Supplemental information:

Study populations:

India- Cornell University(19): Study participants were recruited through the Sanjay Gandhi Post Graduate Institute of Medical Sciences Hospital, Lucknow, India, between 2003 and 2006 as part of an ongoing prostate cancer case-control study. Case status and clinical information were obtained by reviewing medical records. Prostate cancer was diagnosed primarily based on lower urinary tract symptoms, clinical impression of the prostate on digital rectal examination, and high prostate-specific antigen level. Controls, seen for routine checkups and other acute illnesses at the same institution, were ascertained concurrently with the cases and were matched on age. Controls were specifically screened for prostate cancer by prostate-specific antigen tests and excluded from the study if they had an elevated prostate-specific antigen ($\geq$ 4 ng/mL), abnormal digital rectal examination, or previous cancer diagnosis.

University of Washington, St Louis(20): Prostate cancer cases were recruited from the urology and oncology clinics at the University of Washington, St Louis, during the period from May 2000 until March 2005. Criteria for inclusion of cases with advanced disease were as follows: patient must have evidence of metastatic disease. The control group was identified from the University of Washington urology and medicine clinics during the same period of time and all were males greater than 75 years old with no history of prostate carcinoma, and a benign digital rectal examination.

PLCO-Cancer Genetic Markers of Susceptibility (CGEMS)(1): Subjects for this study were participants in the NCI Cancer Genetic Markers of Susceptibility (CGEMS) investigation of SNPs and prostate cancer risk. Of the 38,350 men randomized to the screening arm of the trial, prostate cancer cases were selected from men who were of non-Hispanic white race/ethnicity, had no prior history of prostate of cancer, had at least one (PLCO) prostate cancer screen (PSA testing) before October 1, 2003, had completed a baseline questionnaire about risk factors for cancer, and had provided a blood sample. For participants with suspected or reported prostate cancer, medical and pathology records related to the diagnostic follow-up were obtained from medical care providers to confirm the diagnosis. For this

analysis, 53 cases with clinical stage IV tumors were included. Control subjects were selected by incidence density sampling with a case–control ratio of 1:1 frequency matched by age at cohort entry, time since initial screening, and calendar year of cohort entry.

Fred Hutchinson Cancer Research Center, Seattle, Washington(37): The study population consists of prostate cancer cases originally recruited for a population-based case-control study in Caucasian and African American residents of King County, Washington. Incident cases with histologically confirmed prostate cancer were ascertained from the Seattle-Puget Sound Surveillance, Epidemiology, and End Results (SEER) cancer registry. Cases were diagnosed between January 1, 1993, and December 31, 1996 and were 40 to 64 years of age at diagnosis. Prostate cancer cases (n=753) are under long-term surveillance for outcomes (recurrence/progression and mortality). In 2004 a self-administered follow-up survey with subsequent review of medical records was used to determine recurrence/progression status. Vital status and underlying cause of death data are acquired through linkage to the SEER cancer registry, with death certificates subsequently obtained to confirm cause of death (prostate cancer vs. other cause).

Moffitt Cancer Center: All prostate cancer patients who underwent radical prostatectomy at the Moffitt Cancer Center between 1987 and 2003 were identified. Information on clinical data and demographic variables was collected and study staff routinely conduct annual follow-up on all study participants for vital status, recurrence, and treatment information. Exclusion criteria include recurrent patients who underwent hormonal or radiation treatment before radical prostatectomy, recurrent cases due to residual tumor cells after radical prostatectomy. Paraffin embedded prostate tissue blocks from surgical patients are retrieved, pathology material is characterized by the study pathologist, and clinical data are extracted from the medical chart.

Johns Hopkins University: A case-control study was developed nested in the cohort of 4,860 men who underwent radical retropubic prostatectomy (RRP) for clinically localized prostate cancer at the Johns Hopkins Hospital between 1993 and 2005 and who had not had hormonal or radiation therapy prior to

radical prostatectomy. Cases were the 524 men who experienced biochemical recurrence, metastasis, or prostate cancer death after surgery. For each case, we used incidence density sampling to select a control who had not experienced recurrence by the date of the case's recurrence and who was matched on pathological stage, Gleason sum, age, and race. DNA was available for 450 of the matched pairs, which were used for this analysis.

University of Pennsylvania School of Medicine: Incident prostate cancer cases were identified through Urologic Oncology Clinics at multiple hospitals of the University of Pennsylvania Health System (UPHS) between 1995 and 2008. Case status was confirmed by medical records review using a standardized abstraction form. Cases were excluded from this study if they reported having exposure to finasteride (Proscar) at the time of their prostate cancer diagnosis. Patients who were non-incident cases (i.e., those diagnosed more than twelve months prior to the date of study ascertainment), or had a prior diagnosis of cancer at any site except non-melanoma skin cancer, were also excluded**.** Risk factor, medical history, prostate cancer screening history, and prostate cancer diagnostic information was obtained by using a standardized questionnaire and review of medical records. Information collected included personal history of benign prostatic hyperplasia and vasectomy, previous cancer diagnoses, and demographic information, and prostate cancer screening history. Existence of BPH was confirmed by medical records review. All study participants provided written informed consent for participation in this research under a protocol approved by the Committee for Studies Involving Human Subjects at the University of Pennsylvania.