Risk of early-onset prostate cancer associated with occupation in the Nordic countries

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ABSTRACT

BACKGROUND: Early-onset prostate cancer is often more aggressive and may have a different etiology than later-onset prostate cancer, but has been relatively little studied to date. We evaluated occupation in relation to early-onset and later-onset prostate cancer in a large pooled study. METHODS: We used occupational information from census data in five Nordic countries from 1960-1990. We identified prostate cancer cases diagnosed from 1961-2005 by linkage of census information to national cancer registries and calculated standardized incidence ratios (SIRs) separately for men aged 30-49 and those aged 50 or older. We also conducted separate analyses by period of follow-up, 1961-1985 and 1986-2005, corresponding to pre- and post-prostate-specific antigen (PSA) screening. RESULTS: For early-onset prostate cancer (n=1,521), we observed the highest SIRs for public safety workers (e.g., firefighters) [SIR=1.71, 95% confidence interval (CI): 1.23-2.31] and military personnel (SIR=1.97, 95% CI: 1.31-2.85). These SIRs were significantly higher than the SIRs for later-onset disease (for public safety workers, SIR=1.10, 95% CI: 1.07-1.14, and for military personnel, SIR=1.09, 95% CI: 1.05-1.13; $p_{heterogeneity}$=0.005 and 0.002, respectively). Administrators and technical workers also demonstrated significantly increased risk for early-onset prostate cancer, but the SIRs did not differ from those for later-onset disease ($p_{heterogeneity}$>0.05). While our early-onset finding for public safety workers was restricted to the post-PSA period, that for military personnel was restricted to the pre-PSA period. CONCLUSION: Our results suggest that occupational exposures, particularly for military personnel, may be associated with early-onset prostate cancer. Further evaluation is needed to explain these findings.

INTRODUCTION

The etiology of prostate cancer remains largely unknown, with only a few established risk factors (age, race, family history of prostate cancer and some genetic variants) (1). However, past studies of prostate cancer may have been obscured by including cases diagnosed at an older age, which may have a different etiology than those at younger ages. The relatively high incidental detection of prostate cancer among older men in autopsy studies indicates that many prostate cancers, especially late-onset cases, may be indolent and unlikely to be fatal (2). Early-onset prostate cancer, in contrast, is thought to be more aggressive and more likely to progress, leading to significant morbidity and mortality, and may have a different etiology than later-onset disease (3-4).

Studies of occupation and prostate cancer have yielded some clues about prostate cancer etiology. A number of studies have reported an increased risk of prostate cancer for farmers, suggesting a possible role of pesticides or other agricultural exposures in prostate cancer risk. Meta-analyses of farming and prostate cancer that largely covered studies conducted before uptake of the prostate-specific antigen (PSA) prostate cancer screening test reported meta-rate ratios (RRs) ranging from 1.07 to 1.12 (5-7). However, there was evidence of heterogeneity by geographic location and study design, with higher effect estimates reported for North American than European studies and for proportional mortality ratio or case-control studies than other designs (7). More recent meta-analyses, which covered studies that were predominantly conducted in the post-PSA period, have also reported an increased risk of prostate cancer for pesticide-related occupations, based on meta-RRs ranging from 1.13 to 1.28 (8-10). The U.S. Agricultural Health Study, a large prospective cohort study of pesticide applicators and their

spouses, observed similar results (11, 12), with the most recent analysis (cancer diagnoses from 1993-2006) reporting Standardized Incidence Ratios (SIRs) of 1.19 [95% Confidence Interval (CI): 1.14-1.25] for private pesticide applicators (i.e. farmers) and 1.28 (95% CI: 1.00-1.61) for commercial applicators, respectively (12).

There is also accumulating evidence suggesting an increased risk of prostate cancer for military personnel, night-shift workers and firefighters. A study in the Nordic countries as part of the Nordic Occupational Cancer (NOCCA) project (http://astra.cancer.fi/NOCCA) reported an SIR of 1.10 (95% CI: 1.06-1.14) for military personnel based on prostate cancer diagnoses from 1961-2005 (13). A study of cancer incidence in the U.S. military that included cancer diagnoses from 1990-2004 also reported an increased risk of prostate cancer for this group (14). However, the U.S. findings were more likely to be influenced by screening patterns given the focus on prostate cancer diagnoses in the post-PSA period and prominent U.S. military/political figures such as General Schwarzkopf and Bob Dole advocating for PSA screening in the 1990s. Evidence for an increased risk of prostate cancer for night-shift workers (15) stems from studies covering pre- and post-PSA periods and comprising various study designs and geographic areas (e.g., Sweden, Japan and Canada), with effect estimates ranging from just over 1.0 to about 3.0 (16-19). For firefighters, a 2006 meta-analysis largely based on studies in the pre-PSA period reported a summary effect estimate of 1.28 (20), and more recent studies have supported this finding (21-23). However, an analysis within NOCCA suggested that the increased risk of prostate cancer for firefighters in the Nordic countries may be restricted to the post-PSA period (21). Notably, the Nordic study (21) and a U.S. cohort study (23) conducted stratified analyses by age at diagnosis and observed the highest elevation in prostate cancer risk for cases diagnosed

at younger ages, specifically between the ages of 30-49 (SIR=2.59, 95% CI: 1.34-4.52) (21) or 45-59 (SIR=1.45, 95% CI: 1.28-1.64) (23), respectively. These findings highlight the importance of further investigating etiologic risk factors for prostate cancer by age at diagnosis and calendar time period.

A previous analysis within NOCCA evaluated the association between overall prostate cancer (among other cancer sites) and a number of occupations (13), but early-onset prostate cancer was not considered separately. In the present study, we compare occupation-specific risk of early-onset prostate cancer (i.e., age at diagnosis<50 years) and later-onset prostate cancer within NOCCA. In addition, we separately evaluate risks in two time periods (1961-1985 and 1986-2005) that roughly correspond to the pre- and post-PSA time periods to account for PSA screening.

MATERIALS AND METHODS

Study population

The details of the study population have been described previously (13). Briefly, the study population included individuals in the computerized population censuses from 1960-1990 in five Nordic countries (Denmark, Finland, Iceland, Norway and Sweden) who were aged 30-64 years and still alive and living in the country on January 1 of the year following the census. Up to four consecutive decennial censuses were included per country (Supplementary Table S1). In more recent years, there has been reduced interest in conducting traditional censuses in the Nordic

countries because of the availability of demographic information in central administrative registers (13). However, the administrative registers do not contain the same level of occupational information available in traditional censuses and therefore were not used in the present study. There were approximately 7.4 million male participants included in the present study, comprising roughly 996,000 from Denmark, 1.7 million from Finland, 61,000 from Iceland, 1.3 million from Norway and 3.4 million from Sweden.

Occupation

Information on education, occupation, industry and name and address of employer at the time of the first available census per participant was used to code occupations (13). In Finland, Norway and Sweden, occupation was coded according to national adaptations of the International Standard Classification of Occupations (ISCO) from 1958 (24), and in Iceland according to ISCO 1968 (25). In Denmark, occupation was coded according to a national nomenclature with a distinction between self-employed persons, family workers, salaried employees, skilled workers and unskilled workers. As described previously (13), original national occupational codes were subsequently harmonized into 53 occupational categories and an additional category for economically inactive persons (unemployed).

Follow-up for incidence of prostate cancer

Person-years were calculated for each participant in country, sex, age, period and occupation-specific categories starting from January 1 of the year after the first census of participation (i.e.

January 1, 1961 at the earliest) and ending at the date of emigration, death or December 31 of the most recent year of cancer incidence data available for each of the countries at the time of the NOCCA database creation (2003 for Denmark and Norway, 2004 for Iceland and 2005 for Finland and Sweden), whichever occurred first. Data on dates of emigration and death were obtained from the Central Population Register in each country. Prostate cancer diagnoses from 1961-2005 were identified by linkage to the national cancer registries in each country, which include data on incident cancer cases since 1943 for Denmark, 1953 for Finland and Norway, 1955 for Iceland and 1958 for Sweden. During the period covered in the present study, the registries obtained reports of cancer diagnoses from a variety of sources, including clinics or clinical hospital departments, pathology departments (except Denmark) and the death registry (except Sweden). Death certificate only cases and death certificate initiated cases were not included for Sweden as Sweden does not register such cases. Although there is currently no standard definition, we defined early-onset prostate cancer as a diagnosis before age 50, which has been suggested to arise from a different mechanism than later-onset disease (4). We defined later-onset prostate cancer as a diagnosis at age 50 or older.

Statistical analysis

We calculated SIRs for early-onset or later-onset prostate cancer cases for different occupational categories by comparing observed counts to the counts expected based on the distribution of person-years by country, sex, age and period for each occupational category and the stratum-specific incidence rates for each national population (all occupational categories combined). For each occupation, we computed SIRs separately for each of the five countries, as well as an overall SIR for

all five countries combined. For particular occupational groups of interest, we also performed analyses of subgroups with more specific jobs/exposures. We focus our presentation in the paper (Table 1) on those occupations that were significantly associated with either early- or later-onset prostate cancer (or both) and that had more than 0 observed early-onset cases. SIR findings for the remaining occupations are shown in Supplementary Table S2 (for early-onset prostate cancer) and Supplementary Table S3 (for later-onset prostate cancer). We conducted separate analyses by period of cancer follow-up in two categories, 1961-1985 and 1986-2005 (which roughly correspond to the pre- and post-PSA periods) because of the possible influence of the introduction of the PSA screening test in the Nordic countries (26). For each SIR, we defined the exact 95% confidence interval (95% CI), assuming a Poisson distribution of the observed number of cases. We compared the SIRs for early- and later-onset prostate cancer for a given occupation of interest by computing the ratio of the SIRs, or relative SIR (rSIR), and testing the null hypothesis that the rSIR was equal to 1.0, following the approach described by Breslow and Day (27). For the top occupations associated with early-onset prostate cancer, we also computed the absolute excess risk (AER), defined as [(observed cases – expected cases)/person-years], to estimate the population burden of cancer associated with these occupations.

RESULTS

For early-onset prostate cancer (n=1,521), the highest SIRs were observed for public safety workers (SIR=1.71, 95% CI: 1.23-2.31) and military personnel (SIR=1.97, 95% CI: 1.31-2.85) (Table 1). These SIRs were significantly higher than those observed for later-onset disease (for

public safety workers, SIR=1.10, 95% CI: 1.07-1.14, and for military personnel, SIR=1.09, 95% CI: 1.05-1.13; $p_{heterogeneity}$=0.005 and 0.002, respectively) (Table 1). Absolute excess risk, on the other hand, was much higher for later-onset than early-onset prostate cancer for these occupations. For public safety workers, AERs for early- and later-onset prostate cancer were 1.6 per 100,000 person-years and 30 per 100,000 person-years, respectively, and for military personnel, AERs were 2.1 per 100,000 person-years and 26 per 100,000 person-years, respectively (data not presented). Within the group of public safety workers, firefighters have been previously reported to have a significantly increased risk of early-onset prostate cancer in the NOCCA population, with an SIR of 2.59 (95% CI: 1.34-4.52) (21). After removing firefighters (about 17% of the public safety workers in each country, except in Denmark, where the percentage was about 6%) in the present analysis, the SIR for public safety workers for early-onset disease remained significantly elevated (SIR=1.50, 95% CI: 1.01-2.15). When separately evaluating SIRs by country, the highest SIR for public safety workers (including firefighters) with early-onset prostate cancer was observed for Sweden (SIR=1.99, 95% CI: 1.29-2.93) and the highest SIRs for military personnel were observed for Denmark and Finland (for Denmark, SIR=4.43, 95% CI: 2.21-7.93, and for Finland, SIR=2.43, 95% CI: 1.05-4.79) (Supplementary Table S2). SIRs for later-onset prostate cancer by occupation and country are shown in Supplementary Table S3.

Administrators (SIR=1.41, 95% CI: 1.13-1.73) and technical workers (SIR=1.18, 95% CI: 1.01-1.37) also demonstrated a significantly increased risk of early-onset prostate cancer (Table 1), but their SIRs did not significantly differ from those for later-onset disease (for administrators, SIR=1.17, 95% CI: 1.15-1.19; $p_{heterogeneity}$=0.08, and for technical workers, SIR=1.11, 95% CI:

1.09-1.12; $p_{heterogeneity}$=0.40, respectively). Teachers demonstrated a significantly decreased risk of early-onset prostate cancer (SIR=0.68, 95% CI: 0.48-0.94) in contrast to a significantly increased risk for later-onset prostate cancer (SIR=1.09, 95% CI: 1.07-1.11; $p_{heterogeneity}$=0.005). Gardeners also demonstrated a significantly decreased risk of early-onset prostate cancer (SIR=0.61, 95% CI: 0.35-0.99), which was similar to the pattern observed for later-onset prostate cancer (SIR=0.89, 95% CI: 0.87-0.91; $p_{heterogeneity}$=0.13; Table 1). Farmers did not have a significantly altered risk of early-onset prostate cancer (SIR=0.79, 95% CI: 0.60-1.01; Supplementary Table S2) or later-onset prostate cancer overall (SIR=1.00, 95% CI: 0.99-1.01; Supplementary Table S3; $p_{heterogeneity}$=0.06), although some individual countries demonstrated a significantly increased risk (Norway) or decreased risk (Denmark and Iceland) for later-onset prostate cancer (Supplementary Table S3).

As expected given the predominance of prostate cancer diagnoses at older ages, the SIRs by occupation for later-onset prostate cancer in our study were similar to those reported previously for prostate cancer overall in the NOCCA population (13). The highest SIR in our study for men over age 50 was observed for dentists (SIR=1.22, 95% CI: 1.13-1.31; $p_{heterogeneity}$=0.99) and the lowest SIRs were observed for domestic assistants (SIR=0.62, 95% CI: 0.38-0.98; $p_{heterogeneity}$=0.76) and the economically inactive (SIR=0.80, 95% CI: 0.78-0.81; $p_{heterogeneity}$=0.34) (Table 1).

We also computed SIRs for each occupation with early- and later-onset prostate cancer by period of cancer follow-up (1961-1985 and 1986-2005, which roughly correspond to the pre- and post-PSA periods in the Nordic countries). Table 2 displays findings by period for the subset of

occupations that demonstrated a significant association ($p<0.05$) with early-onset prostate cancer overall or within specific periods in the present study (with the remaining occupations shown in Supplementary Table S4). While several occupations demonstrated a significantly increased risk of early-onset prostate cancer restricted to the 1986-2005 period (for public safety workers, SIR=1.81, 95% CI: 1.23-2.57, for technical workers, SIR=1.22, 95% CI: 1.01-1.46, and for sales agents, SIR=1.35, 95% CI: 1.04-1.72), the associations for the other occupations with early-onset prostate cancer were restricted to the 1961-1985 period (Table 2). For this earlier period, the highest SIRs for early-onset prostate cancer were observed for military personnel (SIR=2.52, 95% CI: 1.44-4.09) and artistic workers (SIR=2.85, 95% CI: 1.30-5.41), and the lowest SIR for smelting workers (SIR=0.35, 95% CI: 0.10-0.89) (Table 2).

DISCUSSION

We conducted the first study to separately evaluate early- and later-onset prostate cancer in relation to a large number of occupations. For later-onset prostate cancer, the SIRs by occupation were similar to those previously published for prostate cancer overall (13), reflecting the large proportion of prostate cancer that occurs at older ages. For early-onset prostate cancer, public safety workers and military personnel demonstrated the highest SIRs, which were also significantly higher than the corresponding SIRs for later-onset prostate cancer. When evaluating absolute excess risk for these two occupations, the opposite pattern was observed, such that higher AERs were observed for later- than early-onset prostate cancer. Administrators and technical workers also demonstrated significantly elevated SIRs for early-onset prostate cancer,

although the SIRs for these occupations did not significantly differ from those for later-onset disease. Gardeners and teachers demonstrated a significantly decreased risk (SIR<1.0) of early-onset prostate cancer, whereas teachers demonstrated a significantly increased risk (SIR>1.0) of later-onset disease. For farmers, we observed a borderline significant decreased risk for early-onset prostate cancer and no overall association for later-onset prostate cancer. While our early-onset finding for public safety workers was restricted to the post-PSA (1986-2005) period, that for military personnel was restricted to the pre-PSA (1961-1985) period.

Public safety workers in our study included firefighters, policemen and detectives, customs officers, guards and watchmen. In addition to some recent evidence for an increased risk of prostate cancer for policemen and detectives (28), several studies have observed an increased risk for firefighters (20-23). Studies of firefighters that have stratified by age at diagnosis (including a previous study in the NOCCA population) have observed greater risk increases for early-onset prostate cancer, consistent with our study results for the larger group of public safety workers (21, 23). The observed excess among public safety workers was not entirely due to excesses among firefighters because the increased risk of early-onset prostate cancer for public safety workers persisted after removing firefighters from this category.

Firefighters may be exposed to a variety of chemicals present in smoke, including benzene, polycyclic aromatic hydrocarbons (PAHs) and fine particulates, among others, as well as diesel exhaust from firefighting vehicles (29, 30). A few studies have suggested an increased risk of prostate cancer associated with exposure to PAHs (31-34) or diesel exhaust (35, 36), although the evidence has been mixed for these exposures (37, 38) and no excess was observed in miners

with very high exposure to diesel exhaust (39). As is common for other public safety workers as well, firefighters frequently conduct night-shift work (29). Some studies have suggested that night-shift work may be associated with an increased risk of prostate cancer (16-19), potentially by disrupting sleep/total sleep, disrupting circadian rhythms or suppressing pineal melatonin secretion (15, 40-42). It is also possible that our findings could have been influenced by detection bias, i.e. if the difference in PSA screening utilization for public safety workers compared to the general population was greater for younger than older men. In addition, due to about 20-year-old EU legislation, night-shift workers such as firefighters, other public safety workers and military personnel are offered a free health examination before the start of night-shift work and at three-year intervals thereafter. This may result in overestimation of prostate cancer at young ages, where night work is more frequent than in older ages, although the PSA test is not included in these examinations.

Military personnel have been previously found to have an increased risk of prostate cancer (13, 14, 43), although to our knowledge, no previous study has specifically evaluated the risk of early-onset prostate cancer in relation to this occupation. Our finding of a significant increased risk of early-onset prostate cancer restricted to the earlier, pre-PSA period suggests that PSA screening patterns likely do not account for our findings. Despite this, it is possible that the increased risk in our study could be due in part to greater detection of prostate cancer for military personnel as a result of more frequent health examinations (44), particularly if the difference in health care utilization for military personnel compared to the general population was greater for younger men. In addition, military personnel may experience exposure to a variety of chemicals on the job, including solvents, pesticides and polychlorinated biphenyls (PCBs) (45, 46), which

have been associated with prostate cancer in some studies (47) and may have also contributed to our findings.

Farmers have tended to demonstrate an elevated risk of prostate cancer in the literature (5-7,11, 12, 48). In our study, we did not observe an overall elevated risk of prostate cancer for farmers for either early- or later-onset disease. Rather, we observed a borderline significant decrease in the risk of early-onset prostate cancer overall and no significant association for later-onset prostate cancer overall, although some individual countries demonstrated a significantly increased risk (Norway) or decreased risk (Denmark and Iceland) for later-onset prostate cancer. Our finding of no association for Finland is consistent with a previous study in a Finnish population that evaluated total prostate cancer (49), and there have been reports in some other countries of an inverse association between farming and prostate cancer (28). Given the evidence for an association between pesticide exposure and prostate cancer in the literature (50-52), it is possible that some of the variation in our results from other studies, as well as the geographic and temporal variation within our study, could be due to differing patterns of pesticide application (e.g., different pesticides applied due to different crops grown or different lengths of the growing season). There could also be a role of exposure to ultraviolet radiation, which has been associated with a decreased risk of prostate cancer in various studies (53-56), or physical activity, as farming can be a physically strenuous occupation; however, there is inconsistent evidence in the literature for a relationship between physical activity and prostate cancer (57).

Although it is noteworthy that the SIRs for early-onset prostate cancer were higher than those for later-onset prostate cancer for public safety workers and military personnel in our study, it is

important to note that the AERs for early-onset prostate cancer for these occupations were relatively small, less than one tenth of the AERs for later-onset disease. The discrepancy between our SIR and AER results is explained by the substantially lower background rate of early-onset prostate cancer when compared with the rate of later-onset prostate cancer.

Our study was limited by the characterization of occupations based on occupational information provided at one point in time and by the lack of information on duration of employment and information on specific exposures in the different occupations. However, military personnel and public safety workers, such as firefighters and policemen, in the Nordic countries tend to retire from active duty around age 60, with some variation (for example, the retirement age for military personnel in Finland is 55), thus reducing the likelihood of holding many other occupations throughout their lifetime. Additionally, we did not have data on prostate cancer screening in our study, and thus could not directly evaluate the impact of screening on our findings. However, we were able to separately evaluate SIRs in two different periods, which helped evaluate the potential impact of PSA screening in the Nordic countries, although there was some variation between countries in PSA uptake, with that in Denmark occurring several years later than the other countries (26). We were also limited by relatively small numbers in some of the occupational categories for early-onset disease, which could have reduced our ability to detect significant associations.

Our study also had several strengths. First, the NOCCA population is large and we had sufficient numbers of cases to study early-onset prostate cancer for many occupations, which was not possible in earlier studies. In addition, the availability of high quality cancer incidence data for

the national cancer registries of the Nordic countries is an improvement over mortality studies (13).

In summary, our study provides some clues about the etiology of early-onset prostate cancer, which has been little studied to date. Although most men with prostate cancer are diagnosed at older ages, it is critical to separately study early-onset disease, which may be more aggressive than later-onset disease and may possess a different etiology. Our results suggest that occupational exposures, particularly for military personnel, may be associated with early-onset prostate cancer. Additional work is warranted to explore specific exposures or other factors that might be contributing to the observed risk increases by occupation.

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Table 1. Observed (Obs) numbers of prostate cancer cases and standardized incidence ratios (SIRs) for men 30-49 years of age and men 50 years of age or older, respectively, in the five Nordic countries combined by occupational category. Occupational categories with 0 observed cases in the 30-49 age category or without a statistically significant SIR in either age category are excluded.

	Men 30-49 years of age		Men 50 years of age or older		$p_{heterogeneity}$[a,b]
Occupational category	Obs	SIR (95% CI)[a]	Obs	SIR (95% CI)[a]	
Technical workers, etc	176	**1.18 (1.01-1.37)**	26265	**1.11 (1.09-1.12)**	0.40
Physicians	10	0.99 (0.48-1.83)	1573	**1.11 (1.06-1.17)**	0.73
Dentists	4	1.21 (0.33-3.11)	732	**1.22 (1.13-1.31)**	0.99
Other health workers	7	0.89 (0.36-1.83)	1133	**1.08 (1.02-1.14)**	0.61
Teachers	36	**0.68 (0.48-0.94)**	9012	**1.09 (1.07-1.11)**	**0.005**
Religious workers, etc	50	1.09 (0.81-1.43)	5785	**1.15 (1.12-1.18)**	0.71
Artistic workers	14	1.40 (0.76-2.34)	1776	**1.10 (1.05-1.15)**	0.37
Administrators	90	**1.41 (1.13-1.73)**	16563	**1.17 (1.15-1.19)**	0.08
Clerical workers	52	1.00 (0.74-1.31)	12405	**1.07 (1.05-1.09)**	0.60
Sales agents	86	1.19 (0.95-1.47)	16346	**1.10 (1.08-1.12)**	0.45
Shop workers	31	0.76 (0.51-1.07)	7728	**1.03 (1.00-1.05)**	0.09
Gardeners	16	**0.61 (0.35-0.99)**	9198	**0.89 (0.87-0.91)**	0.13
Fishermen	8	0.85 (0.37-1.68)	3221	**0.89 (0.86-0.92)**	0.91
Forestry workers	13	0.66 (0.35-1.13)	6502	**0.85 (0.82-0.87)**	0.37
Miners and quarry workers	3	0.51 (0.11-1.49)	1562	**0.89 (0.85-0.94)**	0.33
Seamen	13	0.87 (0.46-1.49)	3600	**1.05 (1.02-1.09)**	0.50
Textile workers	4	0.48 (0.13-1.24)	3105	**0.94 (0.91-0.98)**	0.18
Smelting workers	11	0.57 (0.28-1.01)	4785	**0.94 (0.92-0.97)**	0.09
Mechanics	119	0.96 (0.80-1.15)	22273	**0.96 (0.95-0.98)**	0.99
Wood workers	55	0.81 (0.61-1.05)	18652	**0.97 (0.95-0.98)**	0.18
Other construction workers	37	0.93 (0.65-1.28)	9548	**0.95 (0.93-0.97)**	0.88
Chemical process workers	14	0.95 (0.52-1.60)	3737	**0.90 (0.87-0.92)**	0.81
Glass makers, etc	22	1.17 (0.73-1.77)	3962	**0.94 (0.91-0.97)**	0.31
Public safety workers	42	**1.71 (1.23-2.31)**	4851	**1.10 (1.07-1.14)**	**0.005**
Domestic assistants	1	0.86 (0.02-4.77)	19	**0.62 (0.38-0.98)**	0.76
Military personnel	28	**1.97 (1.31-2.85)**	2688	**1.09 (1.05-1.13)**	**0.002**
Other workers	45	1.10 (0.80-1.47)	11073	**0.96 (0.95-0.98)**	0.39
Economically inactive	78	0.89 (0.70-1.11)	12616	**0.80 (0.78-0.81)**	0.34
All categories	1521	REF	338438	REF	

Abbreviations: 95% CI, 95% Confidence Interval; Obs, observed case number; REF, referent group; SIRs, standardized incidence ratios.
[a]Bolding denotes statistical significance ($p<0.05$)
[b]P-value for heterogeneity

Table 2. Observed (Obs) numbers of prostate cancer cases and standardized incidence ratios (SIR) among men 30-49 years of age and men 50 years or older, respectively, by period (pre- and post-PSA) for occupational categories that were significantly associated with early-onset prostate cancer overall or within specific periods ($p<0.05$) in the five Nordic countries.

	Men 30-49 years of age				Men 50 years of age or older			
	1961-1985		1986-2005		1961-1985		1986-2005	
Occupational category[a]	Obs	SIR (95% CI)[b]	Obs	SIR (95% CI)[b]	Obs	SIR (95% CI)[b]	Obs	SIR (95% CI)[b]
Technical workers, etc	56	1.11 (0.84-1.44)	120	**1.22 (1.01-1.46)**	4512	**1.09 (1.06-1.12)**	21753	**1.11 (1.10-1.13)**
Artistic workers	9	**2.85 (1.30-5.41)**	5	0.73 (0.24-1.70)	373	**1.17 (1.06-1.30)**	1403	**1.08 (1.02-1.14)**
Administrators	50	**1.72 (1.28-2.27)**	40	1.15 (0.82-1.56)	3932	**1.14 (1.11-1.18)**	12631	**1.18 (1.16-1.20)**
Sales agents	22	0.89 (0.56-1.35)	64	**1.35 (1.04-1.72)**	3954	**1.09 (1.06-1.13)**	12392	**1.10 (1.08-1.12)**
Gardeners	8	0.55 (0.24-1.08)	8	0.69 (0.30-1.36)	2776	**0.87 (0.84-0.91)**	6422	**0.90 (0.88-0.92)**
Smelting workers	4	**0.35 (0.10-0.89)**	7	0.87 (0.35-1.80)	1537	1.04 (0.98-1.09)	3248	**0.90 (0.87-0.94)**
Public safety workers	11	1.47 (0.73-2.63)	31	**1.81 (1.23-2.57)**	1017	**1.08 (1.01-1.14)**	3834	**1.11 (1.08-1.15)**
Military personnel	16	**2.52 (1.44-4.09)**	12	1.53 (0.79-2.67)	385	**1.12 (1.01-1.23)**	2303	**1.09 (1.04-1.13)**

Abbreviations: 95% CI, 95% Confidence Interval; Obs, observed case number; SIRs, standardized incidence ratios.
[a]The referent group was all 54 occupational categories combined
[b]Bolding denotes statistical significance ($p<0.05$)