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Usual adult occupation and risk of PCa in West African men:

The Ghana Prostate Study

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B.S. in Psychology, University of Georgia 2016

An abstract of a thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of Master of Public Health in Epidemiology, 2018

ABTSRACT

Usual adult occupation and risk of Prostate Cancer in West African men:

The Ghana Prostate Study

By Colin Harrison Adler

Background: Established PCa (PCa) risk factors include age, family history of PCa in a first degree relative, and African ancestry. Some studies have also suggested that employment in certain occupations, including among farmers and men in military, may be associated with higher risk. These studies have been conducted mostly among highly screened, European ancestry-based populations. Here, we evaluated the association between usual adult occupation and PCa risk in a case-control study of Ghanaian men.

Methods: We analyzed data from a case-control study conducted from 2002-2007 in n=749 PCa cases n=964 controls from Ghana. Structured questionnaires were conducted to assess longest job held by participants. Industrial hygienists classified job titles into occupational categories using the 2010 Standard Occupational Classification (SOC) system. Unconditional logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between longest held occupation and PCa risk, adjusting for birth year, education, region, medical insurance, and smoking. ORs were calculated for PCa overall and for aggressive PCa, defined as Gleason score ≥7.

Results: PCa risk were higher among those in management occupations (SOC 11-0, overall PCa OR = 2.2, 95% CI: 1.4, 3.2 and aggressive PCa OR = 2.2, 95% CI: 1.3, 3.5) and military specific occupations (SOC 55-0, overall PCa OR = 3.4, 95% CI: 1.7, 7.0 aggressive PCa OR = 3.5, 95% CI: 1.5, 8.3). For both management and military occupations, risks were uniformly elevated for jobs based on 3-digit level SOC definitions including for: chief executives, advertising/marketing, operations managers and other management occupations, military officers/special and tactical operations leaders, and specialists and crew members. Sensitivity analyses taking into account possible access to medical care (possible cancer screening), did not show significant differences.

Conclusions: Our study provides some evidence for an increased risk of PCa among men whose longest held job was in management and military occupations. These findings are consistent with the published literature in European populations. However, more studies are needed to adequately address occupational risk factors, and the specific exposures that may be responsible for the observed increased risk for PCa.

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Chapter I: Literature Review

Descriptive Epidemiology

PCa (PCa) is the second most common cancer in American men in the United States with an estimated 164,690 new cases and 29,430 deaths (third-leading cause of cancer related deaths in men) from PCa for 2018 [1]. Data from the National Cancer Institute's Surveillance, Epidemiology, and End Results Program (SEER) show that, on average, 119.8 per 100,000 men will be diagnosed with PCa and 20.1 per 100,000 men will die of the disease each year. It is estimated that approximately 11.6% of men will be diagnosed with PCa at some point during their lifetime. PCa can affect all men, but certain subgroups are at enhanced risk. In 2016, PCa was the most commonly diagnosed cancer among African American men [1]. According to 2014 statistics from the Centers for Disease Control and Prevention, the incidence rate among African American men is 150 cases per 100,000, while whites have a rate of 90 cases per 100,000 men and Hispanics have a rate of 85 cases per 100,000 men [2]. The American Cancer Society reports that PCa is 74% higher in blacks than in whites for reasons that remain unclear [1].

In the late 1980s and early 1990s we observed large increases in PCa incidence, primarily due to widespread screening with prostate-specific antigen (PSA) blood test. Since 1992, at its peak of 237.5 new cases per 100,000 men and 39.2 deaths per 100,000 men, incidence and mortality rates have decreased substantially to 99.7 per 100,000 and 19.1 per 100,000, respectively and the death rate continues to decline about 3% each year [2]. Patients being informed about proper screening protocol (i.e. understanding one's initial risk assessment based on family history, age, and race), being educated about the

different risk factors of PCa, and lifestyle changes (i.e. higher physical activity, healthier dietary choices, etc.) are putative factors for reductions in PCa incidence [3].

The underlying etiology of PCa is unresolved, although there are ongoing efforts to estimate associations with various biologic, lifestyle, and environmental factors [4]. Established risk factors that increase the risk of PCa are age, first degree of family history of PCa, race, and occupation [3]. Of these, the only risk factor that is potentially modifiable is occupation. Thus, it is the focus of this study.

Age

About 1 in 9 men will be diagnosed with PCa during his lifetime [1]. The risk of PCa increases with age, especially after the age of 50. Only 1 in 403 men under the age of 50 will be diagnosed, and the rate increases up to 1 in 58 for ages 50 to 59, and 1 in 21 for ages 60 to 69. Approximately 60% of all PCa cases are diagnosed in men over the age of 65 years [6]. The American Cancer Society recommends men to make informed decision with their healthcare provider about PCa screening [7]. There are three different ages at which screening should be discussed for men. Men who are at average risk of PCa and are expected to live at least ten more years should be screened at age 50. Those who are at a high risk of PCa (i.e. African Americans and men who have a first-degree relative diagnosed with PCa prior to the age of 65) should be screened at age 45. Finally, those who are at higher risk (i.e. those with more than one first-degree relative who had PCa at an early age) should be screened at age 40. PCa often grows slowly so men without symptoms of PCa who do not have a 10-year life expectancy should not be offered testing since they will not benefit from it [7].

Race

Incidence rates are high in Northern and Western Europe, Northern America, Oceania, and some Caribbean island nations, but the most affected group are men of African descent in Northern America and the Caribbean [6]. In 2016, there were over 189,000 cases of PCa in black men, which accounts for 31% of all cancers for black men [8]. It is estimated that 1 in 6 black men will be diagnosed with PCa in his lifetime compared to 1 in 8 white men. The average annual PCa incidence rate was 208.7 cases per 100,000 black men during 2008-2012 (70% higher than the rate in white men) [8].

First Degree Family History

Recent genetic studies have found that strong familial predisposition may be responsible for a sizable quantity of PCa cases [6]. Men with first degree relative with PCa are more than 2.5 times as likely to develop it than a man with no affected family members. Since the 1990s, there have been more frequent screenings of PCA in its earlier stages, and those that have PCa family history, higher educational level, and older age have been associated with frequency of undergoing PSA screening and could bias many study results [9]. Inherited gene mutations also seem to have a role as they cause about 5-10% of PCa cases [6]. For example, BRCA1 and BRCA2 are tumor suppressor genes that repair DNA. While inherited mutations for these two genes are associated with ovarian and breast cancers, there is emerging evidence that they may account for a small proportion of PCa cases [10]. Lynch syndrome (hereditary nonpolyposis colorectal cancer) is another inherited condition that is associated with a 30% increase for lifetime risk of PCa [6]. The American Cancer Society has reports that men with a father or

brother with PCa are 2 to 3 times more likely diagnosed than men without a family history [9].

Occupational Risk

There are certain occupations have been linked to an elevated risk of PCa such as agricultural/farming jobs, military specific/law enforcement, and managerial occupations. Agricultural/farming workers may have a history of reduction in certain cancers (i.e. lung and bronchus), but have elevated risks of PCa because of the exposure to carcinogens (pesticides, dust, and environments with acute toxic gas levels) and whole-body vibration from machine usage [8,9]. The links between military/law enforcement jobs and PCa risk are multifactorial. For example, the United States explained that the military laces their soldiers' suits with protective chemicals against malaria and other vectors when they're deployed [12]. Additionally, military personnel are exposed to large quantities of lead due to their weaponry and ammunition. White collar jobs like management occupations typically entail fewer chemical exposure; however, multiple epidemiological studies have suggested that lower workplace physical activity could be linked to PCa [10-11, 13]. It has also been suggested that men with higher SES are more likely to be screened, thus associations with white collar jobs may be an artifact of enhanced screening in this population.

Farming and Agricultural Occupations and PCa Risk

There have been previous studies that have investigated occupation and industry and the risk of PCa. Farming and agricultural related occupations have been associated with elevated risk for PCa due to different exposures like farming agents [13] (i.e. organochlorines, methyl bromide, and organophosphates), fertilizers, mechanization of farming [11], and organic dust from harvesting that have been well-documented since the 1980s [16, 17]. Multiple meta-analyses that have evaluated farming and agricultural occupations and PCa risk, and have come to the conclusion that farmers tend to have "higher risk for cancers of the lip, melanoma, brain, prostate…" [16]. The most updated meta-analysis evaluated twelve different studies exploring farming and PCa risk found that PCa cases were almost four times more likely to be farmers in comparison to controls with benign prostate hyperplasia [18].

Military Occupations

Military personnel are another grouping of occupations where increased PCa risk is found throughout multiple studies [15, 19, 20]. These are professionals that may exposed to metals, asbestos, fuels, chemical/warfare agents [12], radiation, whole body vibration, and stress and shiftwork [22]. Military personnel tend to be healthier than those of the general population and have constant access to health resources and medical care. Multiple studies on militaries from Canada [23], United States [24], and Australia [25] all found that military men had higher risks for PCa when compared to rates in the general population.

White-Collar Occupations

Men employed in occupations such as administrators, technical workers, management, financiers, lawyers, and politicians have been associated with elevated risk for PCa [15, 19, 20]. Previous studies have reported that men in these occupations usually reflect certain behaviors such as lower workplace physical activity levels and higher socioeconomic status (SES). Men who have higher education and higher income tend to have better access to health resources making them more likely to seek PSA screening and diagnostic history [15, 19-21]. High SES is associated with increased incidence of low- to moderate-risk cancers, which suggests over diagnosis, but also can also explain that people who participate in organized screening are usually healthier and more health-conscious [21]. Different SES levels can propose different thresholds for seeking medical care [21].

Most studies of occupation and PCa risk were conducted in Western or European populations. Although black men in the United States have particularly high risk for PCa, there has been limited data of risk factor profiles among men in Africa. For instance, Ghana's incidence rate is greater than 200 per 100,000 men, and more than 70% of Ghanaians presenting with PCa do so very late with locally invasive and metastatic disease (about 800 men die yearly of PCa out of the 1000 diagnosed) [26]. Though there are established risk factors of age, race, and family history for PCa, there has been a large interest in investigating associations between PCa and occupation title. The present study is the first, to our knowledge, to estimate the association between occupation and PCa among West African men. These data can help us better understand etiology and uncover

intervention that may be useful in this vulnerable population. We are reporting the results of the National Cancer Institute's "Ghana Prostate Study", a case-control, to further estimate the association between occupation and PCa among men in Ghana. We also are evaluating differences due PCa type (overall vs. aggressive) and if there are different differences among certain cancer risk factors (i.e. smoking and medical insurance).

Chapter II: Manuscript

INTRODUCTION

PCa (PCa) is the second most common cancer among men worldwide and the fifth-leading cause of cancer related death in men in 2012 [1]. The incidence rate of PCa varies more than 25-fold worldwide with higher incidence rates in Europe and North American countries where access to prostate-specific antigen (PSA) screening results in greater detection of disease [1]. Risk factors for PCa are still largely unknown, however higher risks have been demonstrated among men of African descent in both epidemiologic and genetic studies. Incidence rates of PCa in certain countries like Ghana are greater than 0.2% with more than 70% of Ghanaians presenting with locally invasive and metastatic disease. Thus, studies of risk factors for PCa among men at high-risk would be informative [1].

Several epidemiologic studies have assessed potential occupational risk factors for PCa and found that workers in certain occupational groups (i.e. military/law enforcement, agriculture, and managerial administration) have a higher risk for PCa compared to men employed in other occupations [11,13-20, 23-25, 27-28]. Most of these studies have largely been conducted in Europe and North America, where PSA screening drives diagnosis of clinically insignificant PCa, making it difficult to attribute observed associations with increased risk. Some studies [13-17] have attempted to focus on more aggressive disease, either those with a high Gleason score or cancers occurring in young men (early-onset), as a way to disentangle possible detection biases cause by PSA, since these cancers are less likely to be detected by screening. For instance, those employed in white-collar occupations (i.e. in higher SES) are usually more eager to participate in screening programs than those in lower SES populations, which has shown that men in

higher SES to have lower grade PCa cases and men in lower SES to have higher PCa cases [21]. Those employed in military occupations tend to satisfy a healthy-worker effect as they have easily-accessible medical resources and possibly screening [23-25].

In light of this, we investigated the association between occupation and PCa in a case-control study of 676 PCa cases and 964 controls in Ghana, a population with high genetic predisposition for PCa and low rates of screen-detected PCa.

METHODS

Study population

The NCI launched a study as to why those of African heritage have higher PCa risk than their other racial/ethnic counterparts. They examined potential etiologies (diet and physical activity, family history, socioeconomic status, occupations, etc.) to PCa and surveyed men in Ghana to examine if they had similar PCa risk to their American equivalents. Thus, the Ghana Prostate Study (2002-2007) was created to assess the burden, risk factor profiles, and biomarkers of PCa in Ghanaian men because West Africa is the principal ancestral origin of an ample proportion of African American men. Participants were recruited through the Ghana Prostate Study which incorporated both a population-based component and clinical component. Controls were derived from the population-based component used the 2000 Ghana Population and Housing Census data to recruit 1,000 men aged 50-74 years in the Greater Accra region. This component successfully consented and enrolled 1,037 healthy men between 2004 and 2006, and had a 98.8% response percentage. These individuals provided a blood sample for prostate specific antigen (PSA) testing, a digital rectal examination (DRE), an in-person

interview, biomarker analyses, and genetic analyses. Participants who had a positive screen by PSA (> 2.5 ng/ml) or DRE underwent a transrectal ultrasound-guided biopsy. From this, 73 histologically-confirmed PCa cases were identified and are included in the case population, which reduced the number of controls to 964.

In the clinical component, we consented and enrolled 676 PCa cases at Korle Bu Teaching Hospital in Accra, Ghana between 2008 and 2012. All cases were under went in-person interviews and provided an overnight fasting blood sample. Combined with the 73 histologically-confirmed cases from the population-based control component, we were able to analyze 749 cases.

The Ghana Prostate Study was approved by institutional review boards in Ghana and at the National Cancer Institute.

Occupation

For both components, occupational information was collected from a structured questionnaire administered by trained interviewers. Subjects reported occupational information on usual occupation ("what is the title of your longest held job") and typical work tasks ("what kind of work did you mainly do"). Each subject's free-text responses were reviewed and coded to three-digit level groups within the 2010 Standard Occupational Classification (SOC) system (http://www.bls.gov/soc) by a trained industrial hygienist.

Statistical Analyses

Unconditional logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (95% CI) for the associations between selected occupations and PCa

risk (overall PCa and aggressive PCa) [29]. Aggressive cancer was defined as a Gleason score greater than or equal to 7. Longest held job in each SOC group was compared to no regular employment (i.e. never employed or not longest held job) in that job. ORs were adjusted for birth year, education (secondary schooling, beyond secondary schooling, unknown); smoking status (ever, never, unknown); and, medical insurance coverage (yes, no, unknown); all impacted the parameter estimates by more than 10%. To explore possible differences in access to care and possible PSA screening, we also conducted stratified analyses by self-reported medical insurance coverage for selected occupations and PCa risk (overall and aggressive). Likelihood ratio tests were used to assess differences between strata (P-interaction). All tests were two-sided and conducted at the α=0.05 level. Analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

Selected characteristics for controls and cases (overall and aggressive) are shown in Table 1. Most cases (74.9%) and controls (67.8%) were born between 1931-1949. Forty percent of controls were from the Greater Accra region, whereas the majority of cases (overall: 76.4%, aggressive: 78.8%) were from regions outside of greater Accra. More than half (63.1%) of the controls had less than secondary schooling, whereas less than half of cases (overall: 42.5%, aggressive: 46.3%) had less than secondary schooling. Almost half of all controls (45.9%), and around a third of all cases (overall: 33.6%, aggressive: 32.1%) identified as being ever smokers. Less than 5% of controls reported having medical insurance coverage (4.1%), whereas more than half of all cases had medical insurance (67.3%).

Table 2 shows the associations between the longest held occupation and PCa risk for overall PCa and aggressive PCa. Men in management occupations (SOC 11-0) had increased odds of having PCa compared with men who were not regularly employed in management occupations (OR = 2.2, 95% CI: 1.5, 3.3) including: chief executives (SOC 11-1; OR = 3.3, 95% CI: 1.2, 9.1), advertising, marketing, promotions, public relations, and sales managers (SOC 11-2; OR = 3.5, 95% CI: 1.1, 10.9), operations specialties managers (SOC 11-3; OR = 2.0, 95% CI: 1.2, 3.5). Results for all management occupations and risk of aggressive PCa risk were similar to the overall associations (SOC-11-0; aggressive PCa OR = 2.2, 95% CI: 1.3-3.5). Men in military occupations (SOC 55-0) also had higher odds of PCa, both for overall and for aggressive PCa, compared with men who were not regularly employed in military specific occupations (overall: OR = 3.4, 95% CI: 1.7, 7.0; aggressive: OR = 3.5, 95% CI: 1.5, 8.3). The majority of these men were employed as special military officers and tactical operations leaders (SOC 55-1), overall and aggressive PCa were OR = 4.4, 95% CI: 1.9, 10.2 and OR = 4.6, 95% CI: 1.6, 13.0, respectively.

We also observed several inverse and null associations between occupations held and PCa risk (Table 2). For the most frequently reported occupations among controls, the odds of PCa were 50% lower for men employed in construction trades workers compared to men not regularly employed in this occupation (SOC 47-2, OR = 0.5, 95% CI: 0.3, 0.9). Men employed in protective service occupations compared to men not regularly employed in this occupation (SOC 33-0, OR=0.5, 95% CI: 0.2, 0.9). Farming occupations (45-0) were also not associated with PCa risk overall (OR = 0.9, 95% CI: 0.5, 1.6, Table 2).

Table 3 shows results between selected occupations and risk of PCa (overall and aggressive) stratified by reported medical insurance coverage. ORs for management occupations (SOC 11-0) by strata of medical insurance were similar to those observed before stratification and were not significantly different (p-interaction=0.87 overall and p-interaction=0.90). The association between employment in military specific occupations was slightly stronger among those without medical insurance coverage (for PCa overall, OR = 4.0, 95% CI: 1.8, 8.7) while the effect estimate among those with medical insurance was 2.4 (95% CI: 0.3, 19.0). However, these were based on small numbers and the p-value for interaction was not statistically significant. Similarly, there was no other statistically significant difference by medical insurance for other occupations examined (all p-interaction>0.05).

We did explore stratified analyses by age to explore the possible differences among older and younger men. Results were similar to those shown here (data not shown) and continue to show a consistent positive association among men regularly employed in management and military occupations.

DISCUSSION

In this analysis, we evaluated occupation as a risk factor for PCa among Ghanaian men. We found higher risks for both overall and aggressive PCa among men regularly employed in management occupations as well as among men with military specific occupations. We also found an inverse association for overall PCa among men regularly employed in protective service occupations.

We found higher risks for PCa among those men who reported military occupations as their longest held job. This finding is supported by other case-control

studies conducted in Canada [15, 19-20, 23], United States [24, Australia [25] and Norway [19, 27], that found that members of the armed forces had significantly higher risks for PCa. Reasons for this may be due to exposure to agents occurring during military deployment including metals, pesticides, fuels, chemical/warfare agents, radiation, or shift-work, some of which have been linked to PCa risk independently [12]. Alternatively, it has been suggested that these increased risks may be driven by greater detection of PCa as a result of more frequently health examination which are required for military personnel, particularly in Europe and North America in the PSA-era [15]. Here, we attempted to look at more aggressive disease, which is less likely to be detected by screening as well as self-reported medical insurance coverage to evaluate if detection of PCa was driving the results in certain occupational groups. For military occupations, associations persist among men with aggressive disease and among those without medical insurance. These data suggest that enhanced PCa detection may not drive the observed results. More work is needed to explore the specific exposures experienced by military personnel and possible risk factors for PCa.

We also observed a higher risk of PCa among those in management occupations. Typical employment in managerial occupations is associated with exposure to fewer chemicals, but also lower workplace physical activity levels. A report from the NIH-AARP Diet and Health Study reviewed the association between vigorous-intensity physical activity, and discovered that when separated by race (white and black men), those that are engaged in four or more hours of moderate/vigorous intensity physical activity compared to infrequent activity during early adulthood provided a 35% lower risk of PCa [30]. However, this is different than sedentary behavior, and should not be

confused. When reviewing a different report from the NIH-AARP Diet and Health Study, it was suggestive of effect modification by body mass index (BMI) categories for television/video viewing time and total PCa risk, and for both daily sitting and television/video viewing time and advanced PCa risk/mortality [31]. Obesity and sedentary behavior have been independently associated with mediating factors (i.e. metabolic dysfunction/metabolic syndrome) in PCa development and progression. However, associations between sedentary behavior and PCa are complex and need further research to elucidate these paths [31].

Alternatively, higher PCa screening practices among this group, or other factors linked to white-collar employment (i.e. socioeconomic status) may explain some of the observed risk [15, 19-21, 28]. Still, our sensitivity analyses suggest that access to medical care does not alter the relationship between regular employment in managerial occupations and risk of PCa, both overall and for aggressive disease.

Interestingly, we did not observe any association between farming occupations and risk of PCa. Although there are several reports in the literature about farming or pesticide exposure and risk of PCa [11,13, 15-20], findings have been quite mixed. We also found a lower risk of PCa among men in protective service occupations; however, this result is inconsistent with those in previous reported studies [14, 19, 22-24, 27]. Pukkala et al., found an excess odds of PCa among those in protective service occupations, such as firefighters and police. Though this study included about 7.4 million people from Nordic countries and similar in our categorization of occupations, the population was predominantly white. Sauve et al., also found that men in protective service occupations were at increased PCA risk; however, the study population (1937

cases) was predominantly of European decent (1696 or 87.6%) and have high PCa screening rates with both cases (99%) and controls (75%) [15, 27].

Strengths of our study include availability of detailed clinical information for defining PCa aggressiveness and expert review of longest held job. In addition, this is the first study conducted among African men, who have a higher genetic susceptibility for PCa and live in a region with low PSA screening (reducing the likelihood of over-diagnosis). However, there were also limitations. Study participants reported only their usual adult occupation, rather than a full lifetime occupational history, and information about the duration of employment for longest held job was unavailable. In addition, numbers of cases and controls were low in some groups, limiting our power to detect effects among certain occupations. Finally, the recruitment strategy for this study resulted in a different age distribution among cases and controls, which may be related to occupation (and types of jobs held over a lifetime).

Our results suggest that Ghanaian men employed in management or military specific occupations may be at higher risk for PCa, and those that are employed in protective service occupations may be at a lower risk for PCa. These findings are consistent with results reported from other studies, conducted in populations of European decent with higher-PSA screening rates. This study provides insight into occupational risk factors for PCa in a region of the world that is rarely studied and suggests a need to identify possible exposures driving these risks.

Tables

Table 1. Selected characteristics among controls and cases (overall and aggressive) from the Ghana prostate study.

Characteristic	Control (n=964) N (%)	Overall PCa cases (n=749) N (%)	Aggressive PCa cases (n=486) N (%)	p-value
Birth year				
1913-1930	15 (1.6)	110 (14.7)	73 (15.0)	
1931-1940	305 (31.7)	342 (45.7)	230 (47.3)	
1941-1949	348 (36.1)	219 (29.2)	136 (28.0)	
1950-1966	296 (30.7)	78 (10.4)	47 (9.7)	<.0001
Ethnicity				
Asante	84 (8.7)	103 (13.8)	62 (12.8)	
Akwapim	52 (5.4)	59 (7.9)	38 (7.8)	
Fante	104 (10.8)	104 (13.9)	70 (14.4)	
Other Akan	73 (7.6)	105 (14.0)	70 (14.4)	
Ga-Adangbe	369 (38.3)	190 (25.4)	118 (24.3)	
Ewe	169 (17.5)	120 (16)	80 (16.5)	
Guan/Mole-Dagbani/Grussi/Gruma/Hausa	60 (6.2)	31 (4.1)	20 (4.1)	
Other	52 (5.4)	35(4.7)	27 (5.6)	
Unknown	1 (0.1)	2 (0.2)	1 (0.2)	<.0001
Region				
Western/Central	117 (12.1)	127 (17.0)	86 (17.7)	
Greater Accra	386 (40.0)	177 (23.6)	103 (21.2)	
Volta	129 (13.4)	105 (14.0)	75 (15.4)	
Eastern	175 (18.2)	173 (23.1)	120 (24.7)	
Ashanti/Brong-Ahafo	85 (8.8)	106 (14.2)	59 (12.1)	
Northern/Upper West/Upper East	39 (4.1)	35 (4.7)	23 (4.7)	
Unknown	33 (3.4)	26 (3.4)	20 (4.1)	<.0001
Education				
Up to Secondary School	608 (63.1)	318 (42.5)	225 (46.3)	

Secondary School or more	343 (35.6)	426 (56.9)	259 (53.3)	
Unknown	13 (1.3)	5 (0.6)	2 (0.4)	<.0001
Smoking Status				
Ever	442 (45.9)	252 (33.6)	156 (32.1)	
Never	521 (54.0)	494 (66.0)	329 (67.7)	
Unknown	1 (0.1)	3 (0.4)	1 (0.2)	<.0001
Medical insurance				
Yes	39 (4.1)	504 (67.3)	363 (74.7)	
No	905 (93.9)	236 (31.5)	117 (24.1)	
Unknown	20 (2.07)	9 (1.2)	6 (1.2)	<.0001

*p-value is chi-square test for difference between all cases and controls

Table 2. Association between selected occupations and prostate cancer for controls and cases (overall and aggressive).

SOC Code	Controls N (%)	All PCa cases N (%)	Aggressive PCa cases N (%)	All PCa OR* (95% CI)	Aggressive PCa¶ OR* (95% CI)
11-0 Management Occupations	77 (7.9)	182 (24.2)	111 (22.8)	2.2 (1.5, 3.3)	2.2 (1.3, 3.5)
11-1 Chief Executives	8 (0.5)	28 (3.7)	13 (2.7)	3.3 (1.2, 9.1)	2.3 (0.6, 8.3)
11-2 Advertising, Marketing, Promotions, Public Relations, and Sales Managers	5 (0.5)	23 (1.3)	12 (2.5)	3.5 (1.1, 10.9)	3.7 (1.0, 13.5)
11-3 Operations Specialties Managers	39 (4.0)	88 (11.7)	59 (12.1)	2.0 (1.2, 3.5)	1.8 (0.9, 3.5)
11-9 Other Management Occupations	25 (2.6)	43 (5.6)	27 (5.6)	1.8 (0.9, 3.7)	2.4 (1.0, 5.4)
13-0 Business and Financial Operations Occupations	74 (7.8)	62 (8.3)	36 (7.4)	0.7 (0.4, 1.2)	0.4 (0.2, 0.9)
13-1 Business Operations	43 (4.5)	34 (4.5)	21 (4.3)	0.7 (0.3,1.6)	0.6 (0.2, 1.6)
13-2 Financial Specialists	31 (3.2)	28 (3.7)	15 (3.1)	0.7 (0.3, 1.5)	0.3 (0.1, 1.0)
17-0 Architecture and Engineering Occupations	20 (2.1)	24 (3.2)	18 (3.7)	1.9 (0.9,4.1)	2.2 (0.9, 5.7)
17-1 Architects, Surveyors, and Cartographers	4 (0.4)	11 (1.5)	10 (2.1)	5.9 (1.3, 26.1)	9.9 (1.9, 51.9)
17-2 Engineers	5 (0.5)	8 (1.1)	6 (1.2)	1.2 (0.3, 5.4)	1.3 (0.2, 7.6)
17-3 Drafters, Engineering Technicians, and Mapping Technicians	11 (1.1)	5 (0.7)	2 (0.4)	1.1 (0.3, 4.0)	0.4 (0.04, 4.8)
25-0 Education, Training, and Library Occupations	36 (3.7)	50 (6.7)	26 5.4)	1.1 (0.6, 2.0)	1.1 (0.5, 2.4)
25-1 Postsecondary Teachers	30 (3.1)	44 (5.9)	23 (4.7)	1.2 (0.6, 2.3)	1.2 (0.5, 2.7)
27-0 Arts, Design, Entertainment, Sports, and Media Occupations	23 (2.4)	13 (1.7)	9 (1.9)	0.4 (0.2, 1.3)	0.5 (0.1, 1.8)

27-1 Arts, Design, Entertainment, Sports, and Media Occupations	17 (1.8)	7 (0.9)	5 (1.0)	0.4 (0.1, 1.6)	0.5 (0.1, 12.2)
29-0 Healthcare Practitioners and Technical Occupations	4 (0.5)	14 (1.7)	8 (1.7)	7.1 (1.9, 25.8)	10.6 (2.4, 46.6)
33-0 Protective Service Occupations	72 (7.5)	23 (3.1)	20 (4.1)	0.5 (0.2, 0.9)	0.8 (0.4, 1.8)
33-1 Supervisors of Protective Service Workers	18 (1.9)	6 (0.8)	6 (1.2)	0.6 (0.2, 2.0)	1.1 (0.3, 4.2)
33-3 Law Enforcement Workers	8 (0.8)	10 (1.3)	9 (1.9)	1.3 (0.4, 4.4)	2.3 (0.6, 8.7)
33-9 Other Protective Service Workers	46 (4.8)	7 (0.9)	5 (1.0)	0.2 (0.1, 0.6)	0.3 (0.1, 1.2)
41-0 Sales and Related Occupations	55 (5.7)	22 (2.9)	19 (3.9)	0.5 (0.2, 1.0)	0.8 (0.3, 1.7)
41-1 Supervisors of Sales Workers	23 (2.4)	14 (1.9)	13 (2.7)	0.5 (0.2, 1.5)	1.0 (0.3, 2.9)
41-2 Retail Sales Worker	19 (2.0)	6 (0.8)	5 (1.0)	0.5 (0.2, 1.7)	0.9 (0.2, 3.3)
43-0 Office and Administrative Support Occupations	50 (5.1)	37 (4.9)	22 (4.5)	0.9 (0.5, 1.7)	0.9 (0.4, 1.9)
43-1 Supervisors of Office and Administrative Support Workers	5 (0.5)	9 (1.2)	5 (1.0)	1.1 (0.3, 4.1)	0.8 (0.2, 4.5)
43-3 Financial Clerks	4 (0.4)	10 (1.3)	5 (1.0)	2.8 (0.6, 11.8)	4.6 (0.9, 22.8)
43-6 Secretaries and Administrative Assistants	9 (0.9)	10 (1.3)	7 (1.4)	0.5 (0.1, 1.7)	0.4 (0.1, 2.0)
43-9 Other Office and Administrative Support Workers	19 (2.0)	6 (0.8)	5 (1.0)	0.7 (0.2, 2.5)	0.9 (0.2, 3.9)
45-0 Farming, Fishing, and Forestry Occupations	78 (8.1)	51 (6.8)	33 (6.8)	0.9 (0.5, 1.6)	0.7 (0.3, 1.6)
45-2 Agricultural Workers	60 (6.2)	51 (6.8)	33 (6.8)	1.0 (0.6, 2.0)	0.8 (0.3, 1.9)
45-3 Fishing and Hunting Workers	18 (1.9)	0 (0.0)	0 (0.0)		
47-0 Construction and Extraction Occupations	110 (11.4)	36 (11.3)	24 (4.9)	0.6 (0.3, 1.0)	0.4 (0.2, 0.9)

47-2 Construction Trades Workers	98 (10.1)	28 (3.9)	19 (3.9)	0.5 (0.3, 0.9)	0.4 (0.2, 0.9)
49-0 Installation, Maintenance, and Repair Occupations	75 (7.8)	31 (4.1)	18 (3.7)	0.5 (0.3, 1.0)	0.4 (0.2, 0.9)
49-1 Supervisors of Installation, Maintenance, and Repair Workers	11 (1.1)	9 (1.2)	6 (1.2)	0.7 (0.2, 2.6)	0.9 (0.2, 4.0)
49-2 Electrical and Electronic Equipment Mechanics, Installers, and Repairers	28 (2.9)	9 (1.2)	5 (1.0)	0.5 (0.2, 1.4)	0.4 (0.1, 1.5)
51-0 Production Occupations	81 (8.4)	27 (3.6)	21 (4.3)	0.6 (0.3, 1.2)	0.8 (0.4, 1.8)
51-6 Textile, Apparel, and Furnishings Workers	34 (3.5)	8 (1.1)	6 (1.2)	0.6 (0.2, 1.7)	0.6 (0.1, 2.9)
53-0 Transportation and Material Moving Occupations	113 (11.8)	58 (7.7)	41 (8.4)	1.2 (0.7, 1.9)	1.3 (0.7, 2.4)
53-3 Motor Vehicle Operators	93 (9.7)	43 (5.7)	30 (6.2)	1.0 (0.6, 1.8)	1.0 (0.5, 2.0)
53-5 Water Transportation Workers	9 (0.9)	6 (0.8)	5 (1.0)	1.3 (0.3, 4.6)	2.6 (0.7, 9.8)
55-0 Military Specific Occupations	17 (1.8)	51 (6.8)	37 (2.6)	3.4 (1.7, 7.0)	3.5 (1.5, 8.3)
55-1 Military Officer Special and Tactical Operations Leaders	11 (1.1)	42 (5.6)	29 (6.0)	4.4 (1.9, 10.2)	4.6 (1.6, 13.0)
55-3 Specialists and Crew Members	5(0.5)	9 (1.2)	8 (1.7)	2.4 (0.6, 10.3)	2.6 (0.5, 13.5)

* Odds ratios (OR) adjusted for birth year, education, region, medical insurance, smoking

¶ Aggressive prostate cancer is defined from the Medical Record Abstracts and Histopathology reports as a case that has a Gleason score of 7 or more

**Occupational group represents longest held job

Table 3. Association between selected occupations and PCa aggressiveness stratified by reported medical insurance coverage.

SOC Code	Medical Insurance		No Medical Insurance		p-interaction
	Case (n)	OR* (95% CI)	Case (n)	OR* (95% CI)	
11-0 Management Occupations					
All PCa	123	2.3 (0.7, 8.2)	56	2.3 (1.5, 3.5)	0.87
Aggressive PCa	80	2.3 (0.6, 8.4)	29	2.2 (1.2, 3.8)	0.9
13-0 Business and Financial Operations Occupations					
All PCa	45	0.3 (0.1, 0.9)	16	0.9 (0.5, 1.6)	0.09
Aggressive PCa	30	0.3 (0.1, 0.8)	6	0.7 (0.3, 1.7)	0.16
33-0 Protective Service Occupations					
All PCa	16	1.1 (0.1, 8.7)	7	0.4 (0.2, 0.8)	0.36
Aggressive PCa	14	1.3 (0.2, 10.7)	6	0.7 (0.3, 1.8)	0.63
43-0 Office and Administrative Support Occupations					
All PCa	21	0.7 (0.1, 3.3)	16	1.0 (0.5, 1.9)	0.78
Aggressive PCa	14	0.6 (0.1, 3.4)	8	0.9 (0.4, 2.2)	0.82
53-0 Transportation and Material Moving Occupations					
All PCa	34	1.1 (0.3, 4.2)	24	1.3 (0.8, 2.1)	0.87
Aggressive PCa	28	1.4 (0.4, 5.3)	13	1.4 (0.7, 2.7)	0.96
55-0 Military Specific Occupations					
All PCa	35	2.4 (0.3, 19.0)	16	4.0 (1.8, 8.7)	0.62
Aggressive PCa	28	2.7 (0.3, 21.9)	9	4.4 (1.7, 11.3)	0.67

* Odds ratios adjusted for birth year, education, region, smoking
**Aggressive PCa is defined from the Medical Record Abstracts and Histopathology reports as a case that has a Gleason score of 7 or more

Chapter III: Conclusion

After evaluating occupation as a risk factor for PCa (PCa) among Ghanaian men, we found higher risks for both overall and aggressive PCa among those regularly employed in management and military specific occupations. Due to the limited knowledge and ambiguity surrounding PCa etiology, the association between occupational status (the only known modifiable risk factor) and PCa incidence is a high-priority topic. Studies in Scandinavia, Canada, and some parts of the United States have asserted that some occupations have increased risk of PCa incidence; however, unknown was whether these findings were generalizable to other regions of the world. It is important to understand whether this risk factor is modified by race and/or ethnicity, or prevalence of other risk factors associated with PCa (i.e. diet, physical activity, family history, etc.) There are broad implications to improving our knowledge around occupation and PCa risk including changes to workplace, lifestyle, or regulatory recommendations (i.e. decreasing occupational sedentary time, enhanced screening, reevaluating what occupational exposures employees are at risk for during their jobs, etc.).

The research that we conducted is novel for Ghana as there has not been prior research investigating links between occupational status and PCa. However, there were some limitations in this study. There was differential selection of cases and controls, including our case expansion from our original case recruitment. Our study initially had 676 cases recruited from the hospital and 1,037 controls selected from the census, but upon further PSA and DRE screenings, there were 73 PCA diagnoses in the control group that were then placed into the case count. This easily can result in misclassification bias.

There was a lack of lifetime history information on occupations for each participant. We were not able to be as specific with our Standard Occupational Classification (SOC) coding and could only code to the third digit out of six digits, so our level of refinement was limited. Our numbers of cases and controls were low in some subgroups, limiting our ability to evaluate certain occupations with precision. There could be possible biases that arise due to residual confounding by age, socioeconomic status, access to care, and detection bias due to frequent health examinations. All these factors should be taken into consideration upon interpreting our results.

There are several considerations to enhance and extend this research. The first step should be expansion by including more regions and countries in these types of studies to garner knowledge about occupational behavior and assess generalizability. The establishment of registry programs that document occupation status in countries that do not already have such programs would help facilitate such studies. Additionally, creation of a global SOC would reduce confusion around definitions between different types of occupations and limit potential for misclassification. Additional documentation of occupation-specific exposures is necessary. Researchers may then begin to examine these associations by grouping subjects by exposure type along with job title.

The etiology for PCa is still ambiguous, but with past research dissecting how occupation could be a strong modifiable risk factor, there is hope that this could help reduce the burden of PCa among Ghana men. Ghana created the National Health Insurance Scheme (NHIS) in 2004 to fund basic healthcare services [26]. However, NHIS membership has been reported to be as low as 18% with the majority of citizens continuing to pay out of pocket for their health care. Governmental officials and

healthcare policy makers are trying to rejuvenate the Community-based Health Planning and Services (CHPS) division as they have identified severe secondary and tertiary gaps within district hospitals [26]. With a country that has low secondary and tertiary care resources, primary prevention is at the vanguard of PCa control. This means that describing the etiologic links between occupation and PCa incidence is crucial, and can be achieved by extrapolating which occupations have higher risk for PCa, uncovering relevant exposure measures, and developing occupation-specific guidelines (i.e. more screenings for occupations with environmental hazards, or activity interventions among those with high sedentary time). These combined efforts can help inform strategies for policymakers who seek to reduce the PCa burden locally and abroad.

References

1. "Key Statistics for PCa." Www.cancer.org. 2018. Accessed March 6, 2018. https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html.

2. "2014 Cancer Types Grouped by Race and Ethnicity." Centers for Disease Control and Prevention. 2017. Accessed March 14, 2018. https://nccd.cdc.gov/uscs/cancersbyraceandethnicity.aspx

3. "Cancer Stat Facts: PCa." Seer.cancer.gov. 2017. Accessed March 6, 2018. https://seer.cancer.gov/statfacts/html/prost.html

4. Schulz, W. A., et al. (2003). "Molecular biology of PCa." MHR: Basic science of reproductive medicine **9**(8): 437-448.

5. Seo, W. I., et al. (2017). "Correlation between postoperative prostate-specific antigen and biochemical recurrence in positive surgical margin patients: Single surgeon series." Prostate Int **5**(2): 53-58.

6. American Cancer Society. Global Cancer Facts & Figures 3rd Edition. Atlanta: American Cancer Society; 2015.

7. American Cancer Society. "American Cancer Society Recommendations for PCa Early Detection." Cancer.org. April 1, 2016. Accessed March 19, 2018. https://www.cancer.org/cancer/prostate-cancer/early-detection/acs-recommendations.html.

8. "PCa Risk Factors. PCF.org. 2018. Accessed March 15, 2018.

9. American Cancer Society. Cancer Facts & Figures for African Americans 2016-2018. Atlanta: American Cancer Society, 2016.

10. Chen, Y.-C., et al. (2008). "Family history of prostate and breast cancer and the risk of PCa in the PSA era." The Prostate **68**(14): 1582-1591.

11. Cerhan, J. R., et al. (1998). "Cancer mortality among Iowa farmers: recent results, time trends, and lifestyle factors (United States)." Cancer Causes Control **9**(3): 311-319.

12. "Military Exposures." Publichealth.va.gov/exposures. 2016. Accessed March 15, 2018

13. Kachuri, L., et al. (2017). "Cancer risks in a population-based study of 70,570 agricultural workers: results from the Canadian census health and Environment cohort (CanCHEC)." BMC Cancer **17**(1): 343.

14. Young, E., et al. (2009). "PCa and driving occupations: could whole body vibration play a role?" International Archives of Occupational and Environmental Health **82**(5): 551-556.

15. Sauve, J. F., et al. (2016). "Occupation, industry, and the risk of PCa: a case-control study in Montreal, Canada." Environ Health **15**(1): 100.

16. Blair, A., et al. (1992). "Clues to cancer etiology from studies of farmers." Scand J Work Environ Health **18**(4): 209-215.

17. Koutros, S., et al. (2013). "Risk of Total and Aggressive PCa and Pesticide Use in the Agricultural Health Study." Am J Epidemiol **177**(1): 59-74.

18. Ragin C, Davis-Reyes B, Tadesse H, Daniels D, Bunker CH, Jackson M, Ferguson TS, Patrick AL, Tulloch-Reid MK, Taioli E. Farming, reported pesticide use, and PCa. Am J Mens Health. 2013;7(2):102–9

19. Barry, K. H., et al. (2017). "Risk of early-onset PCa associated with occupation in the Nordic countries." European Journal of Cancer **87**: 92-100

20. Sritharan, J., et al. (2017). "Occupation and risk of PCa in Canadian men: A case-control study across eight Canadian provinces." Cancer Epidemiol **48**: 96-103.

21. Kilpelainen, T. P., et al. (2016). "PCa and Socioeconomic Status in the Finnish Randomized Study of Screening for PCa." Am J Epidemiol.

22. Gan, Y., et al. (2018). "Association between shift work and risk of PCa: a systematic review and meta-analysis of observational studies." Carcinogenesis **39**(2): 87-97.

23. "Canadian Forces Cancer and Mortality Study: Causes of Death. 2011. Accessed March 15, 2018.

24. Zhu, K., et al. (2009). "Cancer Incidence in the U.S. Military Population: Comparison with Rates from the SEER Program." Cancer Epidemiol Biomarkers Prev **18**(6): 1740-1745.

25. Justine, L., et al. (2006). "Vietnam military service history and PCa." BMC Public Health **6**: 75-75.

26. Laryea, D. O., et al. (2014). "Cancer incidence in Ghana, 2012: evidence from a population-based cancer registry." BMC Cancer **14**(1): 362.

27. Pukkala, E., et al. (2009). "Occupation and cancer – follow-up of 15 million people in five Nordic countries." Acta Oncologica **48**(5): 646-790.

28. Krstev, S., et al. (1998). "Occupational risk factors and PCa in U.S. Blacks and Whites." American Journal of Industrial Medicine **34**(5): 421-430.

29. McNamee R. Regression modelling and other methods to control confounding. *Occupational and Environmental Medicine* 2005;**62:**500-506.

30. Moore, S. C., et al. (2009). "Age-specific physical activity and PCa risk among white men and black men." Cancer **115**(21): 5060-5070.

31. Lynch, B. M., et al. (2014). "Sedentary behavior and PCa risk in the NIH-AARP Diet and Health Study." Cancer Epidemiol Biomarkers Prev **23**(5): 882-889.

32. "Survey of PCa in Accra, Ghana." Clinicaltrials.gov. June 21, 2006. Accessed March 7, 2018.

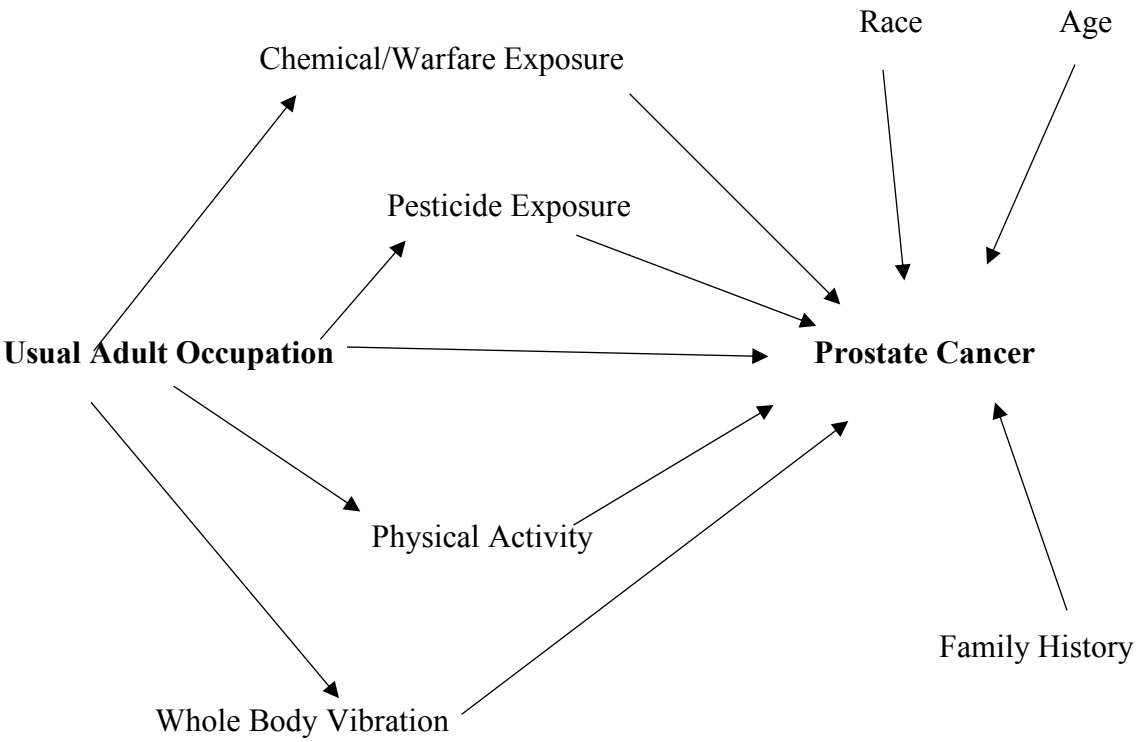
Appendices

4.1 Appendix A. Summary of previous studies examining effect of occupation type, socioeconomic status, screening behaviors, and family history on prostate cancer risk.

Study	**Study Type**	**Population**	**Exposure**	**Prostate Cancer Subtypes/ Biomarkers**	**Results**
Sauve et al., 2016	case control 1937 cases and 1994 controls	Canadian men	**Occupation and Industry**	Gleason score analysis from PSA	Occupations in forestry and logging (OR 1.9, 95% CI 1.2-3.0), social sciences (1.6 95% CI 1.1-2.2), and police officers (OR 1.8, 95% CI 1.1-2.9); other elevated risks included provincial government and financial institutions
Sritharan et al., 2017	case control 1737 cases, 1803 controls	Canadian men	**Occupation and Industry**	PCa definined using International Classification of Diseases for Oncology and were histologically confirmed	Farming and farm management (OR 1.37, 95% CI 1.02-2.93), armed forces (1.33, 95% CI 1.06-1.65), and legal work (OR 2.58, 95% CI 1.05-6.35); Office work (OR 1.2, 95% CI 1.00-1.43)
Kilpelainen et al., 2016	Cohort 80,144 men	Finnish men	**SES in screening for Pca**	PC incidence, mortality, and particpation were outcome measured in screening; SES were educational level, income, and home ownership status;	High SES associated with increased incidence of low to moderate risk cancers in the control arm, but substantially lower incidence of incurable, advanced PCa; men with high SES were significantly more active in participating than were men with low SES;

Chen et al., 2008	cross sectional 51, 529	U.S. males	**Family History**	Family history reviewing how genetics play a role for PCA based on two major cancer types	Increased risk of PCa for men with family history of PCa; PCa risk higher among men with affected brother than affected father; combination of PCa and BCa family history did not increase the risk of PCA and BCA respectively;

4.2 Appendix B Directed acyclic graph (DAG) of the association between usual adult occupation (exposure) and prostate cancer (outcome)



4.3 Appendix C. Table 4. Association between selected occupations and PCa aggressiveness stratified by reported smoking status.

Standard Occupational Classification Code**	Smoker		Not Smoker	
	N Cases	OR 95% CI	N Cases	OR 95% CI
11-0 Management Occupations				
All Prostate Cancer	45	1.5 (0.7, 3.1)	136	2.7 (1.7, 4.5)
Aggressive Prostate Cancer	25	1.1 (0.4, 2.8)	86	2.9 (1.6, 5.3)
13-0 Business and Financial Operations Occupations				
All Prostate Cancer	16	0.5 (0.2, 1.3)	46	0.5 (0.2, 1.3)
Aggressive Prostate Cancer	7	0.3 (0.1, 1.1)	29	0.5 (0.2, 1.3)
25-0 Education, Training, and Library Occupations				
All Prostate Cancer	17	2.1 (0.8, 5.5)	33	0.7 (0.3, 1.6)
Aggressive Prostate Cancer	11	2.9 (0.9, 9.2)	15	0.5 (0.2, 1.6)
33-0 Protective Service Occupations				
All Prostate Cancer	8	0.5 (0.2, 1.4)	15	0.4 (0.2, 1.1)
Aggressive Prostate Cancer	7	0.8 (0.3, 2.8)	13	0.8 (0.3, 2.2)
41-0 Sales and Related Occupations				
All Prostate Cancer	8	0.8 (0.3, 2.5)	14	0.4 (0.1, 0.94)
Aggressive Prostate Cancer	6	1.1 (0.3, 4.0)	13	0.6 (0.2, 1.8)
43-0 Office and Administrative Support Occupations				
All Prostate Cancer	16	0.9 (0.3, 2.3)	21	1.0 (0.5, 2.3)
Aggressive Prostate Cancer	9	0.8 (0.2, 2.8)	13	1.0 (0.4, 2.9)
45-0 Farming, Fishing, and Forestry Occupations				
All Prostate Cancer	16	0.8 (0.3, 1.8)	35	1.0 (0.4, 2.4)
Aggressive Prostate Cancer	8	0.5 (0.1, 1.9)	25	0.9 (0.3, 2.8)
47-0 Construction and Extraction Occupations				
All Prostate Cancer	13	0.6 (0.2, 1.3)	23	0.5 (0.2, 1.2)
Aggressive Prostate Cancer	7	0.3 (0.1, 1.1)	17	0.5 (0.2, 1.4)

49-0 Installation, Maintenance, and Repair Occupations				
All Prostate Cancer	10	0.6 (0.2, 1.5)	21	0.54 (0.2, 1.1)
Aggressive Prostate Cancer	6	0.4 (0.1, 1.5)	12	0.4 (0.1, 1.2)
51-0 Production Occupations				
All Prostate Cancer	15	0.8 (0.3, 1.9)	12	0.5 (0.2, 1.3)
Aggressive Prostate Cancer	11	1.3 (0.5, 3.8)	10	0.5 (0.2, 1.6)
53-0 Transportation and Material Moving Occupations				
All Prostate Cancer	26	1.4 (0.7, 2.8)	32	0.9 (0.5, 1.9)
Aggressive Prostate Cancer	17	1.5 (0.6, 3.5)	24	1.1 (0.5, 2.4)
55-0 Military Specific Occupations				
All Prostate Cancer	26	4.4 (1.7, 11.7)	25	2.4 (0.8, 7.2)
Aggressive Prostate Cancer	19	5.7 (1.8, 17.7)	18	1.9 (0.5, 7.1)

* Odds ratios adjusted for birth year, education, region, medical insurance

**Aggressive PCa is defined from the Medical Record Abstracts and Histopathology reports as a case that has a Gleason score of 7 or more

Appendix D. Supplemental Table 1. Number of cases and controls by 2 and 3-digit SOC code, longest held job.

SOC Code	Controls N (%)	All PCa cases N (%)	Aggressive PCa cases N (%)
11-0 Management Occupations	**77 (8.0)**	**182 (24.2)**	**111 (22.8)**
11-1 Chief Executives	8 (0.5)	28 (3.7)	13 (2.7)
11-2 Advertising, Marketing, Promotions, Public Relations, and Sales Managers	5 (0.5)	23 (1.3)	12 (2.5)
11-3 Operations Specialties Managers	39 (3.9)	88 (11.7)	59 (12.1)
11-9 Other Management Occupations	25 (2.6)	43 (5.6)	27 (5.6)
13-0 Business and Financial Operations Occupations	**74 (7.8)**	**62 (8.3)**	**36 (7.4)**
13-1 Business Operations	43 (4.5)	34 (4.5)	21 (4.3)
13-2 Financial Specialists	31 (3.3)	28 (3.7)	15 (3.1)
15-0 Computer and Mathematical Occupations	**2 (0.2)**	**3 (0.4)**	**1 (0.1)**
15-1 Computer Occupations	2 (0.2)	2 (0.3)	1 (0.1)
15-2 Mathematical Science Occupations	0 (0.0)	1 (0.1)	0
17-0 Architecture and Engineering Occupations	**20 (2.1)**	**24 (3.2)**	**18 (3.7)**
17-1 Architects, Surveyors, and Cartographers	4 (0.4)	11 (1.5)	10 (2.1)
17-2 Engineers	5 (0.5)	8 (1.1)	6 (1.2)
17-3 Drafters, Engineering Technicians, and Mapping Technicians	11 (1.1)	5 (0.7)	2 (0.4)
19-0 Life, Physical, and Social Science Occupations	**4 (0.4)**	**9 (1.2)**	**8 (1.7)**
19-1 Life Scientists	1 (0.1)	0 (0.0)	0 (0.0)
19-3 Social Scientists and Related Workers	3 (0.3)	7 (0.9)	6 (1.2)
19-4 Life, Physical, and Social Science Technicians	0 (0.0)	2 (0.3)	2 (0.4)
21-0 Community and Social Service Occupations	**7 (0.7)**	**10 (1.3)**	**4 (0.8)**
21-1 Service Specialists	0 (0.0)	1 (0.1)	0 (0.0)
21-2 Religious Workers	7 (0.9)	9 (1.2)	4 (0.8)
23-0 Legal Occupations	**1 (0.1)**	**8 (1.1)**	**4 (0.8)**
23-1 Lawyers, Judges, and Related Workers	1 (0.1)	8 (1.1)	4 (0.8)
25-0 Education, Training, and Library Occupations	**36 (3.7)**	**50 (6.7)**	**26 (5.4)**
25-1 Postsecondary Teachers	30 (3.1)	44 (5.9)	23 (4.7)
25-2 Preschool, Primary, Secondary, and Special Education School Teachers	1 (0.1)	0 (0.0)	0 (0.0)
25-3 Other Teachers and Instructors	0 (0.0)	1 (0.1)	0 (0.0)
25-4 Librarians, Curators, and Archivists	2 (0.2)	2 (0.3)	1 (0.2)
25-9 Other Education, Training, and Library Occupations	3 (0.3)	3 (0.4)	2 (0.4)
27-0 Arts, Design, Entertainment, Sports, and Media Occupations	**23 (2.4)**	**13 (1.7)**	**9 (1.9)**
27-1 Arts, Design, Entertainment, Sports, and Media Occupations	17 (1.8)	7 (0.9)	5 (1.0)
27-2 Entertainers and Performers, Sports and Related Workers	3 (0.3)	3 (0.4)	2 (0.4)
27-3 Media and Communication Workers	2 (0.2)	2 (0.3)	1 (0.2)
27-4 Media and Communication Equipment Workers	1 (0.1)	1 (0.1)	1 (0.2)
29-0 Healthcare Practitioners and Technical Occupations	**4 (0.5)**	**15 (2.0)**	**8 (1.7)**

29-1 Health Diagnosing and Treating Practitioners	1 (0.1)	11 (1.3)	6 (1.2)
29-2 Health Technologists and Technicians	0 (0.0)	1 (0.1)	1 (0.2)
29-9 Other Healthcare Practitioners and Technical Occupations	3 (0.3)	3 (0.4)	1 (0.2)
31-0 Healthcare Support Occupations	**2 (0.2)**	**3 (0.3)**	**3 (0.6)**
31-1 Nursing, Psychiatric, and Home Health Aides	0 (0.0)	1 (0.1)	1 (0.2)
31-9 Other Healthcare Support Occupations	2 (0.2)	2 (0.2)	2 (0.2)
33-0 Protective Service Occupations	**72 (7.5)**	**23 (3.1)**	**20 (4.1)**
33-1 Supervisors of Protective Service Workers	18 (1.9)	6 (0.8)	6 (1.2)
33-3 Law Enforcement Workers	8 (0.8)	10 (1.3)	9 (1.9)
33-9 Other Protective Service Workers	46 (4.8)	7 (0.9)	5 (1.0)
35-0 Food Preparation and Serving Related Occupations	**6 (0.6)**	**4 (0.5)**	**3 (0.6)**
35-1 Supervisors of Food Preparation and Serving Workers	1 (0.1)	2 (0.3)	1 (0.2)
35-2 Cooks and Food Preparation Workers	3 (0.3)	0 (0.0)	0 (0.0)
35-3 Food and Beverage Serving Workers	2 (0.2)	1 (0.1)	1 (0.2)
35-9 Other Food Preparation and Serving Related Workers	0 (0.0)	1 (0.1)	1 (0.2)
37-0 Building and Grounds Cleaning and Maintenance	**8 (0.8)**	**3 (0.4)**	**3 (0.8)**
37-1 Supervisors of Building and Grounds Cleaning and Maintenance Workers	2 (0.2)	0 (0.0)	0 (0.0)
37-2 Building Cleaning and Pest Control Workers	5 (0.5)	2 (0.3)	2 (0.4)
37-3 Grounds Maintenance Workers	1 (0.1)	1 (0.1)	1 (0.2)
39-0 Personal Care and Service Occupations	**8 (0.8)**	**2 (0.3)**	**1 (0.2)**
39-1 Supervisors of Personal Care and Service Workers	2 (0.2)	1 (0.1)	1 (0.1)
39-3 Entertainment Attendants and Related Workers	1 (0.1)	0 (0.0)	0 (0.0)
39-5 Personal Appearance Workers	0 (0.0)	1 (0.1)	0 (0.0)
39-6 Baggage Porters, Bellhops, and Concierges	4 (0.4)	0 (0.0)	0 (0.0)
39-9 Other Personal Care and Service Workers	1 (0.1)	0 (0.0)	0 (0.0)
41-0 Sales and Related Occupations	**55 (5.7)**	**22 (2.9)**	**19 (3.9)**
41-1 Supervisors of Sales Workers	23 (2.4)	14 (1.9)	13 (2.7)
41-2 Retail Sales Worker	19 (2.0)	6 (0.8)	5 (1.0)
41-3 Sales Representatives, Services	4 (0.4)	0 (0.0)	0 (0.0)
41-4 Sales Representatives, Wholesale and Manufacturing	1 (0.1)	1 (0.1)	1 (0.0)
41-9 Other Sales and Related Workers	8 (0.8)	1 (0.1)	0 (0.0)
43-0 Office and Administrative Support Occupations	**50 (5.2)**	**37 (4.9)**	**22 (4.5)**
43-1 Supervisors of Office and Administrative Support Workers	6 (0.6)	9 (1.2)	5 (1.0)
43-2 Communications Equipment Operators	2 (0.2)	0 (0.0)	0 (0.0)
43-3 Financial Clerks	4 (0.4)	10 (1.3)	5 (1.0)
43-4 Information and Record Clerks	5 (0.5)	0 (0.0)	0 (0.0)
43-5 Material Recording, Scheduling, Dispatching, and Distributing Workers	4 (0.4)	2 (0.3)	0 (0.)
43-6 Secretaries and Administrative Assistants	9 (0.9)	10 (1.3)	7 (1.4)
43-9 Other Office and Administrative Support Workers	19 (2.0)	6 (0.8)	5 (1.0)

45-0 Farming, Fishing, and Forestry Occupations	**78 (8.1)**	**51 (6.8)**	**33 (6.8)**
45-2 Agricultural Workers	60 (6.2)	51 (6.8)	33 (6.8)
45-3 Fishing and Hunting Workers	18 (1.9)	0 (0.0)	0 (0.0)
47-0 Construction and Extraction Occupations	**110 (11.4)**	**36 (11.3)**	**24 (4.9)**
47-1 Supervisors of Construction and Extraction Workers	7 (0.7)	6 (0.8)	3 (0.6)
47-2 Construction Trades Workers	98 (10.1)	28 (3.9)	19 (3.9)
47-3 Helpers, Construction Trades	1 (0.1)	0 (0.0)	0 (0.0)
47-4 Other Construction and Related Workers	1 (0.1)	1 (0.1)	0 (0.0)
47-5 Extraction Workers	3 (0.4)	1 (0.1)	1 (0.2)
49-0 Installation, Maintenance, and Repair Occupations	**75 (7.8)**	**31 (4.1)**	**18 (3.7)**
49-1 Supervisors of Installation, Maintenance, and Repair Workers	11 (1.1)	9 (1.2)	6 (1.2)
49-2 Electrical and Electronic Equipment Mechanics, Installers, and Repairers	28 (2.9)	9 (1.2)	5 (1.0)
49-3 Vehicle and Mobile Equipment Mechanics, Installers, and Repairers	26 (2.7)	7 (0.9)	3 (0.6)
49-9 Other Installation, Maintenance, and Repair Occupations	10 (1.0)	6 (0.8)	4 (0.8)
51-0 Production Occupations	**81 (8.4)**	**27 (3.6)**	**21 (4.3)**
51-1 Supervisors of Production Workers	1 (0.1)	5 (0.7)	5 (1.0)
51-3 Food Processing Workers	12 (1.2)	1 (0.1)	1 (0.1)
51-4 Metal Workers and Plastic Workers	13 (1.4)	6 (0.8)	3 (0.6)
51-5 Printing Workers	7 (0.7)	3 (0.4)	3 (0.6)
51-6 Textile, Apparel, and Furnishings Workers	34 (3.5)	8 (1.1)	6 (1.2)
51-7 Woodworkers	2 (0.2)	1 (0.1)	1 (0.2)
51-9 Other Production Occupations	12 (1.2)	3 (0.4)	2 (0.4)
53-0 Transportation and Material Moving Occupations	**114 (11.8)**	**58 (7.7)**	**41 (8.4)**
53-1 Supervisors of Transportation and Material Moving Workers	2 (0.2)	1 (0.1)	1 (0.7)
53-2 Air Transportation Workers	0 (0.0)	5 (0.7)	4 (0.8)
53-3 Motor Vehicle Operators	93 (9.7)	43 (5.7)	30 (6.2)
53-4 Locomotive Engineer	1 (0.1)	0 (0.0)	0 (0.0)
53-5 Water Transportation Workers	9 (0.9)	6 (0.8)	5 (1.0)
53-6 Other Transportation Workers	3 (0.3)	1 (0.1)	1 (0.2)
53-7 Material Moving Workers	6 (5.4)	2 (0.3)	0 (0.0)
55-0 Military Specific Occupations	**17 (1.8)**	**51 (6.8)**	**37 (2.6)**
55-1 Military Officer Special and Tactical Operations Leaders	11 (1.1)	42 (5.6)	29 (6.0)
55-2 First-Line Enlisted Military Supervisors	1 (0.1)	0 (0.0)	0 (0.0)
55-3 Specialists and Crew Members	5 (0.2)	9 (1.2)	8 (1.7)
99-9	**41 (4.3)**	**28 (3.7)**	0 (0.0)