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Smoking and Prostate Cancer in a Multi-Ethnic Cohort

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Abstract

BACKGROUND—Prostate cancer (PCa) and smoking-related morbidity disproportionately burdens African American (AA) men. Smoking is associated with high-grade PCa and incidence, but few studies have focused on AA men. This study aims to determine the effect of tobacco-use on odds of PCa and of high-grade PCa in a population of predominantly AA men.

METHODS—This is a cross-sectional study evaluating smoking and PCa status in men with incident PCa and screened healthy controls. Altogether, 1,085 men (527 cases and 558 controls), age ≥ 40 years were enrolled through outpatient urology clinics in two US cities from 2001 to 2012. Validated questionnaires were used to gather clinical and socioeconomic data.

RESULTS—The cases and controls were predominantly AA (79.9% and 71.3%, respectively, $P = 0.01$). AA men smoked more frequently (53.4% vs. 47.9%, $P < 0.001$) and quit less frequently than European American (EA) men (31.5% vs. 40.4%, $P = 0.01$). AA heavy smokers had increased odds of PCa diagnosis (OR 2.57, 95% CI 1.09, 6.10) and high-grade cancer (OR 1.89, 95% CI 1.03, 3.48) relative to never smokers and light smokers. Among AAs, heavy smokers had lower odds of NCCN low PCa recurrence risk stratification. AA former smokers had a trend for increased odds of high-grade cancer compared to never smokers. The associations between smokings, cancer diagnosis and cancer grade did not reach statistical significance in EA men.

CONCLUSION—We found ethnic differences in smoking behavior. Heavy smoking is associated with increased odds of PCa and of higher Gleason grade in AA men.

Keywords

African American; cancer disparities; prostate cancer; smoking

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Folasade Akerenyi and Yaw Nyame have both contributed equally to this work.

INTRODUCTION

Prostate cancer is the leading cause of new cancer diagnoses among men in the United States [1]. The burden of prostate cancer demonstrates a significant degree of disparity along racial and ethnic boundaries among American men. In particular, African American (AA) men demonstrate a higher incidence and poorer outcomes related to the disease [2]. These ethnic differences are a result of biologic, environmental, and socioeconomic differences that promote the development and progression of prostate cancer [3,4]. There are numerous covariates that are associated with increased prostate cancer risk, including age, family history [5], high-fat diet, and obesity. There is an increasing volume of literature that demonstrates that differences in these variables explain some of the ethnic variability demonstrated by prostate cancers.

Tobacco use is a well-known risk factor for many cancers, yet few studies have shown that smoking increases prostate cancer risk among men [6,7]. However, cigarette smoking does demonstrate a significant correlation with aggressive and advanced prostate cancer disease as defined by Gleason grade and TNM stage in non-AA men, respectively [8,9]. Currently, there is a dearth of studies that evaluate the effect of tobacco-use on prostate cancer risk among AA men. This study aims to determine the impact of various patterns and histories of tobacco-use, a modifiable risk factor, on prostate cancer diagnosis and pathologic grade in a sample of predominantly AA men.

MATERIALS ANDMETHODS

Study Population

This study is a cross-sectional study of men newly diagnosed with prostate cancer and controls who self-identified as tobacco users and non-users. The cases and controls are men ≥ 40 years old, ambulatory-, unrelated-men, prospectively enrolled through outpatient urology clinics from numerous urban, academic medical centers in Washington, DC and Chicago, IL. A subset of the controls was recruited from community prostate cancer screening events. Men recently diagnosed with prostate cancer after undergoing prostate biopsy serve as cases. Both cases and controls were enrolled and consented for venipuncture between 2001 and 2012. There were 527 cases of biopsy-confirmed prostate cancer. The controls were men being seen in the clinics for benign urologic conditions (n = 352) or they were recruited from community screening events (n = 145, 29.8%). Controls were excluded from analysis if they had a prior diagnosis of non-prostatic neoplasms. The final population analyzed consisted of 527 prostate cancer cases and 558 controls, for a total of 1,085 subjects. All study participants provided written consent. Approval by the Institutional Review Board was obtained at all participating study sites.

Clinical and Environmental Data

Men in the study were screened for prostate cancer and subsequently were biopsied based on an elevated or abnormal PSA, an abnormal digital rectal exam (DRE), or an elevated PSA velocity. The cases underwent ultrasound-guided transrectal prostate needle biopsy to determine the diagnosis of prostate cancer. Additionally, 37 men with negative prostate biopsies performed for elevated PSA velocity >0.35 ng/ml/year with negative digital rectal exam (DRE) and normal PSA levels were included as controls. This subset of negative biopsy patients was excluded from the control group if they had a subsequent positive prostate biopsy within the follow-up period.

Research coordinators administered questionnaires to study subjects to gather data on age, ancestry, family history of prostate cancer, medical history, occupation, income, education,

alcohol- and tobacco-use, and marital status. A peripheral blood sample was drawn from all participants to measure PSA. Data on tobacco-use consisted of the following parameters: history of tobacco use, current and former history of use, and frequency and duration of use. Never smokers were defined as smoking 0–100 cigarettes in their lifetime, smokers smoked more than 100 cigarettes and former smokers smoked more than 100 cigarettes, but had quit smoking before the time of recruitment. Ethnicity was determined by self-identification by the participants, and included only African Americans (AA) and European Americans (EA). Standing height and weight were used to determine the body mass index (BMI) of all subjects in the sample. Genitourinary pathologists were used to confirm the diagnosis and to verify the Gleason grade.

Statistical Analysis

Univariate comparison of prostate cancer cases and controls were performed using an unpaired, two-sample *t*-test for the measured continuous covariates and a χ^2 test for the categorical covariates. Intensity of tobacco-use was divided into three groups: never smokers (0 cigarettes per day), low-intensity current and former tobacco-users (1–19 cigarettes per day), and high-intensity current and former tobacco-users (20 or more cigarettes per day). Additionally, men were divided into never smokers, current and former smokers. Similarly, current non-smokers were divided into never smoked and quit smoking. We used pack years (years of smoking × average packs of cigarettes smoked per day) as continuous and categorical variables in our analyses based on the previously published literature. A comparison of racial/ethnic differences in smoking history and behavior was conducted using unpaired, two-sample *t*-test and χ^2 analysis. Another comparison was conducted to elicit differences in cigarette smoking history and patterns among prostate cancer cases and controls.

Age, study site, ethnicity, family history and frequency of alcohol-use adjusted models were constructed to calculate odds ratios as an estimate of prostate cancer risk using unconditional logistic regression to independently compare prostate cancer cases and controls with each of the following categorical variables: history of tobacco-use (i.e., ever or never), and the nominal variable (never smoker, current smoker, and former smoker), and smoking intensity (never smoker, <20 cigarettes/day, and ≥20 cigarettes/day). Similarly, models were constructed to compare high-grade prostate cancer cases (Gleason grade ≥7) to controls, and low-grade prostate cancer cases (Gleason grade <7) to controls, and models were stratified by race given the differences in smoking patterns and prostate cancer risk between AA and EA men. All relevant covariates were included in the model, including prostate cancer family history, age, education, martial status, income, alcohol use, and obesity and the models were optimized to increase the magnitude of the −2 log likelihood. Several covariates were excluded from final models (all $P > 0.10$). Because PSA cutoffs were used to select controls, PSA was not included in any of the models to avoid collinearity. All statistical tests were two-sided, and significance is defined as $P < 0.05$. Statistical analysis was performed using SPSS 21 (IBM Corporation 2012, United States).

RESULTS

Table I contains summary characteristics of the cases and controls. The mean age of prostate cancer cases and controls was 63.4 and 56.8 years, respectively (median 63 and 56 years, $P = 0.001$). AA men comprised 79.9% of the cases of prostate cancer and 71.3% of the controls in the population. The cases were more likely to have a history of alcohol use and annual income less than $20,000 US, and less likely to have a high school diploma than controls in the population (all $P < 0.05$). Of the controls, 26% of the men were recruited at community based screening events and were similar to the clinic controls in cigarette use,

years smoked or heavy smoking history and total PSA level (all $P > 0.15$). In total, 363 of the prostate cancer cases had reported Gleason grade (Table I). One hundred and sixty-seven (45.7%) of these patients were classified as high Gleason grade disease (Gleason ≥ 7) and 55 patients (15.3%) had Gleason ≥ 8. Gleason ≥ 7 and total Gleason score on biopsy were positively correlated with a history of heavy tobacco-use on univariate analysis (both $P < 0.05$).

On non-race stratified analysis, 55.7% of prostate cancer cases compared to 49.7% of controls reported current or former cigarette use ($P = 0.02$, data not shown). There were a higher proportion of heavy smokers in the control group versus the prostate cancer cases (21.1% vs. 14.8%, $P = 0.04$).

Approximately 54% of AA men in the sample reported a history of tobacco-use, compared to 48% of EA men, and AA men were significantly more likely to be light smokers (<20 cigarettes/day, see Table II). Tobacco-use was significantly correlated with age (r = 0.22), education (r = −0.17), income (r = −0.20), poverty (r = 0.16), frequency of alcohol-use (r = 0.30), and history of alcohol-use (r = 0.28) on Pearson correlation (all $P < 0.05$). A positive history of alcohol-use and frequency of alcohol consumption were both associated with increased duration (r = 0.24 and 0.31) and frequency of tobacco-use (r = 0.23 and r = 0.30, all $P < 0.05$). AA men in the population smoked significantly fewer cigarettes per day and had less pack-years compared to EA men (Table II). Interestingly, a positive history of heavy cigarette use (at least 20 cigarettes/day) were observed more frequently among cancer subjects when compared to controls among the AA men ($P = 0.003$, Table IIIB). Otherwise trends between AA and EA men were similar for other major covariates including age.

Among African Americans, prostate cancer cases demonstrated statistically significant increased numbers of cigarettes per day, duration of tobacco-use and heavy cigarette smoking (Table IIIB, all $P < 0.01$), but this trend was not observed among European American men (Table IIIA).

The effect of tobacco-use on odds of prostate cancer diagnosis was evaluated using unconditional logistic regression adjusted for covariates of prostate cancer (see Tables IVA and IVB). In our race-stratified logistic regression models, using smoking intensity (never smokers/light smokers versus heavy smokers) as a binary variable produced better-fitting regression models (i.e., higher log likelihood values) than using smoking intensity as an ordinal variable with three levels, except for in the evaluation of high (Gleason ≥7) and low-grade (Gleason <7) tumors versus controls in AAs. It also yielded better fitting models (−2 log likelihood = 870) than using the categorical variable (former smoker/never smoked/current smoker). A positive history of heavy cigarette use (≥20 cigarettes smoked/day) did not confer increased odds of being diagnosed with prostate cancer (OR 1.04, 95% CI 0.65–1.19) among EAs when referenced against light smoking and a negative smoking history (Table IVA). However, among AAs, heavy smoking increased odds of prostate cancer diagnosis in adjusted models (OR 2.57, 95% CI 1.09–6.10, Table IVB).

To evaluate the effect of tobacco on prostate cancer aggressiveness, an unconditional binary logistic regression was done adjusting for covariates of aggressive disease using a dependent binary variable for high- and low-Gleason grade relative to the control patients. We analyzed the effect of heavy smoking on high-grade and low-grade disease stratified by race. For EA men, the smoking variable was dichotomized into heavy smokers versus light smokers/never smokers since the three level variable (i.e., never smoker, light smoker, and heavy smoker) showed a similar OR for light smokers and never smokers in EAs. Smoking 20 or more cigarettes (OR 0.83, 95% CI 0.57–1.22) did not significantly increase odds of

low-grade or high-grade disease among European Americans. Heavy smoking had a non-significant OR of 1.60 ($P = 0.20$) for high-grade cancer in EA men in adjusted models.

Smoking intensity was coded as an ordinal variable with three levels in African Americans to produce better fitting regression models (never smokers/light smokers/heavy smokers, Table IVB). This produced a better fitting model than smoking coded as never smoker/current smoker/former smoker and several other binary and continuous smoking variables. Among AAs however, there is increased odds ratio for high-grade PCa among men who smoke ≥20 cigarettes per day (OR 1.89, $P = 0.03$). There is a potential dose response with light smokers having an intermediate OR estimate for high-grade status. There was no significant association in AA men with heavy smoking and low-grade PCa (see Table IVB). The constellation of covariates was different between AA and EA men on the best-fitting race-stratified analyses. Due to multiple collinear variables, the best overall model for high-grade and low-grade AA cancer versus controls involved only smoking intensity, marital status and alcohol intensity for AAs (Table IVB).

In EA men, high-school completion and marital status were significant covariates in the model and diabetes mellitus (yes/no) improved the prediction accuracy of the regression models comparing high-grade PCa and controls (see Table IVA).

There was a trend for an association with former smoking (OR 1.44, $P = 0.058$) and current smoking (OR 1.39, $P = 0.07$) increasing the odds of prostate cancer diagnosis in unadjusted models in AA men. Former smoking status was not statistically associated with prostate cancer diagnosis, low-grade disease or high-grade disease relative to control patients on unadjusted or adjusted models in EA or AA men (all $P > 0.05$).

Finally, we used a multinomial logistic regression to evaluate the effect of heavy smoking on the 2007 National Comprehensive Cancer Network (NCCN) prostate cancer recurrence risk category (i.e., low vs. intermediate risk and low versus high risk group). In short, men with PSA < 10 ng/ml, clinical stage T1a to T2a, and Gleason <7 were considered low-risk; men with PSA from 10 to 20 ng/ml, or clinical stage T2b–T2c, or Gleason = 7 were considered intermediate risk; men with PSA > 20 ng/ml, clinical stage T3a or greater, or Gleason >7 were considered high-risk. The unadjusted multinomial logistic regression with heavy versus never smokers/light smokers was associated with an OR of 1.47 (CI: 1.09, 1.98) for NCCN intermediate versus low-risk PCa and an OR of 1.56 (CI: 1.15, 2.11) for high risk versus low risk in the non-stratified model. Similar but non-significant trends are seen on adjusted models. In race-stratified models that adjust for alcohol use, age, and marital status, heavy smoking is significant among AA men with an OR of 9.71 for high-risk versus low NCCN risk group (CI: 1.03, 90.91). Due to the smaller sample size in EA men, there is a significant, but unstable estimate for the effect of heavy smoking on high versus low NCCN risk group (OR 1,000, $P = 0.001$).

DISCUSSION

Smoking has been linked to prostate cancer incidence, aggressiveness, and mortality [6,8,10–12]. However, most studies find the strongest association with prostate cancer aggressiveness [6]. The data on incidence usually dichotomizes smoking into the never smokers versus the heaviest smokers with modest relative risk estimates from 1.11 to 1.22 [7]. In our data set, we find no evidence of increased odds of PCa (OR = 1.14, $P = 0.65$) in EA men using heavy smokers versus never smokers. Due to our smaller data set and similar odds ratios for never smokers and light smokers, in EAs, we grouped never smokers and light smokers, but find no evidence of increased odds of PCa cancer for heavy smokers. This was not true among AAs, where heavy smoking was associated with increased odds of

overall cancer diagnosis (Table IV). Heavy smoking also associated with high NCCN PCa recurrence risk group in AA and EA men.

Tobacco use is reportedly correlated with aggressive and advanced prostate cancer disease as defined by Gleason grade and TNM stage, respectively [8,9]. Our data suggests a significant association with high-grade cancer for AA heavy smokers, with 1.89× the odds of high-grade prostate cancer relative to never smokers (see Table IV). When analyzing only the EA men, the effect of heavy smoking is in the same direction as in AA men, but the trend is non-significant. The smaller sample size in EAs in one explanation for the failure to find the association as evidenced by the need for meta-analyses to find the association reliably [7]. There have been multiple possible pathways for cigarette smoking to promote prostate cancer tumorigenesis and progression. One pathway is through the increase in bioavailable serum androgens and decrease in estradiol associated with cigarette smoking [13]. This would produce an environment that promotes carcinogenesis [14,15]. Interestingly, the methylation and inactivation of glutathione S-transferase, which is involved in protecting cells against carcinogens and oxidative stress, is believed to be one of the early processes in mutagenesis of prostate cancer. Glutathione S-transferase also plays an important role in protecting the body from benzopyrene, a tobacco toxin that causes DNA adducts. Inactivation of glutathione S-transferase among tobacco users provides a biologic explanation for increased prevalence of high-grade and advanced stage prostate cancer [16,17]. This does not explain the increased risk of aggressive disease in former smokers however.

According to the CDC, AA, and EA men both have a 21% prevalence of cigarette smoking [18]. However, AA men have lower rates of heavy smoking, but lower rates of smoking cessation [19–26]. Our data is consistent with the literature. Among those with smoking history, 31.5% of AA smokers quit versus 40.4% of EAs. Only 21% of AA men were heavy smokers versus 30.5% of EA men. Studies vary in the estimate of risk for former smokers. It seems likely that the amount of time of cessation would be correlated with risk, but this data is incomplete in our data set. Giovannucci et al. [27] reported in 1999 that the risk of prostate cancer returns to baseline risk after 10 years of smoking cessation.

Studies of smoking habits indicate that AA men have higher plasma nicotine and metabolites, despite smoking the same average number of cigarettes per day as EA men [28]. The higher exposures of nicotine per cigarette smoked by AA men have been attributed to differences in tobacco-use behavior, such as the higher prevalence of menthol cigarette-use, which may confer deeper inhalation of nicotine and tobacco toxins and be associated with increased nicotine dependence [29,30]. Nicotine also binds to melanin and can lead to prolonged clearance of nicotine in AA men [30,31]. Moreover, higher concentrations of plasma nicotine per cigarette smoked per day are associated with increased tobacco addiction among AA men and may contribute to the higher morbidity and mortality reported in this group. It also may explain the difference in odds ratio estimates in AAs and EAs in the study sample.

Former smokers may have a modestly increased risk of prostate cancer relative to never smokers, but the literature is somewhat inconsistent [7]. Our study finds no association with former smokers versus never smokers for PCa status or grade at presentation. In the literature, the heaviest smokers have a 24% greater risk of death from prostate cancer than nonsmokers [7]. In our analysis, we focused on odds of prostate cancer and on odds of higher Gleason grade and NCCN risk group through prostate biopsy Gleason score in a predominantly AA population. AAs have high rates of prostate cancer and cancer-specific mortality, but lower incidence of heavy smoking. AAs are known to have lower rates of heavy smoking [32–36]. Studies suggest that AAs smoke fewer cigarettes than some other

racial groups, but have higher intake of nicotine per cigarette smoked [32,37–40]. These findings correlate with studies showing that AAs tend to smoke menthol cigarettes, which causes a cooling sensation upon inhalation [41]. Thus menthol cigarette use is associated with deeper inhalation of cigarette smoke, which could increase the intake of nicotine and other toxins per cigarette [42]. Some studies fail to show this association [43,44]. Another factor is that smoking mentholated cigarettes is associated with faster time to smoking the first cigarette, a marker of nicotine dependence [29]. Smoking has a modest effect size on PCa risk is and best seen in heavy smokers, making it is possible to miss the association between smoking and PCa since the rates of heavy smoking are lower (see Table II) and the risk of prostate cancer is higher in AAs at baseline. The measures of associations might differ from largely Caucasian study populations as in our sample. Despite these issues in smoking trends, our analysis suggests that the effect of smoking on prostate cancer is modest with an estimated odds ratio of 1.37 ($P = 0.01$) in unadjusted models, since the odds ratio overestimates relative risk in case–control studies. The odds ratio for heavy smoking and prostate cancer diagnosis is estimated at 2.57 for AA men, but fails to reach statistical significance in EA men, possibly due to sample size in the fully adjusted model.

Another mediating factor is that melanin-containing tissues binds nicotine, which is associated with higher degrees of nicotine dependence and accumulation of nicotine and associated carcinogens in AA with higher melanin levels in the skin [28]. This implies that darker pigmented individuals may be predisposed to greater exposure to nicotine and tobacco-specific toxins, and have susceptibility to tobacco-related carcinogens, especially if these toxicants are being slowly released from the reservoir within melanin-containing tissues. Thus, the melanin and nicotine connection has particular relevance for AA smokers, who have higher levels of melanin and have heavy burdens from tobacco-related disease outcomes, including prostate cancer aggressiveness [45].

LIMITATIONS

The largest limitation of the study is the cross-sectional study design, which can have issues with confounding. However, we measured the major confounders of association between smoking and prostate cancer including age, race, cancer family history, BMI, education, marital status, insurance status, alcohol use, and other comorbidities. We recruited most of the PCa cases and controls from urology clinics. The men in the control group were healthy men in the urology clinics for benign urologic conditions such as kidney stone disease and benign prostatic hyperplasia. A small portion of the men from the control group was recruited from prostate cancer screening events and was found to have normal PSA levels. These men may not represent the general population well. The men at screening events were largely African American and uninsured. The direction of the association between odds of overall prostate cancer and aggressive disease were consistent when we stratified our analyses by these factors as well. We were unable to account for exposure to second-hand tobacco smoke. Moreover, we did not collect biological samples to validate smoking status nor data on glutathione S-transferase related genetic polymorphisms in GSTM1 and GSTT1. Because of the difference in age within our cases and controls, we performed several stratifications for age (age <50, <65, and ≥65 y/o) and adjusted for age in our regressions. Our effect estimates for smoking variables were similar with age stratification and with age adjustment. Another limitation in our analysis is that the data does not include the brand of cigarette; consequently information on menthol status and filter use is unavailable. Finally, sample size is limited given the likely modest effect size of tobacco [7], but we did find important associations that were consistent with the literature. A particular strength of our analysis is that both our control and cases group had all been previously screened for prostate cancer. There is always the potential for misclassification in the control group having men with undiagnosed prostate cancer with PSA levels below age-adjusted cutoffs

and a normal rectal examination. This would tend to bias our results to the null hypothesis and lead to underestimation of the effect estimates. Lastly, we cannot reliably separate out the former smokers who quit more than 10 years, as this group seems to have lower PCa risk than those who quit more recently [7].

CONCLUSION

Consistent with the smoking literature, we confirm that there is higher prevalence of smoking and lower prevalence rates of heavy smoking in AAs relative to EAs. Despite these differences, we find no evidence for cigarette smoking increasing the odds of being diagnosed with prostate cancer in EA men, but are associated with prostate cancer diagnosis and higher-grade disease among AA prostate cancer patients. In AA men, we see heavy smokers having increased odds of prostate cancer and particularly high-grade (Table IVB). This trend is consistent with the majority of the literature in EAs. Cigarette smoking is associated with higher-grade prostate cancer among the men with PCa. Larger prospective studies are needed to detect smaller effect sizes for the association of smoking with prostate cancer incidence in EA men.

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TABLE I

Demographic and Clinical Characteristics of Prostate Cancer Cases and Controls

	Cases (N = 527)	Controls (N = 558)	
Continuous variables	**Mean (SD)**	**Mean (SD)**	***P*-value[a]**
Age, years	63.4 (9.3)	56.8 (10.6)	<0.001***
Body-mass index, (kg/m^2)	27.9 (8.6)	29.6 (10.6)	0.02*
Income, $ 000	43.7 (29.5)	48.8 (28.8)	0.02*
Prostate-specific antigen (ng/ml)	81.5 (615.2)	1.2 (1.1)	0.02*

Categorical variables	**%**	**%**	***P*-value[b]**
Cigarette-use			
Never Smoker	44.3	50.3	0.16*
Current Smoker	30.4	28.2	
Former Smoker	25.2	21.5	
Heavy smoking			
Greater than 20 cigarettes per day	14.8	21.1	0.04*
Alcohol-use			
Ever	77.6	74.7	0.29*
Alcohol Frequency			
Greater than 10 drinks per week	14.8	10.5	0.04*
Education			
High school diploma or equivalent	84.8	94.3	<0.001***
Marital status			
Married	29.7	22.2	0.01
Poverty			
Less than $20,000	37.2	26.9	0.003
Obesity			
Obese (BMI ≥ 30)	24.8	34.9	0.003**
Race			
African American	79.9	71.3	
European American	20.1	28.7	0.001**

Tumor characteristics	**%**
Gleason score	
4–6	54.3
7[c]	30.4
8–10	15.3
NCCN risk category	
Low-risk	39.2
Intermediate	30.3

Tumor characteristics	%
High-risk	30.6

[a] Unpaired, two-sample *t*-test.

[b] Chi-square analysis; BMI, body mass index; TNM, Tumor node metastasis staging.

[c] Includes both Gleason 3 + 4 and Gleason 4 + 3 tumors.

* $P < 0.05$.

** $P < 0.01$.

*** $P < 0.001$.

TABLE II

Smoking Characteristics Among African American and European American Men

	African American (N = 822)	European American (N = 262)	
Continuous variables	**Mean ± SD**	**Mean ± SD**	***P*-value[a]**
Cigarettes per day	7.0 ± 8.9	9.1 ± 12.0	0.01
Length of smoking, years	9.35 ± 15.1	10.2 ± 14.1	0.47
Pack-years	5.5 ± 12.3	12.9 ± 24.0	<0.001

Categorical variables	**%**	**%**	***P*-value[b]**
History of tobacco use			
Current	25.0	40.4	
Former	29.4	7.5	
Never	45.6	52.1	<0.001
Smoking intensity			
1–19 cigarettes per day	79.0	69.5	
20 or more cigarettes per day	21.0	30.5	0.003

[a] Unpaired, two-sample *t*-test.

[b] Chi-square analysis.

TABLE III

Smoking Characteristics Among Prostate Cancer Cases and Controls

	EA cases (N = 105)	EA controls (N = 157)	
Continuous variables	**Mean ± SD**	**Mean ± SD**	***P*-value[a]**
IIIA European Americans			
Cigarettes per day	8.5 ± 11.2	9.5 ± 12.5	0.29
Length of smoking, years	10.3 ± 14.2	10.1 ± 14.0	0.79

Categorical variables	**%**	**%**	***P*-value[b]**
Current and former tobacco-users (n = 262)			
Current	41.0	40.4	
Former	4.8	9.0	
Never	54.3	50.6	0.34[c]
Smoking intensity			
1–19 cigarettes per day	70.2	68.2	
20 or more cigarettes per day	29.8	31.8	0.78

	AA cases (N = 422)	AA controls (N = 400)	
Continuous variables	**Mean ± SD**	**Mean ± SD**	***P*-value[a]**
IIIB African Americans			
Cigarettes per day	8.0 ± 9.4	6.0 ± 8.3	0.002
Length of smoking, years	10.4 ± 16.2	8.5 ± 13.0	0.001

Categorical variables	**%**	**%**	***P*-value[b]**
Tobacco use (n = 692)			
Current	27.3	22.6	
Former	31.3	27.3	
Never	41.4	50.1	0.08[c]
Smoking intensity			
1 to 19 cigarettes per day	74.5	84.0	
20 or more cigarettes per day	25.5	16.0	0.003

[a] Unpaired, two-sample *t*-test.

[b] Chi-square analysis.

[c] *P* trend.

TABLE IVA

Association of Prostate Cancer (PCa) Diagnosis and Grade With Smoking in European Americans

European Americans	PCa cases[a] versus control unadjusted OR (95% CI)	PCa cases[a] versus control adjusted OR (95% CI)		Low-grade PCa (n = 56) versus controls[b] OR (95% CI)	High-grade PCa (n = 47) versus controls[b] OR (95% CI)
Smoking categories			Smoking categories		
Never smokers & <20 cigarettes/day	1.00 (reference)	1.00 (reference)	Never smokers & <20 cigarettes/day	1.00 (reference)	1.00 (reference)
≥20 cigarettes/day	0.91 (0.53, 1.57)	1.04 (0.65, 1.19)	≥20 cigarettes/day	0.69 (0.33, 1.46)	1.60 (0.78, 3.31)
PCa family history			Married		
Negative	1.00 (reference)	1.00 (reference)	No	1.00 (reference)	1.00 (reference)
Positive	2.22 (1.24, 3.97)[c]	2.02 (1.06, 3.82)[d]	Yes	0.61 (0.21, 1.78)[d]	0.33 (0.12, 0.90)[d]
Age	1.03 (1.00, 1.06)	1.03 (1.00, 1.06)	Type II diabetes		
Obesity			No	—	1.00 (reference)
BMI <30	1.00 (reference)	1.00 (reference)	Yes	—	8.11 (0.76, 86.57)
BMI ≥30	0.46 (0.24, 0.89)[d]	0.42 (0.21, 0.86)[d]	High school education		
High School Education			Yes	—	1.00 (reference)
Yes	1.00 (reference)	1.00 (reference)	No	—	16.01 (1.03, 249.36)[d]
No	4.60 (0.47, 44.88)	4.59 (0.45, 47.00)			

Table IV A the best unconditional logistic regression model adjusted for known prostate cancer risk factors is presented based on −2 log likelihood scores. Income, 5 alpha-reductase inhibitor use, and city of recruitment failed to reach statistical significance in the analyses and did not improve −2 log likelihood scores and were excluded.

BMI: Body Mass Index

CI: Confidence Interval

PCa: Prostate Cancer

[a] $P < 0.05$.

[b] $P < 0.01$.

[c] N = 157 for EA controls/N = 106 for EA cases.

[d] N = 157 for EA controls.

TABLE IVB

Association of Prostate Cancer (PCa) Diagnosis and Grade with Smoking in African Americans

African Americans	PCa cases[e] versus control unadjusted OR (95% CI)	PCa cases[a] versus control adjusted OR (95% CI)		Low-grade PCa (n = 141) versus controls[d] OR (95% CI)	High-grade PCa (n = 119) versus controls[f] OR (95% CI)
Smoking categories				Smoking categories	
Never smokers & <20 cigarettes/day	1.00 (reference)	1.00 (reference)	Never smokers	1.00 (reference)	1.00 (reference)
≥20 cigarettes/day	1.80 (1.22, 2.65)[c]	2.57 (1.09, 6.10)[d]	<20 cigarettes/day	1.36 (0.84, 2.21)	1.21 (0.69, 2.13)
			≥20 cigarettes/day	1.15 (0.63, 2.11)	1.89 (1.03, 3.48)[d]
PCa family history				Married	
Negative	1.00 (reference)	1.00 (reference)	No	1.00 (reference)	1.00 (reference)
Positive	1.21 (0.82, 1.79)	1.63 (0.83, 3.22)	Yes	0.84 (0.53, 1.33)[c]	0.77 (0.46, 1.29)
Age	1.08 (1.06, 1.10)[c]	1.08 (1.04, 1.12)[c]		Alcohol use	
Obesity			<2 drinks/day	1.00 (reference)	1.00 (reference)
BMI <30	1.00 (reference)	1.00 (reference)	≥2 drinks/day	2.24 (1.18, 4.25)[d]	1.40 (0.65, 3.00)
BMI ≥30	0.60 (0.41, 0.88)[c]	0.87 (0.46, 1.64)			
High school education					
Yes	1.00 (reference)	1.00 (reference)			
No	3.63 (1.94, 6.79)[c]	3.04 (1.35, 6.84)[c]			

Table IV B the best unconditional logistic regression model adjusted for known prostate cancer risk factors is presented based on −2 log likelihood scores. Income, 5 alpha-reductase inhibitor use, and city of recruitment failed to reach statistical significance in the analyses and did not improve −2 log likelihood scores and were excluded.

BMI: Body Mass Index

CI: Confidence Interval

PCa: Prostate Cancer

[a] $P < 0.05$.

[b] $P < 0.01$.

[c] N = 422 for AA controls/N = 400 for EA.

[d] N for AA controls = 400.