas G | 18264096 |
| rs4242384 | 8q24.21 | 128518554 | A | C | 1 | 0.902 | 4,600/2,941 | 0.73 | 0.66 | 0.80 | 5.46E-10 | Eeles RA, Schumacher FR | 18264097, 21743057 |
| rs17694493 | 9p21 | 22041998 | G | C | 0.942 | 0.143 | 4,599/2,941 | 1.08 | 0.98 | 1.18 | 0.12 | Al Olama A | 25217961 |
| rs76934034 | 10q11 | 46082985 | C | T | 0.816 | 0.091 | 4,599/2,941 | 0.79 | 0.69 | 0.90 | 0.0005 | Al Olama A | 25217961 |
| rs3123078 | 10q11.23 | 51524971 | T | C | 1 | 0.559 | 4,600/2,941 | 0.88 | 0.83 | 0.94 | 0.0002 | Eeles RA | 19767753 |
| rs10993994 | 10q11.23 | 51549496 | C | T | 1 | 0.610 | 4,600/2,941 | 0.87 | 0.82 | 0.93 | 5.60E-05 | Thomas G, Eeles RA | 18264096, |

| SNP | Chr | Position | Effect allele | Other allele | Info | EAF | No. cases/ No. controls | OR | Lower CI | Upper CI | P | Reference | PUBMED ID |
|------------|----------|-----------|---------------|--------------|-------|-------|-------------------------|------|----------|----------|----------|--|------------------------------------|
| | | | | | | | | | | | | | 18264097 |
| rs3850699 | 10q24.32 | 104414221 | G | A | 1 | 0.307 | 4,600/2,941 | 0.88 | 0.82 | 0.95 | 0.0009 | Eeles RA | 23535732 |
| rs7127900 | 11p15.5 | 2233574 | G | A | 1 | 0.804 | 4,600/2,941 | 0.92 | 0.85 | 1.00 | 0.05 | Eeles RA | 19767753 |
| rs11228565 | 11q13.3 | 68978580 | A | G | 1 | 0.202 | 4,600/2,941 | 1.15 | 1.06 | 1.24 | 0.0008 | Gudmundsson J | 19767754 |
| rs7931342 | 11q13.3 | 68994497 | G | T | 1 | 0.505 | 4,600/2,941 | 1.15 | 1.08 | 1.23 | 3.05E-05 | Eeles RA | 18264097 |
| rs10896449 | 11q13.3 | 68994667 | G | A | 1 | 0.499 | 4,600/2,941 | 1.15 | 1.08 | 1.23 | 2.16E-05 | Thomas G | 18264096 |
| rs7130881 | 11q13.3 | 68995958 | G | A | 1 | 0.165 | 4,600/2,941 | 1.16 | 1.06 | 1.26 | 0.0007 | Eeles RA, Schumacher FR | 19767753, 21743057 |
| rs11568818 | 11q22.2 | 102401661 | C | T | 1 | 0.458 | 4,600/2,941 | 0.93 | 0.87 | 0.99 | 0.03 | Eeles RA | 23535732 |
| rs11214775 | 11q23 | 113807181 | A | G | 1 | 0.297 | 4,600/2,941 | 0.92 | 0.86 | 0.99 | 0.03 | Al Olama A | 25217961 |
| rs80130819 | 12q13 | 48419618 | C | A | 0.986 | 0.097 | 4,599/2,941 | 0.80 | 0.71 | 0.90 | 0.0002 | Al Olama A | 25217961 |
| rs10875943 | 12q13.12 | 49676010 | C | T | 1 | 0.286 | 4,600/2,941 | 1.04 | 0.97 | 1.12 | 0.31 | Kote-Jarai Z | 21743467 |
| rs902774 | 12q13.13 | 53273904 | A | G | 1 | 0.144 | 4,600/2,941 | 1.20 | 1.10 | 1.32 | 6.36E-05 | Schumacher FR | 21743057 |
| rs1270884 | 12q24.21 | 114685571 | G | A | 0.997 | 0.519 | 4,600/2,941 | 0.91 | 0.85 | 0.97 | 0.007 | Eeles RA | 23535732 |
| rs8008270 | 14q22.1 | 53372330 | C | T | 1 | 0.802 | 4,600/2,941 | 1.14 | 1.05 | 1.24 | 0.002 | Eeles RA | 23535732 |
| rs7153648 | 14q23 | 61122526 | G | C | 0.995 | 0.919 | 4,599/2,941 | 1.02 | 0.90 | 1.15 | 0.78 | Al Olama A | 25217961 |
| rs8014671 | 14q24 | 71092256 | A | G | 1 | 0.421 | 4,600/2,941 | 0.93 | 0.87 | 0.99 | 0.02 | Al Olama A | 25217961 |
| rs7141529 | 14q24.1 | 69126744 | C | T | 1 | 0.515 | 4,600/2,941 | 0.97 | 0.91 | 1.04 | 0.39 | Eeles RA | 23535732 |
| rs12051443 | 16q22 | 71691329 | A | G | 0.994 | 0.326 | 4,599/2,941 | 1.02 | 0.95 | 1.09 | 0.61 | Al Olama A | 25217961 |
| rs684232 | 17p13.3 | 618965 | C | T | 1 | 0.367 | 4,600/2,941 | 1.05 | 0.98 | 1.12 | 0.18 | Eeles RA | 23535732 |
| rs4430796 | 17q12 | 36098040 | A | G | 1 | 0.508 | 4,600/2,941 | 1.22 | 1.14 | 1.30 | 2.86E-09 | Gudmundsson J, Thomas G | 17603485, 18264096 |
| rs7501939 | 17q12 | 36101156 | C | T | 1 | 0.586 | 4,600/2,941 | 1.21 | 1.13 | 1.29 | 2.22E-08 | Eeles RA | 18264097 |
| rs11650494 | 17q21.32 | 47345186 | A | G | 1 | 0.080 | 4,600/2,941 | 1.09 | 0.96 | 1.22 | 0.18 | Eeles RA | 23535732 |
| rs1859962 | 17q24.3 | 69108753 | T | G | 1 | 0.522 | 4,600/2,941 | 0.86 | 0.80 | 0.92 | 4.47E-06 | Gudmundsson J, Eeles RA, Schumacher FR | 17603485, 19767753, 21743057 |
| rs7241993 | 18q23 | 76773973 | T | C | 1 | 0.303 | 4,600/2,941 | 0.95 | 0.89 | 1.02 | 0.18 | Eeles RA | 23535732 |
| rs8102476 | 19q13.2 | 38735613 | T | C | 1 | 0.451 | 4,600/2,941 | 0.92 | 0.86 | 0.98 | 0.02 | Gudmundsson J | 19767754 |
| rs11672691 | 19q13.2 | 41985587 | G | A | 1 | 0.738 | 4,600/2,941 | 1.10 | 1.02 | 1.19 | 0.01 | Amin Al Olama A | 23065704 |
| rs2735839 | 19q13.33 | 51364623 | G | A | 0.992 | 0.853 | 4,600/2,940 | 1.11 | 1.01 | 1.21 | 0.04 | Eeles RA | 18264097 |

| SNP | Chr | Position | Effect allele | Other allele | Info | EAF | No. cases/ No. controls | OR | Lower CI | Upper CI | P | Reference | PUBMED ID |
|------------------------------------|----------|-----------|---------------|--------------|-------|-------|-------------------------|------|----------|----------|----------|---------------|-----------|
| rs12480328 | 20q13 | 49527922 | C | T | 1.000 | 0.077 | 4,600/2,940 | 0.86 | 0.75 | 0.97 | 0.02 | Al Olama A | 25217961 |
| rs2427345 | 20q13.33 | 61015611 | T | C | 1 | 0.376 | 4,600/2,941 | 0.98 | 0.91 | 1.04 | 0.47 | Eeles RA | 23535732 |
| rs6062509 | 20q13.33 | 62362563 | T | G | 1.000 | 0.687 | 4,600/2,941 | 1.09 | 1.01 | 1.17 | 0.02 | Eeles RA | 23535732 |
| rs1041449 | 21q22 | 42901421 | G | A | 1 | 0.440 | 4,600/2,941 | 1.07 | 1.00 | 1.14 | 0.05 | Al Olama A | 25217961 |
| rs2238776 | 22q11 | 19757892 | A | G | 0.991 | 0.221 | 4,600/2,941 | 0.88 | 0.81 | 0.95 | 0.002 | Al Olama A | 25217961 |
| rs5759167 | 22q13.2 | 43500212 | T | G | 1 | 0.514 | 4,600/2,941 | 0.84 | 0.79 | 0.90 | 2.97E-07 | Eeles RA | 19767753 |
| rs2807031 | Xp11 | 52896949 | T | C | 0.993 | 0.839 | 4,625/2,852 | 0.87 | 0.82 | 0.92 | 4.42E-06 | Al Olama A | 25217961 |
| rs1327301 | Xp11.22 | 51210057 | T | C | 0.995 | 0.348 | 4,625/2,853 | 1.10 | 1.05 | 1.16 | 9.77E-05 | Eeles RA | 19767753 |
| rs5945572 | Xp11.22 | 51229683 | G | A | 0.997 | 0.648 | 4,625/2,853 | 0.91 | 0.87 | 0.95 | 0.0001 | Gudmundsson J | 18264098 |
| rs5945619 | Xp11.22 | 51241672 | T | C | 0.994 | 0.647 | 4,625/2,853 | 0.90 | 0.86 | 0.95 | 4.42E-05 | Eeles RA | 18264097 |
| rs5919432 | Xq12 | 67021550 | T | C | 0.995 | 0.795 | 4,625/2,853 | 1.04 | 0.98 | 1.10 | 0.18 | Kote-Jarai Z | 21743467 |
| rs6625711 | Xq13 | 70139850 | T | A | 0.706 | 0.599 | 4,625/2,853 | 0.95 | 0.91 | 1.00 | 0.07 | Al Olama A | 25217961 |
| rs4844289 | Xq13 | 70407983 | G | A | 0.995 | 0.387 | 4,625/2,853 | 1.03 | 0.98 | 1.08 | 0.19 | Al Olama A | 25217961 |
| Discovered in non-Europeans | | | | | | | | | | | | | |
| rs13385191 | 2p24.1 | 20888265 | G | A | 0.997 | 0.236 | 4,599/2,941 | 1.09 | 1.01 | 1.18 | 0.02 | Takata R | 20676098 |
| rs9284813 | 3p12.1 | 87152169 | G | A | 1 | 0.133 | 4,600/2,941 | 1.07 | 0.97 | 1.18 | 0.16 | Takata R | 20676098 |
| rs12653946 | 5p15.33 | 1895829 | T | C | 1 | 0.412 | 4,600/2,941 | 1.14 | 1.07 | 1.22 | 8.67E-05 | Takata R | 20676098 |
| rs1983891 | 6p21.1 | 41536427 | T | C | 1.000 | 0.269 | 4,600/2,941 | 1.14 | 1.06 | 1.22 | 0.0006 | Takata R | 20676098 |
| rs339331 | 6q22.1 | 117210052 | C | T | 1 | 0.310 | 4,600/2,941 | 0.92 | 0.85 | 0.98 | 0.02 | Takata R | 20676098 |
| rs1512268 | 8p21.2 | 23526463 | C | T | 1 | 0.576 | 4,600/2,941 | 0.89 | 0.84 | 0.96 | 0.0010 | Takata R | 20676098 |
| rs1456315 | 8q24.21 | 128103937 | C | T | 1 | 0.681 | 4,600/2,941 | 0.91 | 0.85 | 0.97 | 0.005 | Xu J | 23023329 |
| rs1456315 | 8q24.21 | 128103937 | C | T | 1 | 0.681 | 4,600/2,941 | 0.91 | 0.85 | 0.97 | 0.005 | Takata R | 20676098 |
| rs7837688 | 8q24.21 | 128539360 | G | T | 0.997 | 0.902 | 4,600/2,940 | 0.73 | 0.66 | 0.80 | 5.58E-10 | Takata R | 20676098 |
| rs817826 | 9q31.2 | 110156300 | T | C | 1 | 0.858 | 4,600/2,941 | 1.01 | 0.92 | 1.11 | 0.82 | Xu J | 23023329 |
| rs10993994 | 10q11.23 | 51549496 | C | T | 1 | 0.610 | 4,600/2,941 | 0.87 | 0.82 | 0.93 | 5.60E-05 | Takata R | 20676098 |
| rs9600079 | 13q22.1 | 73728139 | T | G | 1 | 0.444 | 4,600/2,941 | 1.02 | 0.95 | 1.09 | 0.57 | Takata R | 20676098 |
| rs7501939 | 17q12 | 36101156 | C | T | 1 | 0.586 | 4,600/2,941 | 1.21 | 1.13 | 1.29 | 2.22E-08 | Takata R | 20676098 |
| rs103294 | 19q13.42 | 54797848 | T | C | 1 | 0.207 | 4,600/2,941 | 0.99 | 0.91 | 1.07 | 0.74 | Xu J | 23023329 |

Supplementary Table 3. Meta-analysis results of promising SNPs from stage 1 selected for rapid replication

| SNP | Chr | Position ^a | Effect allele | Other allele | Stage | EAF ^b | No. cases / no. controls | OR | 95% CI | P | P _{heterogeneity} ^c |
|------------|----------|-----------------------|---------------|-----------------|---------------------|------------------|--------------------------|--------------------|--------------------|-----------------|---|
| rs2016546 | 15q15.1 | 41,056,440 | T | G | Stage 1 | 0.01 | 4389/2924 | 1.99 | (1.51-2.62) | 5.58E-07 | |
| | | | | | Stage 2 | 0.01 | 2342/2409 | 0.66 | (0.43-1.01) | 0.06 | |
| | | | | | Replication - FHCRC | 0.03 | 1311/1150 | 1.54 | (1.13-2.11) | 6.16E-03 | |
| | | | | | Combined | | 8042/6483 | 1.48 | (1.22-1.78) | 4.19E-05 | |
| rs1635554 | 12q13.11 | 48,374,513 | T | C | Stage 1 | 0.11 | 4583/2926 | 0.77 | (0.69-0.86) | 4.90E-06 | |
| | | | | | Stage 2 | 0.11 | 2487/2524 | 0.93 | (0.82-1.06) | 0.29 | |
| | | | | | Replication - FHCRC | 0.09 | 1309/1144 | 1.01 | (0.83-1.23) | 0.93 | |
| | | | | | Replication - AHS | 0.09 | 574/1157 | 0.85 | (0.66-1.10) | 0.21 | |
| | | | | Combined | | 8953/7751 | 0.86 | (0.80-0.93) | 7.16E-05 | 0.05 | |
| rs10180155 | 2q22.1 | 141,038,006 | A | G | Stage 1 | 0.01 | 4586/2937 | 1.77 | (1.37-2.28) | 1.07E-05 | |
| | | | | | Stage 2 | 0.02 | 2475/2513 | 1.27 | (0.97-1.66) | 0.08 | |
| | | | | | Replication - FHCRC | 0.02 | 1313/1152 | 1.08 | (0.76-1.54) | 0.67 | |
| | | | | | Replication - MEC | 0.02 | 750/733 | 0.66 | (0.39-1.12) | 0.12 | |
| | | | | | Replication - AHS | 0.01 | 577/1166 | 1.41 | (0.81-2.45) | 0.22 | |
| | | | | Combined | | 9701/8501 | 1.32 | (1.14-1.54) | 3.12E-04 | 0.01 | |
| rs2728945 | 3p25.3 | 9,418,510 | A | G | Stage 1 | 0.14 | 4566/2936 | 1.24 | (1.13-1.36) | 5.43E-06 | |
| | | | | | Stage 2 | 0.17 | 2484/2532 | 1.01 | (0.91-1.12) | 0.89 | |
| | | | | | Replication - FHCRC | 0.15 | 1305/1145 | 0.90 | (0.77-1.06) | 0.22 | |
| | | | | | Replication - AHS | 0.15 | 574/1167 | 1.24 | (1.03-1.50) | 0.02 | |
| | | | | Combined | | 8929/7780 | 1.11 | (1.04-1.17) | 9.86E-04 | 0.0009 | |
| rs4624886 | 6q23.3 | 138,341,562 | C | A | Stage 1 | 0.21 | 4562/2921 | 0.83 | (0.76-0.90) | 7.86E-06 | |
| | | | | | Stage 2 | 0.20 | 2486/2520 | 0.98 | (0.89-1.08) | 0.72 | |
| | | | | | Replication - FHCRC | 0.20 | 1303/1150 | 0.93 | (0.81-1.07) | 0.32 | |
| | | | | | Replication - MEC | 0.19 | 740/731 | 1.00 | (0.83-1.20) | 0.98 | |
| | | | | | Replication - AHS | 0.19 | 573/1160 | 1.04 | (0.87-1.24) | 0.70 | |
| | | | | Combined | | 9664/8482 | 0.92 | (0.87-0.97) | 0.001 | 0.03 | |
| rs5979202 | Xp22.2 | 9,871,958 | A | G | Stage 1 | 0.17 | 4342/2920 | 0.78 | (0.71-0.86) | 6.82E-07 | |
| | | | | | Stage 2 | 0.34 | 2482/2516 | 0.95 | (0.90-1.01) | 0.10 | |
| | | | | | Replication - FHCRC | 0.35 | 1312/1148 | 1.03 | (0.95-1.12) | 0.50 | |
| | | | | | Replication - MEC | 0.36 | 747/734 | 0.98 | (0.88-1.09) | 0.76 | |
| | | | | | Replication - AHS | 0.33 | 577/1167 | 0.92 | (0.83-1.03) | 0.14 | |

| SNP | Chr | Position ^a | Effect allele | Other allele | Stage | EAF ^b | No. cases / no. controls | OR | 95% CI | P | P _{heterogeneity} ^c |
|---------------------|---------|-----------------------|---------------|--------------|---------------------|------------------|--------------------------|-------------|--------------------|--------------|---|
| rs79450105 | 8q12.3 | 63,338,261 | C | T | Combined | | 9460/8485 | 0.94 | (0.91-0.98) | 0.001 | 0.0006 |
| | | | | | Stage 1 | 0.05 | 4547/2917 | 1.40 | (1.21-1.61) | 4.93E-06 | |
| | | | | | Stage 2 | 0.05 | 2479/2520 | 0.93 | (0.78-1.12) | 0.46 | |
| | | | | | Replication - FHCRC | 0.07 | 1310/1148 | 1.11 | (0.89-1.37) | 0.35 | |
| | | | | | Replication - MEC | 0.07 | 749/734 | 1.07 | (0.80-1.43) | 0.66 | |
| | | | | | Replication - AHS | 0.06 | 579/1170 | 1.09 | (0.81-1.47) | 0.56 | |
| rs314739 | 5p15.2 | 10,040,199 | T | C | Combined | | 9664/8489 | 1.16 | (1.06-1.27) | 0.001 | 0.01 |
| | | | | | Stage 1 | 0.45 | 4586/2931 | 1.16 | (1.08-1.24) | 1.43E-05 | |
| | | | | | Stage 2 | 0.47 | 2344/2391 | 1.04 | (0.96-1.13) | 0.36 | |
| | | | | | Replication - FHCRC | 0.49 | 1305/1149 | 0.92 | (0.82-1.02) | 0.12 | |
| | | | | | Replication - MEC | 0.50 | 748/735 | 1.00 | (0.86-1.15) | 0.97 | |
| | | | | | Replication - AHS | 0.46 | 554/1134 | 1.08 | (0.94-1.25) | 0.27 | |
| rs2099817 | 15q26.2 | 98,217,064 | G | T | Combined | | 9537/8340 | 1.07 | (1.02-1.11) | 0.003 | 0.006 |
| | | | | | Stage 1 | 0.47 | 4466/2901 | 0.86 | (0.80-0.92) | 8.42E-06 | |
| | | | | | Stage 2 | 0.46 | 2480/2524 | 0.98 | (0.91-1.06) | 0.68 | |
| | | | | | Replication - FHCRC | 0.49 | 1312/1149 | 1.02 | (0.91-1.14) | 0.77 | |
| | | | | | Replication - MEC | 0.48 | 747/733 | 1.05 | (0.91-1.21) | 0.50 | |
| | | | | | Replication - AHS | 0.47 | 574/1162 | 0.97 | (0.84-1.13) | 0.71 | |
| rs4430089 | 8q12.3 | 63,372,633 | A | G | Combined | | 9579/8469 | 0.94 | (0.90-0.98) | 0.004 | 0.01 |
| | | | | | Stage 1 | 0.05 | 4599/2941 | 1.37 | (1.19-1.58) | 1.53E-05 | |
| | | | | | Stage 2 | 0.05 | 2477/2518 | 0.92 | (0.77-1.10) | 0.35 | |
| | | | | | Replication - FHCRC | 0.07 | 1313/1151 | 1.08 | (0.87-1.33) | 0.50 | |
| | | | | | Replication - AHS | 0.05 | 571/1159 | 1.07 | (0.78-1.47) | 0.67 | |
| | | | | | Combined | | 8960/7769 | 1.14 | (1.04-1.26) | 0.005 | |
| Stage 1 | 0.52 | 4581/2927 | 0.86 | (0.81-0.92) | 1.16E-05 | | | | | | |
| Stage 2 | 0.49 | 2468/2506 | 1.00 | (0.92-1.08) | 0.98 | | | | | | |
| Replication - FHCRC | 0.51 | 1304/1146 | 1.03 | (0.92-1.15) | 0.57 | | | | | | |
| Replication - MEC | 0.49 | 746/731 | 1.04 | (0.91-1.20) | 0.55 | | | | | | |
| Replication - AHS | 0.50 | 570/1159 | 0.97 | (0.84-1.11) | 0.63 | | | | | | |
| rs79608926 | 11q24.1 | 123,704,705 | T | G | Combined | | 9669/8469 | 0.95 | (0.91-0.99) | 0.01 | 0.008 |
| | | | | | Stage 1 | 0.19 | 4595/2932 | 0.82 | (0.75-0.90) | 9.20E-06 | |
| | | | | | Stage 2 | 0.17 | 2478/2530 | 1.06 | (0.96-1.18) | 0.26 | |

| SNP | Chr | Position ^a | Effect allele | Other allele | Stage | EAF ^b | No. cases / no. controls | OR | 95% CI | P | P _{heterogeneity} ^c |
|------------|--------|-----------------------|---------------|--------------|---------------------|------------------|--------------------------|-------------|--------------------|-------------|---|
| rs78425081 | 3p14.1 | 65,318,721 | T | G | Replication - FHCRC | 0.15 | 1308/1151 | 1.08 | (0.93-1.26) | 0.30 | 0.001 |
| | | | | | Replication - MEC | 0.17 | 750/733 | 0.98 | (0.81-1.19) | 0.84 | |
| | | | | | Replication - AHS | 0.17 | 575/1171 | 0.89 | (0.73-1.08) | 0.24 | |
| | | | | | Combined | | 9706/8517 | 0.94 | (0.89-0.99) | 0.02 | |
| | | | | | Stage 1 | 0.06 | 4600/2937 | 0.72 | (0.62-0.84) | 1.43E-05 | |
| | | | | | Stage 2 | 0.07 | 2487/2527 | 0.98 | (0.84-1.15) | 0.83 | |
| | | | | | Replication - FHCRC | 0.06 | 1315/1149 | 0.93 | (0.74-1.18) | 0.56 | |
| | | | | | Replication - MEC | 0.05 | 750/733 | 1.34 | (0.97-1.85) | 0.08 | |
| | | | | | Replication - AHS | 0.05 | 576/1161 | 1.27 | (0.94-1.72) | 0.12 | |
| rs74526871 | 7q31.2 | 114,865,325 | A | G | Combined | | 9728/8507 | 0.91 | (0.83-1.00) | 0.04 | 0.0004 |
| | | | | | Stage 1 | 0.03 | 4584/2925 | 0.61 | (0.49-0.76) | 9.00E-06 | |
| | | | | | Stage 2 | 0.02 | 2495/2529 | 1.21 | (0.94-1.56) | 0.14 | |
| | | | | | Replication - FHCRC | 0.02 | 1310/1150 | 1.18 | (0.79-1.78) | 0.42 | |
| | | | | | Replication - MEC | 0.01 | 749/733 | 2.14 | (1.15-3.99) | 0.01 | |
| | | | | | Replication - AHS | 0.02 | 579/1172 | 0.72 | (0.42-1.24) | 0.24 | |
| | | | | | Combined | | 9717/8509 | 0.90 | (0.78-1.03) | 0.13 | |
| | | | | | Stage 1 | 0.06 | 4379/2854 | 0.65 | (0.56-0.76) | 2.11E-08 | |
| | | | | | Stage 2 | 0.12 | 2475/2530 | 1.05 | (0.97-1.14) | 0.25 | |
| rs2075596 | Xq28 | 153,297,392 | A | G | Replication - FHCRC | 0.14 | 1304/1147 | 0.92 | (0.82-1.03) | 0.15 | 1.90E-05 |
| | | | | | Replication - MEC | 0.16 | 747/734 | 1.10 | (0.96-1.26) | 0.16 | |
| | | | | | Replication - AHS | 0.12 | 574/1166 | 0.96 | (0.82-1.12) | 0.60 | |
| | | | | | Combined | | 9479/8431 | 0.96 | (0.91-1.01) | 0.14 | |
| | | | | | Stage 1 | 0.06 | 4379/2854 | 0.65 | (0.56-0.76) | 2.11E-08 | |
| | | | | | Stage 2 | 0.12 | 2475/2530 | 1.05 | (0.97-1.14) | 0.25 | |
| | | | | | Replication - FHCRC | 0.14 | 1304/1147 | 0.92 | (0.82-1.03) | 0.15 | |
| | | | | | Replication - MEC | 0.16 | 747/734 | 1.10 | (0.96-1.26) | 0.16 | |
| | | | | | Replication - AHS | 0.12 | 574/1166 | 0.96 | (0.82-1.12) | 0.60 | |
| rs12013494 | Xq28 | 150,911,107 | A | G | Combined | | 9479/8431 | 0.96 | (0.91-1.01) | 0.14 | 6.50E-07 |
| | | | | | Stage 1 | 0.04 | 4407/2873 | 0.66 | (0.54-0.79) | 1.28E-05 | |
| | | | | | Stage 2 | 0.07 | 2487/2517 | 0.95 | (0.85-1.06) | 0.37 | |
| | | | | | Replication - FHCRC | 0.09 | 1310/1150 | 0.98 | (0.86-1.13) | 0.81 | |
| | | | | | Replication - MEC | 0.10 | 749/733 | 1.08 | (0.91-1.28) | 0.37 | |
| | | | | | Replication - AHS | 0.08 | 571/1149 | 1.18 | (0.99-1.40) | 0.06 | |
| | | | | | Combined | | 9524/8422 | 0.96 | (0.90-1.03) | 0.27 | |
| | | | | | Stage 1 | 0.04 | 4407/2873 | 0.66 | (0.54-0.79) | 1.28E-05 | |
| | | | | | Stage 2 | 0.07 | 2487/2517 | 0.95 | (0.85-1.06) | 0.37 | |

^aPosition based on GRCh37/hg19

^bEAF: Effect allele frequency

^cP-value for the heterogeneity between studies

Supplementary Table 4. Association results for 13 previously reported loci that reach genome-wide significance ($P < 5 \times 10^{-8}$) in the combined meta-analysis

| SNP | Chr | Position | Nearest gene(s) | Effect allele ^a | Other allele | Stage | No. cases/ no. controls | EAF ^b | OR | 95% CI | P |
|------------|----------|-------------|---------------------------|----------------------------|--------------|-----------------|----------------------------|------------------|-------------|--------------------|-----------------|
| rs4242382 | 8q24.21 | 128,517,573 | <i>LOC727677, CASC8</i> | G | A | Stage 1 | 4600/2941 | 0.90 | 0.73 | (0.66-0.80) | 5.03E-10 |
| | | | | | | Stage 2 | 6573/6387 | 0.90 | 0.68 | (0.63-0.74) | 3.77E-22 |
| | | | | | | Stage 3 | 1204/1231 | 0.90 | 0.67 | (0.56-0.80) | 6.64E-06 |
| | | | | | | Combined | 12377/10559 | | 0.69 | (0.65-0.74) | 1.48E-34 |
| rs8064454 | 17q12 | 36,101,586 | <i>HNF1B</i> | C | A | Stage 1 | 4600/2941 | 0.51 | 1.24 | (1.16-1.32) | 2.64E-10 |
| | | | | | | Stage 2 | 6553/6379 | 0.52 | 1.22 | (1.16-1.28) | 7.35E-15 |
| | | | | | | Stage 3 | 1203/1230 | 0.50 | 1.36 | (1.21-1.53) | 2.37E-07 |
| | | | | | | Combined | 12356/10550 | | 1.24 | (1.19-1.29) | 8.03E-29 |
| rs17765344 | 17q24.3 | 69,106,874 | <i>BC039327, CASC17</i> | G | A | Stage 1 | 4600/2941 | 0.52 | 0.86 | (0.80-0.91) | 3.00E-06 |
| | | | | | | Stage 2 | 6569/6387 | 0.52 | 0.84 | (0.80-0.88) | 7.26E-13 |
| | | | | | | Stage 3 | 1203/1230 | 0.52 | 0.78 | (0.70-0.88) | 3.04E-05 |
| | | | | | | Combined | 12372/10558 | | 0.84 | (0.81-0.87) | 4.28E-21 |
| rs5759167 | 22q13.2 | 43,500,212 | <i>BIK</i> | T | G | Stage 1 | 4600/2941 | 0.51 | 0.84 | (0.79-0.90) | 2.97E-07 |
| | | | | | | Stage 2 | 6571/6384 | 0.50 | 0.87 | (0.83-0.91) | 1.53E-08 |
| | | | | | | Stage 3 | 1204/1231 | 0.51 | 0.82 | (0.74-0.92) | 0.0009 |
| | | | | | | Combined | 12375/10556 | | 0.85 | (0.82-0.89) | 1.40E-16 |
| rs10993994 | 10q11.23 | 51,549,496 | <i>PARG, TIMM23, MSMB</i> | C | T | Stage 1 | 4600/2941 | 0.61 | 0.87 | (0.82-0.93) | 5.60E-05 |
| | | | | | | Stage 2 | 6568/6388 | 0.61 | 0.84 | (0.80-0.88) | 9.92E-12 |
| | | | | | | Stage 3 | 1204/1231 | 0.58 | 0.90 | (0.80-1.01) | 0.07 |
| | | | | | | Combined | 12372/10560 | | 0.86 | (0.83-0.89) | 1.05E-15 |
| rs71277158 | 3q26.2 | 169,999,216 | <i>PRKCI</i> | G | T | Stage 1 | 4600/2941 | 0.17 | 0.79 | (0.72-0.87) | 5.75E-07 |
| | | | | | | Stage 2 | 6574/6391 | 0.18 | 0.84 | (0.78-0.89) | 1.09E-07 |
| | | | | | | Stage 3 | 1203/1230 | 0.18 | 0.85 | (0.72-1.00) | 0.05 |
| | | | | | | Combined | 12377/10562 | | 0.82 | (0.78-0.87) | 8.22E-14 |
| rs7929962 | 11q13.3 | 68,985,583 | <i>LOC338694, MYEOV</i> | T | C | Stage 1 | 4600/2941 | 0.50 | 1.16 | (1.08-1.23) | 1.74E-05 |
| | | | | | | Stage 2 | 6561/6385 | 0.51 | 1.13 | (1.08-1.19) | 3.79E-07 |
| | | | | | | Stage 3 | 1204/1231 | 0.53 | 1.21 | (1.08-1.36) | 0.001 |
| | | | | | | Combined | 12365/10557 | | 1.15 | (1.11-1.19) | 2.37E-13 |
| rs7758229 | 6q25.3 | 160,840,252 | <i>SLC22A3</i> | T | G | Stage 1 | 4600/2941 | 0.31 | 1.19 | (1.11-1.27) | 7.16E-07 |

| SNP | Chr | Position | Nearest gene(s) | Effect allele ^a | Other allele | Stage | No. cases/ no. controls | EAF ^b | OR | 95% CI | P |
|------------|----------|-------------|----------------------------|----------------------------|--------------|-----------------|----------------------------|------------------|-------------|--------------------|-----------------|
| rs2430386 | 2p15 | 63,178,111 | <i>EHBP1</i> | T | C | Stage 2 | 6566/6381 | 0.31 | 1.14 | (1.08-1.20) | 1.77E-06 |
| | | | | | | Stage 3 | 1204/1231 | 0.32 | 1.10 | (0.97-1.24) | 0.13 |
| | | | | | | Combined | 12370/10553 | | 1.15 | (1.10-1.20) | 4.40E-12 |
| | | | | | | Stage 1 | 4600/2941 | 0.50 | 1.14 | (1.07-1.22) | 6.81E-05 |
| | | | | | | Stage 2 | 6400/6306 | 0.50 | 1.15 | (1.10-1.21) | 1.41E-08 |
| rs17023900 | 3p12.1 | 87,134,800 | <i>LINC00506, BC050344</i> | G | A | Stage 3 | 1204/1231 | 0.51 | 1.05 | (0.94-1.18) | 0.40 |
| | | | | | | Combined | 12204/10478 | | 1.14 | (1.10-1.18) | 9.04E-12 |
| | | | | | | Stage 1 | 4600/2941 | 0.08 | 1.17 | (1.04-1.31) | 0.009 |
| | | | | | | Stage 2 | 6534/6357 | 0.07 | 1.29 | (1.18-1.42) | 1.19E-08 |
| | | | | | | Stage 3 | 1204/1231 | 0.07 | 1.38 | (1.12-1.70) | 0.003 |
| rs7725218 | 5p15.33 | 1,282,414 | <i>TERT,hTERT</i> | A | G | Stage 3 | 1203/1230 | 0.38 | 0.90 | (0.78-1.02) | 0.10 |
| | | | | | | Combined | 12297/10489 | | 0.87 | (0.84-0.91) | 3.08E-11 |
| | | | | | | Stage 1 | 4600/2941 | 0.35 | 0.88 | (0.82-0.94) | 0.0003 |
| | | | | | | Stage 2 | 6494/6318 | 0.36 | 0.87 | (0.83-0.92) | 9.99E-08 |
| | | | | | | Stage 3 | 1203/1230 | 0.38 | 0.90 | (0.78-1.02) | 0.10 |
| rs10774740 | 12q24.21 | 114,666,202 | <i>TBX5</i> | T | G | Stage 3 | 1203/1231 | 0.39 | 0.87 | (0.77-0.98) | 0.03 |
| | | | | | | Combined | 12368/10558 | | 0.88 | (0.85-0.92) | 2.60E-10 |
| | | | | | | Stage 1 | 4600/2941 | 0.39 | 0.87 | (0.82-0.94) | 0.0001 |
| | | | | | | Stage 2 | 6565/6386 | 0.40 | 0.89 | (0.85-0.94) | 6.18E-06 |
| | | | | | | Stage 3 | 1203/1231 | 0.39 | 0.87 | (0.77-0.98) | 0.03 |
| rs7679673 | 4q24 | 106,061,534 | <i>TET2</i> | A | C | Stage 3 | 1203/1230 | 0.41 | 0.92 | (0.82-1.03) | 0.15 |
| | | | | | | Combined | 12337/10546 | | 0.89 | (0.86-0.93) | 4.03E-09 |
| | | | | | | Stage 1 | 4600/2941 | 0.42 | 0.86 | (0.81-0.92) | 1.06E-05 |
| | | | | | | Stage 2 | 6534/6375 | 0.42 | 0.91 | (0.86-0.95) | 0.0001 |
| | | | | | | Stage 3 | 1203/1230 | 0.41 | 0.92 | (0.82-1.03) | 0.15 |

^aEffect allele is the allele associated with the change in risk

^bFrequency of the effect allele

Supplementary Table 5. New suggestive loci associated with prostate risk ($P < 5 \times 10^{-7}$)

| SNP | Chr | Position | Nearest gene | Risk allele ^a | Other allele | Stage | RAF ^b | No. cases/ no. controls | OR | 95% CI | P |
|------------|---------|------------|--------------|--------------------------|--------------|-----------------|------------------|----------------------------|-------------|--------------------|-----------------|
| rs12597458 | 16q22.2 | 72,030,970 | PKD1L3 | G | T | Stage 1 | 0.55 | 4600/2941 | 1.11 | (1.04-1.19) | 0.001 |
| | | | | | | Stage 2 | 0.56 | 6574/6390 | 1.09 | (1.04-1.15) | 4.16E-04 |
| | | | | | | Stage 3 | 0.55 | 1203/1230 | 1.16 | (1.04-1.32) | 0.01 |
| | | | | | | Combined | | 12377/10561 | 1.11 | (1.06-1.15) | 9.67E-08 |
| rs12198220 | 6p22.3 | 21,330,293 | CDKAL1 | T | G | Stage 1 | 0.74 | 4600/2941 | 1.12 | (1.03-1.20) | 0.005 |
| | | | | | | Stage 2 | 0.74 | 6563/6383 | 1.10 | (1.04-1.16) | 0.002 |
| | | | | | | Stage 3 | 0.71 | 1203/1230 | 1.28 | (1.12-1.46) | 2.40E-04 |
| | | | | | | Combined | | 12366/10554 | 1.12 | (1.07-1.17) | 2.13E-07 |

^aRisk allele is the allele associated with an increased risk of prostate cancer

^bFrequency of the risk allele

Supplementary Table 6. Association results from stage 1 for SNPs previously reported to be associated with aggressive prostate cancer

| SNP | Chr | Position | Effect allele ^a / Other allele | EAF ^b | Info ^c | Case-Only Analysis of Gleason Score (continuous trait) | | | | Case-Control Analysis of Aggressive Prostate Cancer (Gleason \geq 8 vs. controls) | | | | Reference |
|------------|---------|-----------|--|------------------|-------------------|--|--------|-------|------|---|------|-------------|------|--------------------------|
| | | | | | | No. of cases | Beta | SE | P | No. of cases/ No. of controls | OR | 95% CI | P | |
| rs11199874 | 10q26 | 123032519 | G/A | 0.73 | 0.991 | 4545 | -0.003 | 0.025 | 0.89 | 422/2941 | 1.01 | (0.86-1.20) | 0.87 | Nam et al. (2011) |
| rs6497287 | 15q13 | 28440287 | C/T | 0.07 | 1 | 4545 | 0.007 | 0.041 | 0.86 | 423/2941 | 1.26 | (0.94-1.68) | 0.12 | FitzGerald et al. (2011) |
| rs4775302 | 15q21 | 46639808 | A/G | 0.55 | 0.996 | 4544 | -0.007 | 0.021 | 0.74 | 422/2941 | 0.92 | (0.79-1.06) | 0.25 | Nam et al. (2011) |
| rs4054823 | 17p12 | 13625024 | T/C | 0.53 | 1 | 4545 | -0.022 | 0.021 | 0.31 | 423/2941 | 0.83 | (0.71-0.96) | 0.01 | Xu et al. (2010) |
| rs11672691 | 19q13.2 | 41985587 | G/A | 0.74 | 1 | 4545 | -0.010 | 0.024 | 0.66 | 423/2941 | 0.99 | (0.84-1.17) | 0.92 | Al Olama et al. (2013) |
| rs3774315 | 3q26 | 172231986 | G/A | 0.28 | 1 | 4545 | 0.024 | 0.023 | 0.29 | 423/2941 | 1.13 | (0.96-1.32) | 0.15 | FitzGerald et al. (2011) |

^aEffect allele is the allele associated with the change in beta or odds ratio. The results are orientated so that the effect allele corresponds to the risk allele from the published study.

^bEAF=Effect allele frequency among controls

^cInfo=Information score from IMPUTE2

Supplementary Table 7. Case-control association results for prostate cancer risk stratified by disease aggressiveness for the three SNPs associated with Gleason score

| SNP | Cytoband | Position | Risk allele ^a / Other allele | Stage | Gleason ≤ 6 | | | Gleason ≥ 8 | | | P _{heterogeneity} |
|---------------------------------|----------|-------------|--|-----------------|---------------------------|-------------------------|------------------------------|---------------------------|-------------------------|-----------------------------|------------------------------|
| | | | | | No. of cases/ controls | OR (95% CI) | P | No. of cases/ controls | OR (95% CI) | P | |
| Novel loci | | | | | | | | | | | |
| rs35148638 | 5q14.3 | 86,610,989 | C/A | Stage 1 | 2693/2941 | 0.96 (0.88-1.04) | 0.31 | 423/2941 | 1.32 (1.12-1.57) | 1.04x10 ⁻³ | 9.23x10 ⁻⁴ |
| | | | | Stage 2 | 2728/6391 | 0.97 (0.90-1.05) | 0.47 | 747/6391 | 1.24 (1.10-1.40) | 5.18x10 ⁻⁴ | 7.70x10 ⁻⁴ |
| | | | | Stage 3 | 1382/1728 | 1.08 (0.96-1.21) | 0.21 | 468/1728 | 0.99 (0.84-1.15) | 0.87 | 0.38 |
| | | | | Combined | 6803/11060 | 0.99 (0.94-1.04) | 0.57 | 1638/11060 | 1.18 (1.09-1.28) | 8.85x10⁻⁵ | 2.89x10⁻⁴ |
| rs78943174 | 3q26.31 | 175,252,736 | C/T | Stage 1 | 2693/2941 | 0.81 (0.61-1.08) | 0.14 | 423/2941 | 2.00 (1.10-3.70) | 0.02 | 0.008 |
| | | | | Stage 2 | 2723/6378 | 0.98 (0.75-1.28) | 0.88 | 745/6378 | 1.32 (0.81-2.13) | 0.28 | 0.30 |
| | | | | Stage 3 | 1382/1728 | 0.58 (0.42-0.81) | 0.002 | 468/1728 | 0.97 (0.56-1.67) | 0.91 | 0.12 |
| | | | | Combined | 6798/11047 | 0.81 (0.68-0.95) | 0.01 | 1636/11047 | 1.33 (0.97-1.82) | 0.07 | 0.006 |
| Previously reported loci | | | | | | | | | | | |
| rs62113212 | 19q13.33 | 51,360,840 | T/C | Stage 1 | 2692/2941 | 0.70 (0.60-0.81) | 3.05x10 ⁻⁶ | 423/2941 | 1.31 (1.00-1.72) | 0.05 | 7.39x10 ⁻⁵ |
| | | | | Stage 2 | 2728/6389 | 0.70 (0.61-0.80) | 4.16x10 ⁻⁷ | 747/6389 | 1.16 (0.95-1.41) | 0.14 | 3.57x10 ⁻⁵ |
| | | | | Stage 3 | 1382/1728 | 0.83 (0.74-0.93) | 0.002 | 468/1728 | 1.11 (0.95-1.30) | 0.18 | 0.003 |
| | | | | Combined | 6802/11058 | 0.75 (0.70-0.81) | 3.51x10⁻¹³ | 1638/11058 | 1.16 (1.04-1.30) | 0.01 | 1.44x10⁻¹⁰ |

^aRisk allele is the allele associated with an increased risk of aggressive prostate cancer (Gleason ≥ 8)

Supplementary Table 8. Association results for prostate cancer risk stratified by disease aggressiveness from the African American Prostate Cancer (AAPC) Consortium for the three SNPs associated with Gleason score

| SNP | Chr | Position | Info | Risk allele/ other allele | RAF | Gleason ≤ 6 | | | Gleason ≥ 8 | | |
|------------|----------|-----------|-------|------------------------------|-------|----------------------------|------------------|------|----------------------------|------------------|------|
| | | | | | | No. cases/ No. controls | OR (95% CI) | P | No. cases/ No. controls | OR (95% CI) | P |
| rs35148638 | 5q14.3 | 86610989 | 1 | C/A | 0.092 | 2311/4678 | 1.11 (0.98-1.26) | 0.10 | 1091/4678 | 0.97 (0.82-1.15) | 0.72 |
| rs78943174 | 3q26.31 | 175252736 | 0.394 | C/T | 0.999 | 2311/4678 | 0.75 (0.31-5.68) | 0.69 | 1091/4678 | 1.11 (0.11-7.33) | 0.92 |
| rs62113212 | 19q13.33 | 51360840 | 0.997 | T/C | 0.015 | 2311/4678 | 0.71 (0.51-0.99) | 0.04 | 1091/4678 | 1.10 (0.74-1.63) | 0.63 |

Supplementary Table 9. HaploReg results for SNPs reaching genome-wide significance ($P < 5 \times 10^{-8}$) for Gleason score among cases

| DNase enrichment analysis | | | | | | | |
|---------------------------|------------------------------|-----------|--------|-----|-----|------|-------|
| Cell type | | DNase | | | | | |
| ID | Description | Treatment | Center | Obs | Exp | Fold | p |
| GM12891 | B-lymphocyte, lymphoblastoid | None | Duke | 1 | 0 | 38.9 | 0.025 |
| HSMM_emb | embryonic myoblast | None | Duke | 1 | 0 | 44.4 | 0.022 |
| GM12878 | B-lymphocyte, lymphoblastoid | None | AWG | 1 | 0 | 31.9 | 0.031 |

Query SNP: [rs35148638](#) and variants with $r^2 \geq 0.8$

| SNP | chr: pos (hg19) | LD (r^2) | LD (D') | Ref | Alt | EUR Freq | SiPhy cons | Promoter histone marks | Enhancer histone marks | DNase | Proteins bound | eQTL tissue | Motifs changed | GENCO DE genes | dbSNP funct annot |
|----------------------------|-----------------|--------------|-------------|-----|-----|----------|------------|------------------------|------------------------|---------------|----------------|-----------------|------------------|----------------|-------------------|
| rs7719891 | chr 5: 86577352 | 0.8 | 0.93 | A | G | 0.28 | | | | | | | 7 altered motifs | RASA1 | intronic |
| rs1428438 | chr 5: 86598808 | 0.86 | 1 | T | A | 0.23 | | | NHLF, HMEC | 7 cell types | | EWSR1-FLI1,PPAR | RASA1 | intronic | |
| rs35148638 | chr 5: 86610989 | 1 | 1 | A | C | 0.26 | | | | | | Foxm1,SIX5,YY1 | RASA1 | intronic | |
| rs4421140 | chr 5: 86656964 | 0.82 | 0.97 | T | C | 0.24 | | | NHLF, HSMM, NHEK | 28 cell types | | | RASA1 | intronic | |

Query SNP: [rs78943174](#) and variants with $r^2 \geq 0.8$

| | | | | | | | | | | | | | | | |
|----------------------------|------------------|---|---|---|---|------|--|--|--|--|--|--|------|----------|----------|
| rs78943174 | chr 3: 175252736 | 1 | 1 | C | T | 0.01 | | | | | | | NF-Y | NAALADL2 | intronic |
|----------------------------|------------------|---|---|---|---|------|--|--|--|--|--|--|------|----------|----------|

Query SNP: [rs62113212](#) and variants with $r^2 \geq 0.8$

| | | | | | | | | | | | | | | |
|-----------------------------|------------------|------|------|---|---|------|--|--|----|----------------------------------|--|------------------|---------------------|----------|
| rs62113212 | chr 19: 51360840 | 1 | 1 | C | T | 0.08 | | | | GM12878,G M12891,HS MM_emb | | Sin3Ak-20,Znf143 | KLK3 | intronic |
| rs17632542 | chr 19: 51361757 | 1 | 1 | T | C | 0.08 | | | H1 | GM12892 | | NF-AT,STAT | KLK3 | missense |
| rs62113214 | chr 19: 51362537 | 1 | 1 | T | G | 0.08 | | | H1 | HMEC | | 7 altered motifs | KLK3 | intronic |
| rs76765083 | chr 19: 51362715 | 1 | 1 | T | G | 0.08 | | | H1 | | | 4 altered motifs | KLK3 | intronic |
| rs111362352 | chr 19: 51365440 | 0.96 | 0.98 | C | T | 0.08 | | | | BE2_C | | HIF1,HIF1::Arnt | 1.4kb 3' of KLK3 | |