Published in final edited form as:
J Urol. 2010 December ; 184(6): 2297–2302. doi:10.1016/j.juro.2010.08.005.

Androgen Receptor CAG Repeat Length and Association with Prostate Cancer Risk: Results from the Prostate Cancer Prevention Trial

Douglas K. Price[1], **Cindy H. Chau**[1], **Cathee Till**[2], **Phyllis J. Goodman**[2], **Caitlin E. Baum**[1], **Sandy B. Ockers**[1], **Bevin C. English**[1], **Lori Minasian**[3], **Howard L. Parnes**[3], **Ann W. Hsing**[4], **Juergen K. V. Reichardt**[5], **Ashraful Hoque**[6], **Catherine M. Tangen**[2], **Alan R. Kristal**[2,7], **Ian M. Thompson**[8], and **William D. Figg**[1,*]

[1]Medical Oncology Branch, National Cancer Institute, Bethesda, MD

[2]Cancer Prevention Program, Fred Hutchinson Cancer Research Center, Seattle, WA

[3]Division of Cancer Prevention, National Cancer Institute, Bethesda, MD

[4]Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD

[5]Plunkett Chair of Molecular Biology (Medicine), University of Sydney, Australia

[6]Department of Clinical Cancer Prevention, The University of Texas M.D. Anderson, Cancer Center, Houston, TX

[7]Department of Epidemiology, University of Washington, Seattle, WA

[8]Department of Urology, University of Texas Health Science Center at San Antonio, San Antonio, TX

Abstract

PURPOSE—We investigated the association between the length of the polymorphic trinucleotide CAG microsatellite repeats in exon 1 of the androgen receptor (AR) gene and the risk of prostate cancer.

METHODS—This is a nested case-control study of 1159 cases and 1353 controls drawn from the Prostate Cancer Prevention Trial, a randomized, placebo-controlled trial testing whether finasteride, a 5α-reductase inhibitor, could reduce the 7-year period prevalence of prostate cancer. During the course of the PCPT, men underwent annual DRE and PSA measures and a prostate biopsy was recommended for all men with an abnormal DRE or a finasteride-adjusted PSA of > 4.0 ng/mL. Cases were drawn from men with biopsy-determined prostate cancer identified either by a for-cause or end-of-study biopsy and controls were selected from men who completed the end-of-study biopsy procedure.

RESULTS—CAG repeat mean lengths were not different between cases and controls. The frequency distribution for cases and controls for the *AR* CAG repeat length is similar. There were no significant associations of CAG repeat length with prostate cancer risk, either when stratified by treatment arm (finasteride or placebo) or when combined together. There was also no significant association between CAG repeat length and the risk of low- or high-grade prostate cancer.

*Corresponding author: William D. Figg, Bldg 10/Room 5A01, 9000 Rockville Pike, Bethesda, MD 20892, Tel: 301-402-3623, Fax: 301-402-8606, wdfigg@helix.nih.gov.

CONCLUSIONS—There were no associations of the *AR* CAG repeat length and prostate cancer risk. Knowledge of *AR* CAG repeat length provides no clinical useful information for predicting prostate cancer risk.

Keywords

androgen receptor; CAG repeat length; prostate cancer

Introduction

Prostate cancer is the most common non-cutaneous malignancy and the second leading cause of cancer deaths among men in the United States, with approximately 192,280 men being diagnosed with prostate cancer and about 27,360 men expected to die of the disease in 2009 [1]. The etiology of prostate cancer remains poorly defined; age, family history and ethnicity (such as African ancestry) are the only established risk factors for prostate cancer [2]. The global ethnic variation and family clustering of prostate cancers implicate that certain genetic variations may be related to a higher risk of the disease.

Androgens, through androgen receptor (AR) signaling, play a critical role in prostate cancer growth. The *AR* gene is located at Xq11.2–q12 and is more than 90 kb in length, with the open reading frame separated over eight exons. The large amino-terminal domain of the *AR* gene is encoded by exon one, which includes the highly polymorphic CAG repeat sequence [3]. The CAG repeat sequence normally ranges from 8 to 35 repeats and averages 20 [4]. Shorter *AR* CAG repeats are associated with increased AR activity such as binding affinity for androgens and a higher transactivation activity [5], and a number of androgen-related clinical conditions including benign prostatic hyperplasia [6].

Coetzee and Ross initially suggested that variations in CAG repeat length are associated with prostate cancer [7]. Since then, multiple studies have evaluated the association of the *AR* gene CAG repeat length polymorphisms and prostate cancer risk. Meta-analyses suggest that the presence of shorter CAG repeat lengths is modestly associated with increased prostate cancer risk, although the absolute mean difference in the number of CAG repeats between cases and controls is < 1 repeat [8,9]. Recent publications continue to present inconsistent findings regarding AR CAG repeat length and prostate cancer risk in different ethnic groups [10–14].

Herein, we report results on the association of the *AR* gene CAG repeat length and risk of prostate cancer from the Prostate Cancer Prevention Trial (PCPT). One unique aspect of the PCPT is that presence or absence of prostate cancer was determined for each participant by prostate biopsy, minimizing potential bias and error due to latent, undetected cancer in the study population. In addition, cancer diagnoses were confirmed centrally and tumor grade was assigned by a single pathologist. Thus, this study provides a strong test of the association of the *AR* CAG repeat length with prostate cancer risk.

Methods

Study Design, Study Population, and Data Collection

All data for this study are from the PCPT, a randomized, placebo-controlled trial testing whether finasteride, a 5α-reductase inhibitor, could reduce the 7-year period prevalence of prostate cancer. Details of the study design and participant characteristics have been described previously [15,16]. Briefly, 18,882 men age 55 years and older with a normal digital rectal exam (DRE), prostate specific antigen (PSA) level of 3 ng/mL or below, and no history of prostate cancer or other clinically significant co-morbid conditions that would

have precluded successful completion of the study protocol, were randomized to receive either finasteride (5 mg/day) or placebo daily for seven years. Enrollment took place between 1994 and 1997. During the course of the PCPT, men underwent annual DRE and PSA measures and a prostate biopsy was recommended for all men with an abnormal DRE or a finasteride-adjusted PSA of > 4.0 ng/mL. At the conclusion of the trial, either a prostate cancer diagnosis or end-of-study biopsy was available from 59.6% of the participants in the finasteride treatment arm, and 63% from the placebo arm. This level of ascertainment agreed well with the study design assumption that 60% of men who have an endpoint were assessed.

This report presents data from a nested case-control study in the PCPT. Cases were men with biopsy-determined prostate cancer identified either by a for-cause or end-of-study biopsy and who had baseline DNA from white blood cells available. Controls were selected from men who completed the end-of-study biopsy procedure, had no evidence of prostate cancer and had archived baseline DNA samples. Controls were frequency matched to cases on distributions of age (in 5-year age groups), PCPT treatment arm (finasteride vs. placebo) and positive family history for first degree relative with prostate cancer; controls were oversampled to include all eligible non-whites. From this sample of cases and controls, DNA was available from the 1159 cases and 1353 controls who had consented to a special blood draw for lymphocyte collection.

Details regarding age, race/ethnicity, family history, physical activity (type, frequency, duration, pace, and intensity), usual alcohol consumption and history of smoking were collected at baseline using self-administered questionnaires. Clinic staff measured height and weight at randomization, and body mass index (BMI) was calculated as weight (kg) divided by height^2 (m). Tumors were graded and categorized and we retained the low and high-grade classifications as used in the original trial report for these analyses (low grade = Gleason < 7; high grade = Gleason ≥ 7).

Blood Collection and Genotyping

Blood for lymphocyte collection was drawn into a 7 ml EDTA vacutainer tube and shipped overnight to a central storage facility, where it was centrifuged, aliquoted and stored at −70 °C until analysis. DNA was extracted on a Qiagen BioRobot M48 Workstation using the MagAttract DNA Blood Midi M48 Kit (Qiagen, Valencia, CA). The DNA was amplified by polymerase chain reaction (PCR) using 5ul of the extracted DNA (~20ng/ul), 20pmol of each primer (ARF1=5′-ACAGCCTGTTGAACTCTTCTGAG-3′, ARR1=5′-CCAGCAGGGACAACGTGGATG-3′), 1 x PCR buffer (Invitrogen, Carlsbad, CA), 1.5mM $MgCl_2$, and 1 unit of Platinum Taq polymerase (Invitrogen, Carlsbad, CA) in a reaction volume of 50ul. After a 5 minute (95° C) denaturation period, the reaction was subjected to 40 cycles of PCR (94°C, 30 secs.; 70°C, 30 secs.; 72°C, 30 secs.) followed by a 7 minute extension at 72°C on the final cycle. Upon completion of amplification, 10ul of amplified product was electrophoresed on a 2% agarose gel to view quality and quantity of the DNA. Excess oligonucleotide primers were eliminated by column purification (Microcon YM-100, Millipore Corp., Bedford, MA) according to the manufacturer's instructions. Sequencing was performed using the Big Dye terminator v3.1 cycle sequencing reaction kit (Applied Biosystems, Foster City, CA) primed with either ARF2 (5′-GATTCAGCCAAGCTCAAGGATG-3′) or ARR2 (5′-CTCTGGGACGCAACCTCTCTC-3′). Sequenced DNA was analyzed on an ABI 3130xl Genetic Analyzer, and CAG repeat length was determined using Sequencing Analysis 5.3.1 (Applied Biosystems) and read independently by two individuals. Any questionable findings were repeated to gain a conclusive result.

Statistical Analysis

Descriptive statistics were used to characterize the study sample and distribution of *AR* CAG repeat length in cases and controls. Unconditional logistic regression was used to calculate the relative odds ratios (OR) and their 95% confidence intervals associated with CAG repeat length, using categories from previously published studies (<19, 19–25 and ≥26 and <20, 20–25 and ≥26) and based on the sample median (<22 and ≥22). Results are given for statistical models controlled for matching variables only since results did not change when diabetes, smoking status or alcohol were adjusted for in the model. All p-values were two-sided and considered statistically significant at $p<0.05$. Statistical analyses were conducted using SAS (version 9.0 Cary, NC).

Results

Distributions of demographic and health-related characteristics in cases (n=1159) and controls (n=1353) are given in Table 1. There were no differences in age and family history due to frequency matching of the larger case/control group. Because minorities were oversampled (all eligible non-Caucasians were included) in the control group, there were more African-American race or other ethnicity (non-whites) in the control group. The proportion of men with diabetes and obesity were also significantly higher in controls compared to cases. There were no differences between cases and controls in physical activity, smoking, alcohol consumption, or CAG repeat length (case mean = 22.03, SD = 3.05; control mean = 21.94, SD = 3.14). As expected, the African-Americans in our study population (cases + controls) have shorter CAG repeat lengths (<19) than the Caucasians (blacks, n=65/175 vs whites, n=199/2162). The frequency distribution for cases and controls for the *AR* CAG repeat length is similar (data not shown).

There were no significant associations of CAG repeat length with total prostate cancer risk (Table 2), either when stratified by treatment arm (finasteride or placebo) or when pooled together after adjusting for age, BMI, race, and family history of prostate cancer. There was also no significant association between CAG repeat length and low- or high-grade prostate cancer when evaluated separately as endpoints. There is a single significant finding for longer CAG repeat length (26+) associating with lower risk for low-grade disease in the placebo arm (OR = 0.67, 95%CI 0.46–0.98, p trend = 0.05). This is most likely a chance finding because it is inconsistent across treatment arms. Additionally, there were many tests done so the nominal significance of this finding does not reflect multiple testing. The lack of relationship between CAG repeat length and prostate cancer risk was still seen when CAG repeat length was categorized into different cutpoints (<20, 20–25 and ≥26 or <22 and ≥22, data not shown).

Because there was no indication of an interaction of treatment arm with CAG repeat length and the limitations of the sample size, analyses within the African American subset are shown in Table 3. We found no association between *AR* CAG repeat length and prostate cancer risk among controls and patients with low-grade and high-grade prostate cancer in this subset of the African-American population.

Discussion

This study found no significant association between the *AR* CAG repeat length and the risk of total, low- or high-grade prostate cancer. This is in agreement with other studies that did not observe any association between *AR* CAG repeats and prostate cancer risk including a multiethnic cohort study of 1014 cases [17] and another study of 460 cases [18]. Although our study participants were mostly Caucasians, we found that the *AR* CAG repeat length association with prostate cancer risk was not affected by race.

To date, results regarding the *AR* CAG repeat polymorphism and association with prostate cancer risk remain controversial (as reviewed by Simard *et al*. [19]). Several studies found positive associations between shorter CAG repeat length (20 or 22) and higher risk for prostate cancer [20–22]. In a nested case-control Caucasian population, Giovanucci et al. found that men with less than 18 CAG repeats had a higher risk of prostate cancer than men with more than 26 repeats [23]. Others have reported a reduced risk of prostate cancer associated with short alleles (≤22) such as in an analysis of a large Swedish population (n=1461) [24] and in British men with early-onset prostate cancer (n=288) [25]. In a Caucasian study consisting of 1045 prostate cancer patients and 814 controls, an association was also observed between the presence of a short *AR* CAG repeat (<17 repeats) and patients with late onset prostate cancer (diagnosed >64 years) [13]. This is in contrast to results reported by Hardy *et al*., which found a positive correlation between CAG repeats (≥23) and increased age at diagnosis [26]. In a meta-analysis of 19 case-control studies comprising a total of 4274 cases and 5275 controls with 79% of Caucasians, the authors concluded that a modest association existed between the shorter repeats (21) and prostate cancer risk (OR=1.19, 95% CI=1.07–1.31) [9]. However, because the absolute difference in mean repeat length between cases and controls was less than one repeat, it is questionable whether this minimal difference could be strong enough to cause biological impact.

CAG repeat lengths are different across ethnic groups, which has been hypothesized to explain the large racial differences in prostate cancer risk. Among populations studied to date, African-Americans have the highest frequency of short CAG repeats [4,27,28]. Our study confirmed previous findings of no association between the *AR* CAG repeat length and prostate cancer risk in the African-American population. Lange *et al.* found no evidence to support the association between *AR* CAG repeat polymorphisms and prostate cancer in a population-based study of 471 African American men (131 cases and 340 controls) [10]. Moreover, a study on 118 African American men diagnosed with prostate cancer and 567 African-American controls revealed no evidence for an association between *AR* CAG repeat length and prostate cancer [29]. A multiethnic cohort study with 635 African-American prostate patients and 664 African-American controls also failed to identify any association between *AR* CAG repeat length and prostate cancer [17]. Taken together, these studies suggest that the observation of shorter CAG repeats in African-Americans does not explain their increased risk of prostate cancer.

Other ethnic differences may also account for the influence of genetic determinants on prostate cancer risk. A population-based case-control study in China found that men with a CAG repeat length shorter than 23 (median length) had a 65% increased risk of prostate cancer (OR = 1.65 [95% CI 1.14–2.39]), compared to men with a CAG repeat length of 23 or longer [22]. The study demonstrates that Chinese men have a longer CAG repeat length than western men and that even in this very low-risk Chinese population, a shorter CAG repeat length confers a higher risk of clinically significant prostate cancer. Similarly, in a case-control study from a Brazilian population that presents with one of the highest incidences of prostate cancer in Brazil, the risk for prostate cancer was higher for CAG repeats ≤ 21 (OR = 2.44 [95% CI 1.03–5.81]) [14]. However, in another Brazilian study, Santos *et al.* found no significant correlation between cases and controls; however, they did find a significant association between early age of onset (< 55 years old) and CAG repeat length (< 21 repeats) [30]. Bratt et al. found no association between CAG repeat length and prostate cancer in patients and controls in a Swedish population [31]. Based on these findings, the evidence remains inconsistent regarding *AR* CAG repeat length and prostate cancer risk in different ethnic groups. Clearly larger studies are needed to have sufficient power to conclusively determine whether the *AR* CAG repeat length plays a role in genetic susceptibility to prostate cancer in specific ethnic populations.

Conclusions

We found no association of the *AR* CAG repeat length and prostate cancer risk. This lack of association of prostate cancer with the androgen receptor gene CAG repeat length refutes the hypothesis that this factor notably influences the risk or development of early-stage prostate cancer disease. The contradictory results across the many studies conducted thus far may be influenced by the complexity of several factors such as the number of cases investigated, the various ethnicities evaluated, the various cutpoints of CAG repeats which may indicate a sub-population responsible for the higher risk of developing prostate cancer, and classification bias due to not utilizing biopsy-negative controls. Nevertheless, based on the results given here, it is unlikely that knowledge of *AR* CAG repeat length will be of any clinical utility in predicting prostate cancer risk.

Acknowledgments

Supported by the Intramural Research Program at the National Cancer Institute, National Institutes of Health and funding from the American College of Clinical Pharmacy/Research Institute, the NIH's National Center for Minority Health and Health Disparity, and the NCI's Prostate Cancer Prevention Trial PO1 grant (CA108964).

We would like to thank Drs. Eddie Reed, Scott Lippman, Charles Coltman, Shannon Dixon, Elizabeth Platz, and Oliver Sartor for their helpful suggestions throughout the process of this project.

References

1. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2009. CA Cancer J Clin. 2009; 59:225–49. [PubMed: 19474385]
2. Bostwick DG, Burke HB, Djakiew D, et al. Human prostate cancer risk factors. Cancer. 2004; 101:2371–490. [PubMed: 15495199]
3. Trapman J, Cleutjens KB. Androgen-regulated gene expression in prostate cancer. Semin Cancer Biol. 1997; 8:29–36. [PubMed: 9299579]
4. Edwards A, Hammond HA, Jin L, et al. Genetic variation at five trimeric and tetrameric tandem repeat loci in four human population groups. Genomics. 1992; 12:241–53. [PubMed: 1740333]
5. Rajender S, Singh L, Thangaraj K. Phenotypic heterogeneity of mutations in androgen receptor gene. Asian J Androl. 2007; 9:147–79. [PubMed: 17334586]
6. Giovannucci E. Is the androgen receptor CAG repeat length significant for prostate cancer? Cancer Epidemiol Biomarkers Prev. 2002; 11:985–6. [PubMed: 12376496]
7. Coetzee GA, Ross RK. Re: Prostate cancer and the androgen receptor. J Natl Cancer Inst. 1994; 86:872–3. [PubMed: 8182772]
8. Nelson KA, Witte JS. Androgen receptor CAG repeats and prostate cancer. Am J Epidemiol. 2002; 155:883–90. [PubMed: 11994226]
9. Zeegers MP, Kiemeney LA, Nieder AM, et al. How strong is the association between CAG and GGN repeat length polymorphisms in the androgen receptor gene and prostate cancer risk? Cancer Epidemiol Biomarkers Prev. 2004; 13:1765–71. [PubMed: 15533905]
10. Lange EM, Sarma AV, Ray A, et al. The androgen receptor CAG and GGN repeat polymorphisms and prostate cancer susceptibility in African-American men: results from the Flint Men's Health Study. J Hum Genet. 2008; 53:220–6. [PubMed: 18217192]
11. Mishra D, Thangaraj K, Mandhani A, et al. Is reduced CAG repeat length in androgen receptor gene associated with risk of prostate cancer in Indian population? Clin Genet. 2005; 68:55–60. [PubMed: 15952987]
12. Mittal RD, Mishra D, Mandhani AK. Role of an androgen receptor gene polymorphism in development of hormone refractory prostate cancer in Indian population. Asian Pac J Cancer Prev. 2007; 8:275–8. [PubMed: 17696745]
13. Nicolaiew N, Cancel-Tassin G, Azzouzi AR, et al. Association between estrogen and androgen receptor genes and prostate cancer risk. Eur J Endocrinol. 2009; 160:101–6. [PubMed: 18952763]

14. Silva Neto B, Koff WJ, Biolchi V, et al. Polymorphic CAG and GGC repeat lengths in the androgen receptor gene and prostate cancer risk: analysis of a Brazilian population. Cancer Invest. 2008; 26:74–80. [PubMed: 18181049]
15. Thompson IM, Goodman PJ, Tangen CM, et al. The influence of finasteride on the development of prostate cancer. N Engl J Med. 2003; 349:215–24. [PubMed: 12824459]
16. Feigl P, Blumenstein B, Thompson I, et al. Design of the Prostate Cancer Prevention Trial (PCPT). Control Clin Trials. 1995; 16:150–63. [PubMed: 7540965]
17. Freedman ML, Pearce CL, Penney KL, et al. Systematic evaluation of genetic variation at the androgen receptor locus and risk of prostate cancer in a multiethnic cohort study. Am J Hum Genet. 2005; 76:82–90. [PubMed: 15570555]
18. Platz EA, Leitzmann MF, Rifai N, et al. Sex steroid hormones and the androgen receptor gene CAG repeat and subsequent risk of prostate cancer in the prostate-specific antigen era. Cancer Epidemiol Biomarkers Prev. 2005; 14:1262–9. [PubMed: 15894683]
19. Simard J, Dumont M, Labuda D, et al. Prostate cancer susceptibility genes: lessons learned and challenges posed. Endocr Relat Cancer. 2003; 10:225–59. [PubMed: 12790786]
20. Andersson P, Varenhorst E, Soderkvist P. Androgen receptor and vitamin D receptor gene polymorphisms and prostate cancer risk. Eur J Cancer. 2006; 42:2833–7. [PubMed: 17010601]
21. Ingles SA, Ross RK, Yu MC, et al. Association of prostate cancer risk with genetic polymorphisms in vitamin D receptor and androgen receptor. J Natl Cancer Inst. 1997; 89:166–70. [PubMed: 8998186]
22. Hsing AW, Gao YT, Wu G, et al. Polymorphic CAG and GGN repeat lengths in the androgen receptor gene and prostate cancer risk: a population-based case-control study in China. Cancer Res. 2000; 60:5111–6. [PubMed: 11016637]
23. Giovannucci E, Stampfer MJ, Krithivas K, et al. The CAG repeat within the androgen receptor gene and its relationship to prostate cancer. Proc Natl Acad Sci U S A. 1997; 94:3320–3. [PubMed: 9096391]
24. Lindstrom S, Zheng SL, Wiklund F, et al. Systematic replication study of reported genetic associations in prostate cancer: Strong support for genetic variation in the androgen pathway. Prostate. 2006; 66:1729–43. [PubMed: 16998812]
25. Forrest MS, Edwards SM, Houlston R, et al. Association between hormonal genetic polymorphisms and early-onset prostate cancer. Prostate Cancer Prostatic Dis. 2005; 8:95–102. [PubMed: 15711606]
26. Hardy DO, Scher HI, Bogenreider T, et al. Androgen receptor CAG repeat lengths in prostate cancer: correlation with age of onset. J Clin Endocrinol Metab. 1996; 81:4400–5. [PubMed: 8954049]
27. Irvine RA, Yu MC, Ross RK, et al. The CAG and GGC microsatellites of the androgen receptor gene are in linkage disequilibrium in men with prostate cancer. Cancer Res. 1995; 55:1937–40. [PubMed: 7728763]
28. Cude KJ, Montgomery JS, Price DK, et al. The role of an androgen receptor polymorphism in the clinical outcome of patients with metastatic prostate cancer. Urol Int. 2002; 68:16–23. [PubMed: 11803263]
29. Gilligan T, Manola J, Sartor O, et al. Absence of a correlation of androgen receptor gene CAG repeat length and prostate cancer risk in an African-American population. Clin Prostate Cancer. 2004; 3:98–103. [PubMed: 15479493]
30. Santos ML, Sarkis AS, Nishimoto IN, et al. Androgen receptor CAG repeat polymorphism in prostate cancer from a Brazilian population. Cancer Detect Prev. 2003; 27:321–6. [PubMed: 14585317]
31. Bratt O, Borg A, Kristoffersson U, et al. CAG repeat length in the androgen receptor gene is related to age at diagnosis of prostate cancer and response to endocrine therapy, but not to prostate cancer risk. Br J Cancer. 1999; 81:672–6. [PubMed: 10574254]

Table 1

Demographics and characteristics of study population by control subjects and case patients: The Prostate Cancer Prevention Trial.

	Controls (n=1353)	Cases (n=1159)	p-value
Diabetes n(%)	170 (12.57)	82 (7.08)	<0.0001
Family History of Prostate Cancer n(%)	288 (21.29)	246 (21.23)	0.97
Age mean(sd)	63.6 (5.61)	63.4 (5.57)	0.51
55–59 n(%)	367 (27.12)	328 (28.30)	
60–64	443 (32.74)	378 (32.61)	
65–69	319 (23.58)	270 (23.30)	
70+	224 (16.56)	183 (15.79)	
BMI (kg/m^2) mean(sd)	27.7 (4.02	27.4 (4.04)	0.04
Normal (<25) n(%)	324 (24.2)	324 (28.17)	
Overweight (25 – <30)	712 (53.17)	593 (51.57)	
Obese (>=30)	303 (22.63)	233 (20.26)	
Physical Activity n(%)			0.36
Sedentary	233 (17.31)	208 (17.99)	
Light	557 (41.38)	474 (41)	
Moderate	414 (30.76)	378 (32.7)	
Active	142 (10.55)	96 (8.3)	
Race n(%)			<0.0001
Caucasian (Non-Hispanic)	1080 (79.82)	1082 (93.36)	
African American	128 (9.46)	47 (4.06)	
Other	145 (10.72)	30 (2.59)	
Smoking Status n(%)			0.16
Non-Smoker	1251 (92.46)	1088 (93.87)	
Current Smoker	102 (7.54)	71 (6.13)	
Alcohol Consumption n(%)			<0.01
<1 drink/week	613 (46.94)	451 (41.61)	
1 to <7 drinks/week	345 (26.42)	296 (27.31)	
7+ drinks/week	348 (26.65)	337 (31.09)	
CAG Repeat Length mean(sd)	21.9 (3.14)	22.0 (3.05)	0.46
<19 n(%)	168 (12.42)	117 (10.09)	
19–25	1032 (76.27)	923 (79.64)	
25+	153 (11.31)	119 (10.27)	

Table 2

Association between AR CAG repeat length and prostate cancer risk among controls and patients with low-grade and high-grade prostate cancer, stratified by study arm: The Prostate Cancer Prevention Trial. *

	Combined						
	Control	All prostate cancer		Low-Grade (Gleason 2–6)		High-Grade (Gleason 7–10)	
	N	N	OR (95% CI)	N	OR (95% CI)	N	OR (95% CI)
<19	168	116	0.91 (0.70, 1.19)	86	0.97 (0.72, 1.30)	27	0.80 (0.51, 1.25)
19–25 [a]	1019	916	1.00	649	1.00	235	1.00
26+	152	118	0.92 (0.7, 1.19)	84	0.92 (0.69, 1.23)	30	0.92 (0.60, 1.4)
p_{trend}			0.41		0.59		0.43
	Finasteride						
	Control	All prostate cancer		Low-Grade (Gleason 2–6)		High-Grade (Gleason 7–10)	
	N	N	OR (95% CI)	N	OR (95% CI)	N	OR (95% CI)
<19	75	44	0.97 (0.63, 1.49)	28	1.01 (0.61, 1.66)	15	0.93 (0.50, 1.71)
19–25 [a]	441	376	1.00	230	1.00	132	1.00
26+	53	53	1.26 (0.82, 1.93)	38	1.52 (0.95, 2.43)	14	0.91 (0.48, 1.72)
p_{trend}			0.37		0.11		0.72
	Placebo						
	Control	All prostate cancer		Low-Grade (Gleason 2–6)		High-Grade (Gleason 7–10)	
	N	N	OR (95% CI)	N	OR (95% CI)	N	OR (95% CI)
<19	93	72	0.89 (0.63, 1.25)	58	0.95 (0.66, 1.37)	12	0.70 (0.36, 1.34)
19–25 [a]	578	540	1.00	419	1.00	103	1.00
26+	99	65	0.74 (0.53, 1.04)	46	0.67 (0.46, 0.98)	16	0.98 (0.55, 1.74)
p_{trend}			0.07		0.05		0.67

* Adjusted for age, BMI, race (whites vs. blacks vs. others), and family history of prostate cancer.

[a] Reference category

Table 3

Association between AR CAG repeat length and prostate cancer risk among controls and patients with low-grade and high-grade prostate cancer, black participants only. *

	Black Only, Combined Treatment Arms						
	Control	Case	Total	Low-Grade (Gleason 2–6)		High-Grade (Gleason 7–10)	
	N	N	OR (95% CI)	N	OR (95% CI)	N	OR (95% CI)
<19	48	17	0.93 (0.45, 1.92)	10	0.95 (0.39, 2.33)	6	0.89 (0.30, 2.67)
19–25 *a*	71	27	1.00	16	1.00	10	1.00
26+	9	3	0.77 (0.19, 3.19)	2	0.92 (0.17, 4.92)	1	0.66 (0.07, 6.02)
p_{trend}			0.78		0.95		0.74
$p_{interacvtion}$ *b*			0.91		0.78		0.94

*Adjusted for age, BMI, and family history of prostate cancer.

*a*Reference category

*b*Interaction p-value tests the interaction between CAG repeat length and race (black vs. white).