TITLE	**Occupational exposure to solar ultraviolet radiation and the risk of prostate cancer**
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ABSTRACT

Objectives

Preventable risk factors for prostate cancer are poorly understood; sun exposure is a possible protective factor. The goal of this study was to investigate prostate cancer risk in outdoor workers, a population with high sun exposure.

Methods

Prostate cancer cases and controls from a large study (conducted between 1994 and 1997) were used for this analysis. A job exposure matrix was used to assign solar UVR at work as moderate (2-<6 hours outside/day) or high (≥6). Average daily satellite UV-B measures were linked to the latitude/longitude of the residences of each subject. Several other exposure metrics were also examined, including ever/never exposed and standard erythemal dose by years (SED*years). Logistic regression was used to evaluate the association between solar UVR exposure and the odds of prostate cancer.

Results

A total of 1638 cases and 1697 controls were included. Men of Indian and Asian descent had reduced odds of prostate cancer (ORs 0.17 (0.08 – 0.35) and 0.25 (0.15 – 0.41), respectively) compared to Caucasian men, as did single men (OR 0.76, (0.58 - 0.98)) compared to married. Overall, no statistically significant associations were observed between sun exposure and prostate cancer with one exception. In the satellite-enhanced JEM that considered exposure in high category jobs only, prostate cancer odds in the highest quartile of cumulative exposure was decreased compared to unexposed men (OR 0.68 (0.51 – 0.92)).

Conclusion

This study found limited evidence for an association with prostate cancer, with the exception of one statistically significant finding of a decreased risk among workers with the longest-term and highest sun exposure.

WHAT THIS PAPER ADDS

- Despite being the second most common cancer in men (after skin cancer), the preventable causes of prostate cancer remain unclear. Ecological evidence suggests a possible role of sun exposure in prostate cancer prevention.
- Outdoor workers have the highest level of sun exposure, but exposure assessment methods for sun-related ultraviolet radiation are relatively crude.
- This study improves upon exposure assessment methods for solar radiation in outdoor workers by including a job exposure matrix with satellite data on available sun by location, and links exposure to prostate cancer outcomes in a population-based case-control study in Canada.

- Limited evidence for a link between high solar ultraviolet radiation exposure and reduced risk of prostate cancer was found with the exception of very high, long-term exposures.

INTRODUCTION

Excluding skin cancers, prostate cancer is the most common malignancy diagnosed in Canadian men (1). Despite this, risk factors for prostate cancer remain unclear. Other than personal and genetic characteristics (older age, African ancestry, screening history, family history), consistent risk factors have not been identified (2). The only modifiable risk factor with strong evidence for a link with prostate cancer is overweight and obesity (3). Interest in identifying environmental causes for prostate cancer is strong (4), both as a result of interest in cancer prevention, and for explaining varying rates by country; the incidence rates of prostate cancer vary by more than 25 times between different areas of the world (3).

The geographical variation in cancer rates in the United States (lower in the south compared to the north) and Europe (lower in Southern Europe than Northern) (5,6) prompted researchers to investigate ultraviolet radiation (UVR) exposure, and ecological studies have shown that exposure to UVR may lead to lower risks of colorectal, breast, ovarian and prostate cancers (7–9). This was seen as plausible because of a hypothesized protective effect of vitamin D, and racial differences in prostate cancer risk; darker-skinned people (especially those of African ancestry) have less ability to produce vitamin D endogenously and also have higher prostate cancer risk (10). However, the relationship between pigmentation, vitamin D synthesis, and sun protection practices in sun-sensitive individuals complicates the relationship between UVR exposure and prostate cancer (11). As evidence of these complex relationships, several studies have not found a relationship between either sun exposure or vitamin D and prostate cancer (12–14). Evidence also exists showing the opposite relationship, that sun exposure may increase the risk of prostate cancer, particularly in areas of high UVR (15,16). In addition, a review on vitamin D and cancer risk by the International Agency for Research on Cancer in 2008 did not find evidence for a protective effect of vitamin D on prostate cancer (17).

Despite these complexities, a decreased risk of prostate cancer with increased solar UVR exposure has been detected in some studies. Bodiwala et al. carried out a study of English men that collected detailed information on lifetime solar UVR exposure and showed statistically significant reductions in risk of prostate cancer, especially in the highest exposed (9,18). Typically, studies designed to examine UVR exposure and cancer risk rely on residential histories (7,19) or self-reported indicators of solar UVR as their exposure metrics (18,20). In addition, a large American prospective study of UVR exposure and the risk of various cancers used ground-level estimates of residential UVR derived from satellite data to examine cancer risk; they found significantly decreased risks of prostate cancer in all exposure categories relative to the comparison group (21).

Since outdoor workers receive about six to eight times the yearly exposure to solar UVR than indoor workers, a useful identifier of cumulative UVR exposure is whether a person works outdoors (22). In a Netherlands-based study of prostate cancer in patients with previous skin cancer diagnosis, a significantly decreased standardized incidence ratio for prostate cancer was found for all skin cancer types, and was lowest for those with squamous cell carcinoma (SIR: 0.84), the cancer most strongly linked to cumulative, occupational exposure (23).

The purpose of the current study was to test the hypothesis, in the context of a Canadian population-based case-control study, that higher cumulative occupational UVR exposure reduces the risk of prostate cancer; the purpose was also to improve on UVR exposure measures for epidemiological studies. Exposure assessment and epidemiological analysis was done in two phases: 1) using a previously-developed job exposure matrix (SUNJEM) to assign all jobs into high, moderate and low categories of exposure based on time spent outside each workday; and 2) enhancing this job exposure matrix (JEM) by applying ground-level UVR exposure measures (from satellite data) to each exposed job over time for more refined measures.

METHODS

Study population

The National Enhanced Cancer Surveillance System (NECSS) is a large, multi-site population-based case-control study that was designed to investigate the environmental causes of cancer in Canada (24). Detailed methods for the NECSS are published elsewhere (24–26); briefly, mailed questionnaires were used to obtain full residential and occupational histories, and detailed information on risk factors for cancer. The response rate was the same for cases and controls (69%). Questions included ethnicity, relationship status, education (total years of education), income, smoking (pack-years), height, weight, physical activity (number of hours per month of strenuous or moderate activity), diet (60-item food frequency measure), and exposure to occupational carcinogens (pesticides, cadmium, radiation, coal, tar, pitch, soot). The current study was approved by the Behavioral Research Ethics Board at the University of British Columbia.

Prostate cancer cases and controls were interviewed between 1994 and 1997 within 6 months after diagnosis in all provinces except Ontario, where this lag time was approximately one year. Prostate cancer cases were identified from the provincial cancer registries (which identifies nearly all cancer cases), and were histologically confirmed. Controls were obtained differently by province. In Prince Edward Island, British Columbia, Nova Scotia, Saskatchewan and Manitoba, controls were selected randomly from provincial health insurance registries. In Ontario, Ministry of Finance data was used to generate a stratified random sample of controls, and in Newfoundland and Alberta random digit dialing was used to recruit controls. Controls were age-matched based on the entire set of cancer cases (not just prostate), so the controls were slightly younger than cases for prostate cancer in particular (due to recruitment to examine cancers in younger men, such as testicular cancer). The subjects were limited to men aged 50 to 75 years for the current analysis because younger diagnoses for prostate cancer are rare and more likely to reflect genetic susceptibility than occupational exposure, and people over 75 were excluded from the NECSS at the outset due to expected logistical difficulties in tracing these individuals, as well as anticipated recall difficulties (25). People were excluded from the analysis if they had missing job information (title or years), or missing residential histories for an outdoor job and location could not be determined otherwise.

Exposure assessment

A previously-created job exposure matrix (SUNJEM) was used to assign exposure for all outdoor jobs in either low (intermittent or partly-shaded exposure), moderate (2 to <6 hours) or high (≥6 hours) categories based on time spent outdoors by job(27). Exposure was defined as being an outdoor worker, which requires that at least 2 hours are expected to be spent outdoors per day on average. Briefly, SUNJEM categories were based on: 1) European CAREX (CARcinogen EXposure) defining jobs as primarily outdoors (high exposure) when 75% or more of each work day (i.e. 6+ hours assuming an 8-hour day) was spent outside (28); 2) time spent outside per day available from career selection websites; and 3) task descriptions allowing the delineation of intermittent exposure (such as for a truck driver with exposed arms) (27). It was possible for survey respondents to record up to 2 simultaneous jobs; if more than one job title was recorded, both were coded. If the primary job (where most time was spent) was flagged as exposed by SUNJEM, then the secondary job was not generally considered, unless it implied that the person worked in management; in which case the level of exposure was dropped by one scale point. If the primary job was not exposed but the secondary one was, exposure was added on a case-by-case basis by an industrial hygienist to decide if the job-time should be considered exposed. If the secondary job (normally noted as part time or seasonal) was likely to be outdoors, these were weighted in time-relevant exposure metrics by dividing the number of years in that job by half (so as not to overestimate exposure). In SUNJEM, if there is uncertainty about whether a low exposed job should be flagged or not, the default is to leave it as unexposed unless there is a compelling reason to flag it as exposed. Only 50 jobs were flagged as low exposed, so these jobs were combined with the moderate category.

Satellite measures of UV-B were available from the Global UV (glUV) project (29). These data were linked to the latitude/longitude of each residence for each person, assuming the home would be relatively close to the work location. The unit of measure for this data is Joules/m^2/day, which can be converted to the average Standard Erythemal Dose (SED) per day by dividing by 100. This daily average SED (averaged over one year) was multiplied by years of outdoor employment to obtain a UV-weighted variable of the type exposure*years.

Statistical analyses

The analysis was comprised of six separate models (denoted Models 1-6) based on the type of exposure measure: Model 1: ever had an outdoor job (yes/no); Model 2: ever had an outdoor job in the high category of exposure (6+ hours outdoors per day) (yes/no); Model 3: the number of years in outdoor work; Model 4: the number of years in an outdoor job in the high category of exposure (6+ hours outdoors per day; Model 5: quartiles of total UVR exposure*years (in units of SED*years); and Model 6: quartiles of UVR exposure*years considering only jobs in the >6 hours per day outdoors JEM category (in units of SED*years).. For the cumulative UVR*years measures, quartiles of exposure were used (units of SED*years). Models 2, 4, and 6 were limited to just jobs in the high category of exposure according to the JEM (6+ hours) in order to limit some of the misclassification of exposure more inherent to the moderate category of exposure. These models consider those workers where there is more certainty of regular high exposure to solar UVR.

SAS PROC LOGISTIC (version 9.3) was used to create separate models for each of the six exposure metrics as mentioned above, modeling prostate cancer case as the outcome, and using people without outdoor work as the comparison group in each model. Due to the sampling differences for controls across provinces and the age structure of cases compared to controls, all bivariate analyses were calculated as minimally adjusted odds ratios so that these two variables were always accounted for in the presentation of results. Predictive models to ascertain prostate cancer risk factors have been previously published on this dataset (25), and so were not considered here. The covariates considered were ethnicity (grouped as European, European with higher likelihood of darker skin types (Italian, Spanish, Greek, Portuguese) Asian, Indian, First Nations, Black, or Other), smoking (in pack-years), marital status (married/common-law, single/divorced/separated, widowed), percent of lifetime lived in urban areas (estimated from residential histories), total career length, education (in years, by category), income adequacy (household income accounting for number of people per household), body mass index (BMI), hours of moderate and strenuous physical activity per month (summed), total servings of dairy, fruit, and vegetables per week, and self-reported exposure to pesticides, cadmium, or asphalt fumes (suspected occupational risk factors for prostate cancer).

Each potential confounder was considered in a minimally-adjusted logistic model with each of the six exposure metrics only, to evaluate its influence on each exposure variable alone. Variables that changed the odds ratios of the exposure metrics appreciably (>10%) were added to the multivariable models. Ethnicity was always included (along with age and province) because it is one of the few known risk factors. Variables that could be related to screening behaviour were also included in the analyses (marital status, education, income, and urban living), as screening information was not collected in the NECSS. If any subject had missing data for a covariate, a category of 'missing' was created so that the subject could be retained in analyses.

RESULTS

There were 4,346 men in the original dataset; 634 were outside the age range (50-75 years) for the current analyses; and 377 had missing job information, including no recorded job histories (n=104), no job titles or dates (n=264), and no job location during times when they worked outdoors (n=9). The final analytic sample included 3,335 people (1638 cases, 1697 controls) (Figure 1). Nearly 19% of jobs held were outdoor jobs (n=2,496), and of these the small number of low exposure category jobs (n=50) were combined with the moderate category for a total of 711 jobs, leaving 1,785 in the high category (>75% of workdays outdoors).

Bivariate relationships between all of the covariates and the odds of prostate cancer are presented in Table 1 (controlling for province and age). People of Indian and Asian heritage had a reduced odds of prostate cancer (ORs of 0.15 (0.07 – 0.31) and 0.22 (0.14 – 0.36), respectively), consistent with previous evidence for ethnicity. Men who spent less time living in urban areas had a higher odds of prostate cancer, which is the opposite of what was expected based on access to screening services. Those in the lowest categories of income adequacy and physical activity had significantly reduced odds of prostate cancer (ORs of 0.7 (0.5 – 0.9) and 0.6 (0.4 – 0.9), respectively), perhaps reflecting a screening effect whereby less affluent and healthy men were less likely to get screened. Men with less than 5 servings of dairy products per week also had a reduced odds of prostate cancer (OR of 0.7, 95%CI of 0.5 – 0.8). No other covariate was significantly related to the odds of prostate cancer (relationship status, smoking, education, fruit and vegetable consumption, or any occupational exposures).

The relationships between the metrics of occupational UVR exposure and the odds of prostate cancer are presented as six final models (Table 2; data for covariates not shown). Each model has minimally-adjusted odds ratios (OR) (age, province), and a fully-adjusted model. The covariates that remained in fully-adjusted models were the same for all models (race/ethnicity, relationship status, time in urban areas, career length). People of Indian and Asian heritage remained at reduced risk of prostate cancer in the fully adjusted models (OR 0.17 and 0.25, respectively), while black and First Nations people were at increased risk, but the 95% confidence intervals included 1. Stratified analyses by ethnicity were not possible due to small numbers of non-Caucasian men. People with less time in urban areas also remained more likely to have prostate cancer in the full-adjusted models (OR 1.45 for those in the category of >0-50% of their lives in urban areas compared to those who always lived in urban areas, 95%CI 1.10-1.91). Finally, single men were at lower risk of prostate cancer than married men in the fully adjusted models (OR 0.76, 95%CI 0.58 – 0.98). Length of career was included to control for the healthy worker effect in the fully-adjusted models (OR 1.01, 95%CI 1.00 – 1.02.

Table 1. Bivariate relationships between covariates and prostate cancer, adjusted for province and age

Variable name	Cases (n, %) (n=1638)	Controls (n, %) (n=1697)	Minimally adjusted odds ratios (OR)[a]
Race/ethnicity			
Western European Caucasian	1480 (90%)	1435 (85%)	1.0
Italian/Spanish/Greek/Portuguese	87 (5.3%)	111 (6.5%)	0.75 (0.56 – 1.02)
Asian	23 (1.4%)	75 (4.4%)	0.22 (0.14 – 0.36)
Indian	9 (0.6%)	43 (2.5%)	0.15 (0.07 – 0.31)
First Nations	22 (1.3%)	17 (1.0%)	1.30 (0.67 – 2.52)
Black	10 (0.6%)	8 (0.5%)	1.47 (0.56 – 3.86)
Other	7 (0.4%)	8 (0.4%)	1.04 (0.36 – 2.97)
Relationship status			
Married/Common law	1437 (88%)	1467 (86%)	1.0
Single/Divorced/Other	121 (7.4%)	161 (9.5%)	0.78 (0.60 – 1.00)
Widowed	80 (4.9%)	69 (4.1%)	1.17 (0.83 – 1.65)
% Time lived in urban areas			
100%	622 (38%)	721 (42%)	1.0
≥50% to <100%	727 (44%)	692 (41%)	1.31 (1.12 – 1.53)
>0 - 50%	156 (9.5%)	130 (7.7%)	1.58 (1.21 – 2.06)
0	133 (8.1%)	154 (9.1%)	1.27 (0.97 – 1.67)
Pack-years smoking			
0	405 (25%)	394 (23%)	1.0
>0 – 10	296 (18%)	287 (17%)	1.0 (0.8 – 1.2)
≥10 – 25	443 (27%)	435 (26%)	1.0 (0.8 – 1.2)
≥25 – 40	269 (16%)	298 (18%)	0.8 (0.7 – 1.0)
40+	225 (14%)	283 (17%)	0.7 (0.6 – 0.9)
BMI category			
<25 (Normal)	572 (35%)	621 (37%)	1.0
25 – 30 (Overweight)	832 (51%)	808 (48%)	1.2 (1.0 – 1.4)
30+ (Obese)	234 (14%)	268 (16%)	1.0 (0.8 – 1.3)
Income adequacy[b]			
Low	208 (13%)	266 (16%)	0.7 (0.5 – 0.9)
Lower middle	290 (18%)	293 (17%)	0.9 (0.7 – 1.1)
Upper middle	419 (26%)	437 (26%)	0.9 (0.7 – 1.1)
High	342 (21%)	318 (19%)	1.0
Missing or prefer not to answer	379 (23%)	383 (23%)	0.9 (0.7 – 1.1)
Education (years)			
≤9 (middle school or less)	471 (29%)	513 (30%)	1.1 (0.9 – 1.3)
10 to <12 (some high school)	339 (21%)	337 (20%)	1.2 (0.9 – 1.5)
≥12 to <16 (graduated high school + some college)	517 (32%)	488 (29%)	1.2 (0.9 – 1.4)
≥16 (graduated college)	292 (18%)	334 (20%)	1.0
Missing data	19 (1%)	25 (1%)	0.8 (0.4 – 1.5)

Physical activity category (hours per month)[c]			
0	537 (33%)	672 (40%)	0.6 (0.4 – 0.9)
>0 – 10	318 (19%)	333 (20%)	0.8 (0.7 – 1.1)
≥10 – 30	434 (27%)	409 (24%)	0.9 (0.7 – 1.1)
≥30	349 (21%)	283 (17%)	1.0
# dairy products consumed/week			
<5	291 (18%)	415 (24%)	0.7 (0.5 – 0.8)
≥5 - <10	430 (26%)	425 (25%)	1.0 (0.8 – 1.2)
≥10 - <20	557 (34%)	514 (30%)	1.0 (0.8 – 1.2)
≥20	360 (22%)	343 (20%)	1.0
# vegetables consumed/week			
<10	210 (13%)	246 (15%)	0.9 (0.7 – 1.1)
≥10 - <20	731 (45%)	720 (42%)	1.0 (0.8 – 1.3)
≥20 - <30	451 (28%)	495 (29%)	0.9 (0.7 – 1.1)
≥30	246 (15%)	236 (14%)	1.0
# fruits consumed/week			
<5	405 (25%)	479 (28%)	1.0 (0.8 – 1.2)
≥5 - <10	491 (30%)	460 (27%)	1.2 (0.9 – 1.5)
≥10 - <20	543 (33%)	535 (32%)	1.1 (0.9 – 1.4)
≥20	199 (12%)	223 (13%)	1.0
Occupational exposures (ever exposed)[d]			
Cadmium	21 (1%)	23 (1%)	0.9 (0.5 – 1.7)
Asphalt fumes	229 (14%)	222 (13%)	1.1 (0.9 – 1.3)
Pesticides	153 (9%)	163 (10%)	0.9 (0.7 – 1.2)

[a]Adjusted for age and province
[b]Low: Household income <$20,000 or income $20,000 - $29,999 and 4+ persons in the household. Lower middle: Income $20,000 - $29,999 and <4 persons in the household, or income $30,000 - $49,999 and 4+ persons in the household. Upper middle: Income $30,000 - $49,999 and <4 persons in the household or income $50,000 - $99,999 and 4+ persons in the household. High: income $50,000 - $99,999 and <4 persons in the household or income >$100,000
[c]Total number of strenuous and moderate hours of exercise per month (summed across all physical activities)
[d]Models for occupational exposure show the odds of being a prostate cancer case for those that reported ever being exposed to the agent.

Table 2. Exposure to Occupational Solar Ultraviolet Radiation (UVR) and Prostate Cancer Risk: Minimally Adjusted and Fully Adjusted Models

	Cases (n=1638)	Controls (n=1697)	Minimally adjusted odds ratio (OR)[a]	Fully adjusted odds ratio (OR)[b]
MODEL 1				
Ever had an outdoor job (Yes vs. No)	45%	42%	1.10 (0.95 – 1.30)	0.99 (0.85 – 1.20)
MODEL 2				

Ever had an outdoor job with high exposure (6+ hours outdoors per day) (Yes vs. No)	36%	35%	1.03 (0.89 – 1.20)	0.92 (0.78 – 1.10)
MODEL 3: Exposure years (number of years in any outdoor job)				
0	55%	58%	1.0	1.0
>0 - <10	18%	15%	1.19 (0.98 – 1.45)	1.08 (0.89 – 1.32)
10 - <35	16%	15%	1.17 (0.95 – 1.43)	1.05 (0.85 – 1.29)
≥35	11%	12%	0.89 (0.40 – 1.12)	0.71 (0.55 – 0.93)
p-value for trend			*0.907*	*0.147*
MODEL 4: Exposure years, number of years in high category (6+ hours per day outdoors) jobs				
0	64%	65%	1.0	1.0
>0 - <10	15%	13%	1.10 (0.90 – 1.35)	0.99 (0.80 – 1.23)
10 - <35	13%	12%	1.05 (0.84 – 1.30)	0.93 (0.74 – 1.23)
≥35	8.7%	9.4%	0.91 (0.70 – 1.17)	0.74 (0.55 – 0.99)
p-value for trend			*0.832*	*0.095*
MODEL 5: UV quartiles, all exposed jobs (in Standard Erythemal Dose * years)				
0	55%	58%	1.0	1.0
>0 – <76 SED-yrs	11%	10%	1.17 (0.93 – 1.48)	1.08 (0.86 – 1.37)
76 – <232 SED-yrs	12%	10%	1.20 (0.95 – 1.51)	1.07 (0.84 – 1.36)
232 – 523 SED-yrs	11%	11%	1.07 (0.85 – 1.35)	0.95 (0.74 – 1.21)
≥523 SED-yrs	10%	11%	0.96 (0.75 – 1.21)	0.78 (0.60 – 1.03)
p-value for trend			*0.738*	*0.229*
MODEL 6: UV quartiles, only high category jobs				
0	64%	66%	1.0	1.0
>0 – <86 SED-yrs	9.0%	8.5%	1.07 (0.84 – 1.38)	0.99 (0.77 – 1.29)
86 – <245 SED-yrs	9.4%	8.4%	1.09 (0.85 – 1.40)	0.97 (0.75 – 1.26)
245 – 629 SED-yrs	9.4%	8.1%	1.14 (0.83 – 1.46)	0.99 (0.76 – 1.29)
≥629 SED-yrs	8.1%	9.4%	0.85 (0.66 – 1.10)	0.68 (0.51 – 0.92)
p-value for linear trend			*0.849*	*0.087*

[a]Adjusted for age and province

[b]Adjusted for age, province, length of career (total), race/ethnicity, relationship status, and time lived in urban areas (the variables that remained in the models as significant)

Models represented: Model 1: ever had an outdoor job (yes/no); Model 2: ever had an outdoor job in the high category of exposure (6+ hours outdoors per day) (yes/no); Model 3: the number of years in outdoor work; Model 4: the number of years in an outdoor job in the high category of exposure (6+ hours outdoors per day; Model 5: quartiles of total UVR exposure*years; and Model 6: quartiles of UVR exposure*years considering only jobs in the >6 hours per day outdoors JEM category.

Models 1 through 4 in Table 2 considered exposure based only on SUNJEM. Overall, 737 cases (45%) and 713 controls (42%) were ever-exposed to solar UVR at work (Table 2, Model 1). When low/moderate jobs were excluded from that number, 590 cases and 594 controls ever had a high category outdoor job (outside >75% of a typical workday) (Table 2, Model 2). In the adjusted models, both of these variables led to very slightly reduced odds of prostate cancer (OR 0.99 and 0.92, respectively), however the 95% confidence intervals included 1. In Model 3, the number of exposure years (years in any outdoor job) in quartiles ranging from 0 (never had an outdoor job) to 35+ outdoor job years showed a trend (not statistically significant) of decreasing prostate cancer risk with increasing exposure-years (test for trend, p=0.147). In Model 4, where only the number of exposure years in high category jobs were considered as exposed, this same trend occurs, with an OR of 0.74 (95%CI 0.55 – 0.99) for the highest quartile of exposure-years (test for trend, p=0.095).

Models 5 and 6 expand upon SUNJEM by adding in cumulative measures of UVR exposure from satellite data. Similarly to Models 3 and 4, Model 5 considers all outdoor jobs, and Model 6 considers just those jobs with high category exposure as assigned by SUNJEM. In Model 5, the general pattern of decreasing odds of prostate cancer with increasing exposure persists, with an OR of 0.78 (0.6 – 1.0) in the highest category of exposure. Interestingly, a small increased odds of prostate cancer is noted when comparing the two lowest exposure categories to those without any occupational exposure, though the 95% confidence intervals contain 1. In Model 6, which sums satellite-measured values across high exposure outdoor jobs (≥6 hours per day), the odds of prostate cancer were close to 1.0 for all exposure categories compared to those with no exposure, with the exception of the highest category of exposure (longer duration at high ambient levels), where the OR for prostate cancer was 0.68 (95%CI 0.51 – 0.92).

DISCUSSION

This study found limited evidence that long-term occupational exposure to solar UVR could be linked to a lower risk of prostate cancer, in particular at high levels of solar UVR. As the sensitivity of the exposure metric for UVR increased (i.e. as the potential for misclassification of exposure decreased), so did the strength of this relationship. It is likely that some of the workers identified by SUNJEM as unexposed were misclassified due to their recreational exposure; however since this has the effect of biasing to the null, the reduced risk of prostate cancer in the highest exposure group of Model 6 could be lower. Some evidence generated in recent years suggests that more sunlight exposure leads to a lower risk of both prostate cancer diagnosis and death (13,20,23,30,31). The exact biological mechanism for this relationship is not known, but it has long been presumed to be linked with vitamin D that is increased most effectively via endogenous production in the skin from sun exposure. Prostate cells contain vitamin D receptors and enzymes necessary for vitamin D metabolism, and vitamin D metabolites have anti-proliferative influences on prostate cancer cell lines *in vitro* and *in vivo* (32). It has also been noted that Japanese men have a rate of prostate cancer 10 times lower than American men, and also have a diet richer in fish oils, an excellent source of dietary vitamin D (7). Many researchers have postulated that the burden of disease related to solar UVR is likely U-shaped (i.e. both low levels *and* high levels have negative health impacts) (33). However, the International Agency for Research on Cancer's summary report on the evidence for vitamin D lowering the risk of prostate cancer found insufficient evidence to support this hypothesis in the epidemiologic literature (17), and it is therefore important to consider alternate explanations for the apparent link between UVR exposure and reduced prostate cancer risk. Measures of vitamin D were not available for subjects in the NECSS, and so it was not possible to directly test the vitamin D hypothesis in this analysis; dietary variables (fruit, vegetable, and dairy consumption) were also not associated with the odds of prostate cancer.

Since Models 3 through 6 all considered time-dependent exposure metrics, the healthy-worker effect is a concern for interpretation of these results. Outdoor jobs are more physically demanding than indoor work, and thus attract and retain healthier workers. It is therefore possible that the relationship observed between long-term solar UVR exposure and reduced risk of prostate cancer could be explained by the fact that those workers who held an outdoor job for 35 years are simply healthier than those who did not. Firstly, this dataset is less prone to the healthy worker effect because all of the subjects were able to work; the minimum career length recorded was 5 years and 90% of the subjects had career lengths of >30 years. Additionally, career length was included in the models to adjust for potentially less-healthy workers with shorter careers (length of career was correlated with age, but the Pearson correlation coefficient was small, at 0.32). To further examine this potential bias, several sensitivity analyses were performed. Firstly, the dataset was limited to those people with long careers (35+ years and then 40+ years (results not shown). The same pattern of decreasing risk with increasing UVR exposure was observed, though the ORs were closer to 1.0 (for 35+ years only model: OR 0.71, 95%CI 0.52 – 0.98 in the highest category of exposure from Model 6; for 40+ years only: OR 0.82, 95%CI 0.59 – 1.01). The most common long-term outdoor jobs were farmers and fisherman, and these groups might be either less likely to undergo cancer screening since they have little contact with health professionals in general (34), or more likely to have other unique characteristics that could lower their risk (35). For this reason, the analysis was repeated without people who had these jobs as their most common profession, and the interpretation of the results remained unchanged. As another consideration, the markers of good health available in this dataset (BMI, smoking behaviour, diet, and physical activity levels) were not significantly different between the cases and controls.

Very few of the variables that were considered as potential confounders actually had any influence on the exposure-response relationship in this study. This was not a surprising finding, as the original work on this dataset by Villeneuve and colleagues did not find many significant relationships between most of the potential risk factors and prostate cancer (25). In particular, physical activity and BMI did not impact the relationship between exposure to solar UVR at work and prostate cancer risk, which was interesting as it was thought that at least part of the benefit of being a long-term outdoor worker would have been linked to physical activity levels and healthier weight. This, however, lends more credence to solar UVR being specifically linked with prostate cancer risk itself.

The main limitations of this study are the lack of information on prostate cancer severity, and the lack of information on prostate cancer screening behaviours. Autopsy studies have found that prevalence of prostate cancer in American Caucasian men over 50 was >40%, and this increased to over 80% by aged 80 (36). Since we do not know if prostate cancer was discovered from routine screening (37) or presentation of symptoms, cases might have been more likely to be screened than the controls for some reason that we could not detect. To address this, several variables related to screening behaviour, including marital status, education, income, urban home, and race/ethnicity (38) were considered in the analysis, and all of these except income and education remained important in the final models. Prostate cancer cases were more likely to be married or widowed than single, which suggests a screening effect; and more educated and wealthier people had higher risk of prostate cancer (though these variables did not remain in the final models), which also suggests there could be a minor effect of increased screening among cases. However, people who lived more of their lives in rural areas were actually at higher risk of prostate cancer, when easier access to healthcare is expected in urban areas. This finding may reflect underlying risk factors that differ by location. Questionnaires were not sent to cases that were deceased or known to have advanced disease, which is likely to have excluded those with aggressive disease. However, this would lead to an attenuation of risk estimates, since the case population were more likely to have similar risk profiles to the control population (25). A further limitation of this study is a lack of participant information sun protection used at work. However, outdoor workers tend not to use sun protection (such as seeking shade, wearing sunscreen, etc.) in large numbers (37). There is some reason to believe that those workers in the highest and long-term category of solar UVR exposure may be more resilient to the effects of the sun, but these are also men who are less likely to wear sun protection.

The strength of association between UVR exposure and prostate cancer increased slightly from the use of 'ever/never' had an outdoor job to the use of time spent outdoors multiplied by the average available UVR at each location. However, misclassification of exposure is still possible, particularly because leisure time sun behaviours were not available. Some people counted as unexposed may have had high sun exposure outside of work. Outdoor workers spend more leisure time outdoors than indoor workers (39), so it is likely that the truly highly exposed people were captured. Yearly average UVR dose was used as a metric, even though maximum average monthly dose was available. These values were highly correlated so the more stable yearly average was selected to calculate SED*years. This procedure was considered as a relative 'weighting' for the JEM, as it cannot be determined how much UVR was actually absorbed by the workers. Categorical weighting was used to assess exposure, rather than to consider it as a true dose.

This study found no association between sun exposure and prostate cancer, except for in workers with long-term, high UVR exposure (where limited evidence for a decreased risk of prostate cancer was noted). Since people with the highest cumulative occupational exposure to solar UVR were the only group with a statistically significantly reduction in risk, there could be a threshold for this effect. The study also addressed the need for improved assessment of occupational exposure to solar UVR, whereby the more specific and refined measures of exposure reduced misclassification and were associated with prostate cancer risk. Further research is required to examine the biological mechanism for the observed association, should one exist.

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CONTRIBUTORSHIP STATEMENT

Dr. Peters led the study as part of her PhD work, including data acquisition, cleaning and analysis, and wrote the manuscript. Drs. Demers, Kalia, and Nicol were on Dr. Peters' supervisory committee during this work, and gave methodological guidance in the design phase of the work through to its completion; all also provided a critical review and comments on the manuscript drafts. Dr. Hystad worked on the ultraviolet radiation exposure assessment using satellite data, both in planning it as well as in generating the files; he also provided critical feedback on the manuscript. Dr. Villeneuve is the data steward for the case control study on which the manuscript is based and provided feedback at the study design stage, as well as on the manuscript drafts. Dr. Kreiger was on the Canadian Cancer Registries Board who were responsible for the design and implementation of the case control study, and she also provided critical feedback on the manuscript. Dr. Koehoorn supervised the work, helped to design the analytical strategy, and helped with interpretation of results; she too reviewed and critiqued the manuscript.

COMPETING INTERESTS

None declared.

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