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A case-control study of occupational sunlight exposure and renal cancer risk

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Abstract

Epidemiological evidence of a relationship between vitamin D and kidney cancer risk has been inconsistent despite experimental data indicating that vitamin D and its metabolites may inhibit carcinogenesis. Previously we reported an inverse association between renal cell carcinoma (RCC) risk and occupational ultraviolet (UV) exposure among European men. In the current study, we examined the association between occupational UV exposure and RCC risk among US residents and investigated whether this association varied by race and sex. Lifetime occupational data for 1,217 RCC cases and 1,235 controls in a population-based case-control study, conducted from 2002-2007, were assessed for occupational UV exposure. We evaluated exposure metrics in quartiles based on control exposure levels and calculated associations between RCC risk and occupational UV exposure using unconditional logistic regression adjusted for sex, race, body mass index, smoking, hypertension, center, education, family history of cancer, and dietary vitamin D intake. A general pattern of decreasing RCC risk with increasing UV exposure was observed. Cases had significantly lower cumulative occupational UV exposure than controls (fourth quartile vs. first: odds ratio=0.74 [95% confidence interval=0.56-0.99], *P*-trend=0.03). Similar results were observed for other UV exposure metrics. The association with occupational UV exposure was stronger for women than men, but did not differ by race. Our findings suggest an inverse association between occupational UV exposure and RCC, particularly among women. Given the sex finding discrepancies in our current versus previous study, additional research is need to clarify whether the protective effects of occupational UV exposure and RCC risk are real.

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Keywords

sunlight; occupational UV; kidney cancer; race

INTRODUCTION

Nearly 65,000 Americans are diagnosed with kidney cancer annually,[1] accounting for roughly 4% of newly detected cancers and 2% of cancer deaths.[1] Higher incidence rates are observed among men than women and blacks than whites.[2] Etiologic risk factors include smoking, obesity, and hypertension.[2] Other risk factors have not been well established, although emerging scientific evidence indicates a possible protective role for vitamin D.

Vitamin D may impede carcinogenesis by inhibiting cell proliferation, stimulating cell differentiation, and suppressing tumor invasiveness, angiogenesis, and metastasis.[3,4] Typically synthesized in the skin after solar ultraviolet (UV) B exposure, vitamin D remains biologically inert until hepatic hydroxylation and renal transformation to the biologically active 1,25-dihydoxy vitamin D form.[4] Observational studies have shown lower incidence and mortality rates for various cancers, including kidney, for residents of higher UV light areas.[5,6] Laboratory and ecological findings have shown vitamin D may increase kidney cancer survival, reducing risk by 12%-20%.[7] Yet, evidence linking vitamin D/UV exposure and kidney cancer risk from cohort or case-control studies is limited.[8,9]

Previously, we conducted a hospital-based case-control study designed partly to assess renal cell carcinoma (RCC) risk associated with occupational sunlight exposure. We found evidence suggesting an inverse association between occupational sunlight exposure and RCC risk, particularly among men.[8] To replicate and extend findings, we investigated the association between RCC risk and occupational sunlight exposure in the US Kidney Cancer Study.

MATERIAL and METHODS

Study Population

The US Kidney Cancer Study was conducted in Chicago, Illinois and Detroit, Michigan. Details on recruitment and data collection have been described.[10] Briefly, black and white participants, 20-79 years, with histologically confirmed incident RCC (International Classification of Diseases for Oncology, Third Edition, Code 64.9) from 2002-2007 were identified from Chicago hospital pathology reports and the Metropolitan Detroit Cancer Surveillance System. Frequency-matched to cases on sex, age, race, and residential area, population controls (<65 years) were identified from Department of Motor Vehicle (DMV) records and (65-75 years) from Centers for Medicare and Medicaid Services (CMS).

To increase enrollment of blacks, all eligible black cases were invited to participate, whereas only a subset of eligible white cases were recruited. Our targeted control:case matching ratio was 2:1 for blacks and 1:1 for whites.[10] Among the 1,918 eligible cases identified, we contacted 1,571 cases for enrollment and recruited 1,217 for participation. Among the 2,718 potentially eligible controls identified, we contacted 2,269 controls for enrollment and

recruited 1,235 for participation. Study procedures were approved by Institutional Review Boards at collaborating institutions. Written informed consent was obtained from all subjects.

Data Collection

Demographics, diet, occupation, smoking, medical and medication history data were collected using in-home, computer-assisted personal interviews. Before interviews, work history calendars were mailed to participants asking to record information on job title, tasks performed, employer, and years of employment for all jobs held ≥12 months. During interviews, work history calendars were reviewed by trained interviewers and detailed questions were asked on tasks preformed and equipment and chemicals regularly used.

Occupational Exposure Assessment

All jobs were classified according to Standard Occupational and Industry Classification schemes by coders blinded to case/control status.[11,12] Classification schemes were used to categorize frequency, duration, intensity, and confidence of occupational sunlight exposure for each job considering responses to open-ended questions. Occupational sunlight exposure frequency was estimated as the percentage of time per 8-hour workday during which exposure was possible (<30%, 30%-<70%, ≥70%) considering the likelihood and location (indoor/outdoor) of tasks performed. To compute sunlight exposure across jobs with varying exposure frequencies, frequency weights (0.15, 0.50, 0.85) were assigned, corresponding to the midpoints of the range for each category. Occupational sunlight exposure confidence, coded as “possible” (<40%), “probable” (40%-90%), or “certain” (>90%), represented the degree of confidence in our exposure frequency assignment. Exposure intensity was coded as “high” (2 units) for jobs likely entailing strong UV exposure reflected from the sea or for outdoor occupations in rural settings.[13] All other jobs, suspected to involve weak UV exposure, were coded as “low” (1 unit).[13]

To assess quality of exposure assessment, occupational sunlight exposure frequency, confidence, and intensity assignments were independently reviewed by an industrial hygiene expert (P.S.) for each job held per participant. Inter-rater agreement for these variables was calculated using the Cohen kappa statistic.[14]

Statistical Analysis

Occupational sunlight exposure across jobs was evaluated using several metrics: (1) cumulative exposure, calculated as the product of duration (years), frequency midpoint, and exposure intensity unit for each job and summed over jobs; (2) frequency-adjusted duration of exposure, calculated as the product of duration (years) and frequency midpoint for each job and summed over jobs; (3) frequency-adjusted duration of exposure among participants that held only low-intensity jobs (excludes participants with any high-intensity job); and (4) frequency-adjusted duration of exposure among participants who held any high-intensity job (excludes participants with only low-intensity jobs).

Occupational sunlight exposure-response relationships were assessed in quartiles (Q_1:<25%, Q_2:25%-<50%, Q_3:50%-<75%, Q_4:≥75%) using control exposure levels. Frequency-

adjusted duration of exposure among participants who held any high-intensity job was evaluated dichotomously (Q_1 vs. Q_2-Q_4) due to small numbers. We conducted stratified analyses by race, sex, median age, body mass index (BMI: <30kg·m^{-2}/≥30kg·m^{-2}), hypertension (ever/never), smoking (ever/never), center (Detroit/Chicago), education (≤high school graduate/≥some college), family history of cancer (yes/no) and kidney cancer (yes/no), histologic subtype (clear cell RCC/RCC), and jobs assigned a high confidence level (probable or certain). Because >99% of occupations were assigned a high confidence UV exposure level, we present findings for this subset only.

As described previously,[10] sample weights were developed to reduce the potential for bias arising from differential sampling rates for controls and cases, from survey non-response, and deficiencies in coverage of the population at risk in DMV and CMS files. [15] We compared the sample-weighted frequency distribution of selected characteristics and known RCC risk factors between cases and controls using a Wald F-test.[16] Unconditional weighted logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) associated with occupational sunlight exposure. We performed trend tests by modeling the median of the exposure-response categories for occupational sunlight exposure as ordinal variables and applying the Wald Chi-Square test.[16] We used the jackknife replicate weight method to estimate standard errors.[17]

We adjusted regression models for sex, race, smoking, age (continuous), BMI (continuous), hypertension, family history of cancer, education (<12 years, high school graduate, some college, college graduate), center, and dietary vitamin D intake (continuous). Interactions were tested using a t-test and Wald test. Analyses were conducted with SAS 9.2 using procedures for sample weighted data. Statistical significance was determined at a two-sided *P*-value<0.05.

RESULTS

Nearly 12,000 jobs were assessed for occupational sunlight exposure frequency, intensity, and confidence. Inter-rater agreement scores for assessment of exposure frequency (kappa=0.80) and intensity (kappa=0.81) was very good and moderate (kappa=0.52) for confidence of exposure between raters.

Cases and controls were comparable by sex and age, but cases had a higher BMI, prevalence of hypertension, history of smoking, and a lower education level (Table 1). Similar distributions of characteristics were observed for sex and race stratified analyses (data not shown).

Inverse RCC associations with occupational sunlight exposure were observed for cumulative (*P*-trend=0.03), frequency-adjusted duration (*P*-trend=0.01), and frequency-adjusted duration of exposure among those who held only low-intensity jobs (*P*-trend=0.003) (Table 2). Compared to participants in the lowest exposure quartile, significant risk reductions were observed for those in the highest two quartiles for cumulative (OR_{Q3}=0.67, 95%CI=0.50-0.90; OR_{Q4}=0.74, 95%CI=0.56-0.99), frequency-adjusted duration (OR_{Q3}=0.66, 95%CI=0.49-0.89; OR_{Q4}=0.70, 95%CI=0.52-0.94), and frequency-adjusted

duration of exposure among those who held only low-intensity jobs (OR_{Q3}=0.63, 95%CI=0.47-0.86; OR_{Q4}=0.56, 95%CI=0.40-0.79). ORs for frequency-adjusted duration of exposure among those who held any high-intensity job were non-significant. Stratification by race revealed similar association patterns without significant interactions.

Sex stratified analyses (Table 3) revealed inverse associations significant for women but not men. Among women, we observed a monotonic decrease in RCC risk with increasing levels of cumulative (*P*-trend=0.007), frequency-adjusted duration (*P*-trend=0.003), and frequency-adjusted duration of exposure for only-low intensity jobs (*P*-trend=0.002). For women, similar association patterns were observed by race; though, slightly stronger associations were observed for white women while associations were weaker and non-significant for black women. For men, non-significant inverse association patterns with increasing UV exposure were observed; association patterns did not vary by race.

Stratified analyses by sex and other RCC risk factors did not suggest the presence of effect modification (data not shown).

DISCUSSION

Our study findings for several exposure metrics suggest a protective association for RCC risk and occupational UV exposure. A general decreasing risk pattern with increasing sunlight exposure was observed for blacks and whites and for both sexes. Associations were significant only among white women, however interaction by race and sex were non-significant. Stratification by exposure intensity showed inverse associations between occupational UV exposure and RCC risk restricted to subjects with low-intensity sunlight exposure.

Although our findings are supported by ecological studies,[5-7] the association between UV exposure and kidney cancer risk has rarely been examined using other study designs. We previously assessed occupational UV exposure and RCC risk in a European hospital-based case-control study utilizing identical exposure assessment techniques.[8] Significant inverse associations were observed, but only among men suspected of lower intensity UV exposure (i.e., residence at the highest latitude, 55.8°North). In the current study, participants resided at lower latitudes (Chicago: 41.9°North; Detroit: 42.3°North). To our knowledge, no other case-control study has examined the link between UV exposure and RCC risk. In an occupational cohort study of Swedish construction workers, a significant 30% decreased kidney cancer risk was observed among men exposed to the highest level of sunlight.[18] In another cohort of over 400,000 skin cancer and 3.7 million non-skin cancer cases, increased epidermal vitamin D production was associated with lower risk of second primary cancers, including kidney.[9] Recently, significantly reduced kidney cancer risk with increasing ambient UV exposure was observed among 450,934 US adults followed prospectively.[19] Similarly, evidence from the Cohort Consortium Vitamin D Pooling Project showed a significant 69% reduction in kidney cancer risk among females in the highest quintile concentration of circulating 25-dihydoxy vitamin D (25(OH)D).[20] However, the authors concluded that no protective effect was evident for kidney cancer and serum vitamin D levels given power limitations and lack of a statistical association for trend. It should be

noted that blood 25(OH)D levels have a short half-life, therefore a single measurement may not reflect long-term vitamin D status.[4]

The kidney is the major organ of vitamin D metabolism and activity.[4] While epidemiological studies of vitamin D and kidney cancer are limited, laboratory findings support the plausibility of an inverse association. *In vitro* and *in vivo* studies have shown vitamin D and its analogues to inhibit growth of kidney cancer cell lines.[3,4] Observations from *in vitro* systems indicate that vitamin D can affect the cell cycle process by inhibiting the G1-to-S phase transition and regulating tumor suppressor protein expression.[3,4] Although the exact anti-carcinogenic mechanism of vitamin D is unclear, epidemiological and laboratory evidence suggest that this vitamin may impede carcinogenesis by disrupting cellular processes involved in differentiation, proliferation, apoptosis, angiogenesis, and metastasis.[4]

Our current and previous case-control study findings revealed that the relationship between occupational UV exposure and RCC risk varied by sex. Here, protective RCC risk patterns were generally confined to white females with low-intensity occupational UV exposure. In our previous case-control study, significant association patterns were limited to men with low-intensity occupational UV exposure. Earlier studies have noted gender differences related to UV sensitivity and cancer risk.[21,22] Laboratory findings indicate that sex-related hormonal differences may influence acute UVB exposure response and UV-induced tumor development.[23,24] Alternatively, differential validity of UV exposure assessment for men and women may explain the observed variation by sex. Still, the question remains whether these sex differences are hormonally linked, due to behavioral differences which alter UV exposure, or chance related.

In our investigation trends were limited to low-intensity UV occupations. Sufficient vitamin D levels can be generated in a short period of time (10-20 minutes) following sunlight exposure to unprotected fair skin.[4] With prolonged exposure, vitamin D transformation becomes saturated forming inert metabolites and actually begins to photodegrade.[25] Therefore, shorter bursts or low-intensity UV exposures may be more advantageous. This saturation level may partially explain the lack of significant associations observed for males and those with high-intensity jobs. Interestingly, estimated occupational UV exposure levels in our study were approximately two-times higher for males and those with high-intensity jobs than for females and those with only low-intensity jobs. The contrast in vitamin D levels across groups with various exposure frequencies among males and those with high-intensity jobs may not have been sufficient to detect an association, since these individuals could conceivably be exposed beyond saturation though everyday activities. In our study, estimated occupational UV exposure levels were similar for blacks and whites. Yet, the lack of association among blacks, particularly black females, is likely related to their increased melanin content which reduces vitamin D synthesis. Consequently, longer periods of solar UV exposure are required for equivalent vitamin D synthesis in blacks compared to whites.

Strengths of our study include its population-based design, analyses by race, restriction to histologically confirmed RCC cases, and use of self-reported data on occupational tasks performed and equipment used to assign individual exposure. Although actual occupational

UV exposure measurements were unavailable, the inter-rater agreement scores confirmed consistency of the exposure assessment methodologies applied. Study limitations include inaccurate or incomplete recall of occupational histories and exposure misclassification. Our inability to account for other UV exposure sources like sunbathing activities, use of tanning beds, and recreational UV exposure may have led to exposure misclassification, possibly biasing results towards the null. However, we believe that occupational UV exposure would contribute substantially to one's vitamin D level as synthesis from sunlight is most likely to occur when UV index levels reach their peak between 11am-1pm,[13] times when individuals are generally working. Although race was known, information on subjects' tanning habits, hair and eye color, and use of sunscreen and personal protective equipment (e.g., hat, long sleeves, etc.) was unavailable. Other potential risk modifiers (e.g., genetics, other occupation and non-occupational exposures) were not considered. However, known RCC risk factors and potential confounders like dietary vitamin D intake, family history of cancer, and education (a surrogate for socioeconomic status) were considered for analyses presented. While we had sufficient statistical power to detect relatively small associations, race and sex analyses were underpowered. Lastly, control response rates were low; however, the sample weights used included adjustments for differences among demographic categories that may have reduced bias due to non-response.[15]

To our knowledge, this is the largest case-control study to investigate occupational UV exposure and RCC risk and the first study to compare this association by race. Our findings offer support for a protective association between RCC and occupational UV exposure for Detroit and Chicago residents, and suggest more pronounced associations among women. Our findings did not indicate that risk varied by race. Given the sex finding discrepancies between our current and previously published study, additional research is need to clarify whether the protective occupational UV exposure effects for RCC are real. Future studies considering recreational UV exposure and behaviors that influence sunlight exposure are needed to extend these findings.

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Abbreviations used

25(OH)D	25-dihydoxy vitamin D
BMI	body mass index
CIs	confidence intervals
CMS	Centers for Medicare and Medicaid Services
DMV	Department of Motor Vehicle
OR	Odd ratio
Q	quartile

RCC	renal cell carcinoma
SIC	Standard Industry Classification
SOC	Standard Occupational Classification
US	United States
UV	ultraviolet

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Novelty & Impact Statements

Our findings suggest that occupational ultraviolet exposure is associated with reduced risk of renal cell carcinoma, particularly among women. Additional studies are needed to investigate whether the protective effects of occupational UV exposure and renal cancer risk are real and to clarify the discrepancies observed by sex.

Table 1

Weighted characteristics of study participants

	Case	Control
Characteristics	**N (%[a])**	**N (%[a])**
Total	1217	1235
Sex		
Male	720 (61.8)	689 (61.4)
Female	497 (38.2)	546 (38.6)
Race		
White	856 (73.9)	712 (73.9)
Black	361 (26.1)	523 (26.1)
Age (in years)		
<45	147 (10.5)	179 (10.5)
45-54	287 (21.6)	270 (21.6)
55-64	372 (29.4)	350 (29.4)
65-74	303 (27.1)	329 (27.1)
75+	108 (11.5)	107 (11.3)
Mean Age (std)	58.8 (11.4)	58.3 (12.6)
Center		
Chicago	199 (16.7)	197 (17.3)
Detroit	1018 (83.3)	1038 (82.7)
Body Mass Index ($kg \cdot m^{-2}$)[b]		
<25	240 (19.5)	366 (29.1)
25-<30	436 (37.4)	493 (41.7)
30+	528 (43.1)	368 (29.2)
History of Hypertension		
No	500 (40.8)	718 (59.0)
Yes	701 (59.2)	508 (41.0)
Smoking Status		
Never	432 (35.3)	471 (38.4)
Occasional[c]	55 (4.7)	55 (4.0)
Regular Former Smoker	410 (34.7)	445 (38.0)
Regular Current Smoker	320 (25.3)	264 (19.7)
Education		
<12 years	200 (16.7)	165 (12.0)
High School Graduate	419 (34.5)	390 (31.5)
Some College	328 (26.3)	356 (27.3)
College Graduate	270 (22.5)	324 (29.3)
Family History of Cancer		

	Case	Control
Characteristics	**N (%[a])**	**N (%[a])**
No	517 (42.0)	566 (42.3)
Yes- Other than Kidney	636 (53.8)	633 (55.8)
Yes- Kidney Cancer	52 (4.3)	24 (2.0)

Abbreviations: BMI- body mass index; N- number; std- standard deviation.

[a] A sample-weighted frequency distribution.

[b] BMI five years before interview.

[c] Smoked 100 cigarettes in the lifetime, but never >1 cigarette a day for six months or longer.

Table 2

Weighted analysis for RCC risk and occupational sunlight exposure, stratified by race

	ALL				WHITES				BLACKS				
	Cases	Controls			Cases	Controls			Cases	Controls			
Sunlight	N (%[a])	N (%[a])	OR (95%CI)	*P*-trend[b]	N (%[a])	N (%[a])	OR (95%CI)	*P*-trend[b]	N (%[a])	N (%[a])	OR (95%CI)	*P*-trend[b]	lrt
Cumulative Exposure (low exposure-unit years)													
<4.19	315 (24.8)	301 (21.8)	1.00 [Ref]		227 (24.3)	156 (21.5)	1.00 [Ref]		88 (26.5)	145 (22.8)	1.00 [Ref]		
≥4.19-<6.30	281 (23.0)	300 (24.1)	0.80 (0.61 to 1.06)		191 (21.7)	163 (23.4)	0.78 (0.57 to 1.07)		90 (26.8)	137 (26.0)	0.88 (0.55 to 1.42)		
≥6.30-<9.00	262 (23.2)	303 (26.5)	0.67 (0.50 to 0.90)		194 (24.3)	192 (27.5)	0.69 (0.49 to 0.97)		68 (20.0)	111 (23.4)	0.65 (0.38 to 1.12)		
≥9 .00	321 (29.0)	301 (27.7)	0.74 (0.56 to 0.99)		228 (29.8)	186 (27.7)	0.78 (0.54 to 1.11)		93 (26.7)	115 (27.7)	0.68 (0.42 to 1.11)		
				0.03				0.20				0.07	0.83
Frequency-Adjusted Duration of Exposure (years)													
<4.17	315 (24.8)	301 (21.7)	1.00 [Ref]		227 (24.3)	156 (21.3)	1.00 [Ref]		88 (26.5)	145 (22.7)	1.00 [Ref]		
≥4.17-<6.24	285 (23.2)	302 (24.1)	0.80 (0.61 to 1.06)		194 (22.0)	161 (23.1)	0.79 (0.58 to 1.08)		91 (26.8)	141 (27.1)	0.85 (0.54 to 1.35)		
≥6.24-<8.68	263 (23.5)	301 (26.1)	0.66 (0.49 to 0.89)		193 (24.4)	188 (27.0)	0.67 (0.48 to 0.94)		70 (20.9)	113 (23.6)	0.68 (0.40 to 1.16)		
≥8.68	316 (28.5)	301 (28.1)	0.70 (0.52 to 0.94)		226 (29.3)	192 (28.7)	0.70 (0.48 to 1.03)		90 (25.9)	109 (26.6)	0.69 (0.42 to 1.13)		
				0.01				0.07				0.09	0.81
Frequency-Adjusted Duration of Exposure Among Only Low Intensity Jobs (years)													
<4.17	309 (28.7)	294 (24.1)	1.00 [Ref]		222 (28.0)	152 (23.5)	1.00 [Ref]		87 (30.6)	142 (25.8)	1.00 [Ref]		
≥4.17-<6.24	273 (26.3)	286 (26.0)	0.81 (0.61 to 1.07)		186 (25.0)	154 (24.8)	0.80 (0.58 to 1.10)		87 (29.9)	132 (29.6)	0.86 (0.53 to 1.39)		
≥6.24-<8.68	235 (24.9)	274 (27.1)	0.63 (0.47 to 0.86)		174 (26.1)	175 (28.1)	0.64 (0.45 to 0.90)		61 (21.4)	99 (24.0)	0.65 (0.38 to 1.10)		
≥8.68	188 (20.2)	212 (22.9)	0.56 (0.40 to 0.79)		135 (20.9)	141 (23.7)	0.55 (0.36 to 0.85)		53 (18.1)	71 (20.6)	0.60 (0.34 to 1.05)		
				0.0003				0.004				0.04	0.54
Frequency-Adjusted Duration of Exposure Among Any High Intensity Jobs (years)													
<8.68	46 (25.4)	50 (30.6)	1.00 [Ref]		32 (24.9)	24 (27.9)	1.00 [Ref]		14 (27.2)	26 (36.2)	1.00 [Ref]		

	ALL				WHITES				BLACKS				
	Cases	Controls			Cases	Controls			Cases	Controls			
Sunlight	**N (%[a])**	**N (%[a])**	**OR (95%CI)**	***P*-trend[b]**	**N (%[a])**	**N (%[a])**	**OR (95%CI)**	***P*-trend[b]**	**N (%[a])**	**N (%[a])**	**OR (95%CI)**	***P*-trend[b]**	**lrt**
≥8.68	128 (74.6)	89 (69.4)	1.23 (0.72 to 2.11)		91 (75.1)	51 (72.1)	1.06 (0.48 to 2.33)		37 (72.8)	38 (63.8)	1.78 (0.57 to 5.56)		
													0.66

Abbreviations: BMI- body mass index; CI- confidence interval; lrt- likelihood ratio test; N, number; OR- odd ratio; RCC- renal cell carcinoma; Ref- reference.

Analyses adjusted for sex, race, smoking status, age, BMI, hypertension, family history of cancer, education, center and dietary vitamin D intake.

[a] A sample-weighted frequency distribution.

[b] *P*-value from sample Wald F-test.

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Table 3

Weighted analysis for RCC risk and occupational sunlight exposure, stratified by sex and race

	Cases	Controls			Cases	Controls			Cases	Controls			
Sunlight	**N (%[a])**	**N (%[a])**	**OR (95% CI)**	***P*-trend[b]**	**N (%[a])**	**N (%[a])**	**OR (95% CI)**	***P*-trend[b]**	**N (%[a])**	**N (%[a])**	**OR (95% CI)**	***P*-trend[b]**	**lrt**
WOMEN					WHITE WOMEN				BLACK WOMEN				
Cumulative Exposure (low exposure to unit years)													
<4.19	236 (50.4)	230 (44.4)	1.00 [Ref]		185 (51.9)	127 (47.1)	1.00 [Ref]		51 (45.3)	103 (37.0)	1.00 [Ref]		
≥4.19-<6.30	148 (31.3)	167 (29.6)	0.90 (0.63 to 1.28)		110 (31.5)	68 (26.2)	0.98 (0.66 to 1.46)		38 (30.8)	99 (38.6)	0.68 (0.35 to 1.31)		
≥6.30-<9.00	63 (14.2)	100 (19.6)	0.54 (0.35 to 0.84)		40 (12.5)	49 (19.3)	0.47 (0.28 to 0.79)		23 (19.5)	51 (20.2)	0.68 (0.29 to 1.63)		
≥9 .00	20 (4.1)	27 (6.5)	0.48 (0.21 to 1.00)		14 (4.0)	16 (7.3)	0.42 (0.16 to 1.12)		6 (4.4)	11 (4.3)	0.72 (0.22 to 2.43)		
				0.007				0.008				0.33	0.46
Frequency to Adjusted Duration of Exposure (years)													
<4.17	236 (50.4)	230 (44.1)	1.00 [Ref]		185 (51.9)	126 (46.7)	1.00 [Ref]		51 (45.3)	104 (37.3)	1.00 [Ref]		
≥4.17-<6.24	149 (31.5)	167 (29.1)	0.92 (0.64 to 1.31)		111 (31.8)	68 (25.3)	1.03 (0.69 to 1.53)		38 (30.8)	99 (39.3)	0.65 (0.33 to 1.28)		
≥6.24-<8.68	66 (14.8)	102 (21.0)	0.52 (0.34 to 0.79)		41 (12.8)	52 (21.6)	0.42 (0.25 to 0.70)		25 (21.0)	50 (19.1)	0.86 (0.42 to 1.73)		
≥8.68	16 (3.3)	25 (5.8)	0.39 (0.16 to 0.98)		12 (3.4)	14 (6.4)	0.35 (0.13 to 0.99)		4 (2.9)	11 (4.3)	0.47 (0.09 to 2.60)		
				0.003				0.002				0.33	0.29
Frequency to Adjusted Duration of Exposure Among Only Low Intensity Jobs (years)													
<4.17	233 (51.6)	227 (45.4)	1.00 [Ref]		182 (52.9)	125 (48.1)	1.00 [Ref]		51 (47.6)	102 (38.0)	1.00 [Ref]		
≥4.17-<6.24	145 (31.9)	161 (29.2)	0.96 (0.67 to 1.38)		108 (32.1)	66 (25.7)	1.06 (0.71 to 1.60)		37 (31.4)	95 (39.0)	0.68 (0.35 to 1.34)		
≥6.24-<8.68	60 (14.2)	97 (20.5)	0.49 (0.32 to 0.76)		39 (12.8)	49 (21.0)	0.42 (0.25 to 0.71)		21 (18.7)	48 (19.3)	0.71 (0.34 to 1.47)		
≥8.68	10 (2.3)	20 (4.8)	0.33 (0.11 to 0.97)		7 (2.2)	11 (5.2)	0.28 (0.08 to 0.95)		3 (2.4)	9 (3.7)	0.47 (0.06 to 3.83)		
				0.002				0.001				0.19	0.45
Frequency to Adjusted Duration of Exposure Among Any High Intensity Jobs (years)													
<8.68	13 (70.4)	14 (66.5)	1.00 [Ref]		8 (64.1)	6 (57.3)	1.00 [Ref]		5 (85.7)	8 (83.9)	1.00 [Ref]		

	Cases	Controls			Cases	Controls			Cases	Controls			
Sunlight	**N (%[a])**	**N (%[a])**	**OR (95% CI)**	***P*-trend[b]**	**N (%[a])**	**N (%[a])**	**OR (95% CI)**	***P*-trend[b]**	**N (%[a])**	**N (%[a])**	**OR (95% CI)**	***P*-trend[b]**	**lrt**
≥8.68	6 (29.6)	5 (33.6)	0.17 (0.00 to 86.59)		5 (35.9)	3 (42.7)	2.20 (0.80 to 6.02)		1 (14.3)	2 (16.1)	-----		
													0.92
MEN					WHITE MEN				BLACK MEN				
Cumulative Exposure (low exposure to unit years)													
<4.19	79 (9.9)	71 (8.1)	1.00 [Ref]		42 (7.7)	29 (6.2)	1.00 [Ref]		37 (16.1)	42 (13.7)	1.00 [Ref]		
≥4.19-<6.30	133 (18.1)	133 (20.7)	0.78 (0.49 to 1.25)		81 (15.8)	95 (21.6)	0.63 (0.34 to 1.19)		52 (24.5)	38 (18.1)	1.34 (0.66 to 2.70)		
≥6.30-<9.00	199 (28.5)	203 (30.6)	0.79 (0.50 to 1.25)		154 (31.3)	143 (32.4)	0.80 (0.43 to 1.47)		45 (20.3)	60 (25.5)	0.75 (0.36 to 1.57)		
≥9 .00	301 (43.6)	274 (40.5)	0.87 (0.57 to 1.32)		214 (45.2)	170 (39.8)	0.88 (0.47 to 1.65)		87 (39.0)	104 (42.7)	0.84 (0.47 to 1.50)		
				0.98				0.42				0.17	0.054
Frequency to Adjusted Duration of Exposure (years)													
<4.17	79 (9.8)	71 (8.1)	1.00 [Ref]		42 (7.7)	30 (6.3)	1.00 [Ref]		37 (13.4)	41 (16.1)	1.00 [Ref]		
≥4.17-<6.24	136 (18.3)	135 (21.1)	0.78 (0.49 to 1.23)		83 (16.2)	93 (21.7)	0.65 (0.35 to 1.22)		53 (19.2)	42 (24.6)	1.28 (0.65 to 2.54)		
≥6.24-<8.68	197 (28.6)	199 (29.2)	0.81 (0.52 to 1.28)		152 (31.3)	136 (30.1)	0.85 (0.46 to 1.54)		45 (26.5)	63 (20.8)	0.73 (0.35 to 1.52)		
≥8.68	300 (43.2)	276 (41.6)	0.84 (0.54 to 1.30)		214 (44.9)	178 (41.9)	0.84 (0.44 to 162)		86 (40.9)	98 (38.5)	0.86 (0.48 to 1.52)		
				0.83				0.72				0.22	0.13
Frequency to Adjusted Duration of Exposure Among Only Low Intensity Jobs (years)													
<4.17	76 (12.1)	67 (9.2)	1.00 [Ref]		40 (9.4)	27 (6.9)	1.00 [Ref]		36 (19.5)	40 (16.5)	1.00 [Ref]		
≥4.17-<6.24	128 (22.2)	125 (23.7)	0.76 (0.47 to 1.24)		78 (19.7)	88 (24.2)	0.61 (0.31 to 1.20)		50 (29.0)	37 (22.4)	1.27 (0.61 to 2.62)		
≥6.24-<8.68	175 (32.6)	177 (31.6)	0.76 (0.46 to 1.24)		135 (36.0)	126 (32.8)	0.74 (0.38 to 1.45)		40 (23.1)	51 (27.7)	0.74 (0.35 to 1.56)		
≥8.68	178 (33.2)	192 (35.5)	0.65 (0.40 to 1.06)		128 (34.9)	130 (36.1)	0.60 (0.28 to 1.29)		50 (28.4)	62 (33.5)	0.72 (0.39 to 1.35)		
				0.10				0.38				0.09	0.48
Frequency to Adjusted Duration of Exposure Among Any High Intensity Jobs (years)													
<8.68	33 (20.8)	36 (25.9)	1.00 [Ref]		24 (21.2)	18 (24.2)	1.00 [Ref]		9 (19.4)	18 (29.6)	1.00 [Ref]		

	Cases	Controls			Cases	Controls			Cases	Controls			
Sunlight	**N (%[a])**	**N (%[a])**	**OR (95% CI)**	***P*-trend[b]**	**N (%[a])**	**N (%[a])**	**OR (95% CI)**	***P*-trend[b]**	**N (%[a])**	**N (%[a])**	**OR (95% CI)**	***P*-trend[b]**	**lrt**
≥8.68	122 (79.2)	84 (74.1)	1.72 (0.92 to 3.21)		86 (78.8)	48 (75.8)	1.54 (0.61 to 3.90)		36 (80.6)	36 (70.4)	2.72 (0.73 to 10.10)		
													≥0.99

Abbreviations: BMI- body mass index; CI- confidence interval; lrt- likelihood ratio test for interaction; N- number; OR- odds ratio; RCC- renal cell carcinoma; Ref.- reference.

Analyses adjusted for sex, race, smoking status, age, BMI, hypertension, family history of cancer, education, center and dietary vitamin D intake.

[a] A sample to weighted frequency distribution.

[b] P to value from sample Wald F to test.

Years of exposure among female participants: range=0.09 to 32.82, mean=4.53, median=4.35; years of exposure among white female participants: range=0.09 to 32.82, mean=4.41, median=4.07; years of exposure among black female participants: range=0.18 to 18.66, mean=4.72, median=4.73.

Years of exposure for only low intensity jobs for female participants: range=0.09 to 26.23, mean=4.37, median=4.29; years of exposure for only low intensity jobs among white female participants: range=0.09 to 26.23, mean=4.21, median=4.05; years of exposure for only low intensity jobs among black female participants: range=0.18 to 16.40, mean=4.61, median=4.65.

Years of exposure for any high intensity jobs for female participants: range=0.99 to 32.82, mean=8.65, median=7.67; years of exposure for any high intensity jobs among white female participants: range=1.09 to 32.82, mean=9.58, median=7.11; years of exposure for any high intensity jobs among black female participants: range=0.99 to 18.66, mean=7.36, median=7.74.

Years of exposure among male participants: range=0.12 to 58.88, mean=9.81, median=7.93; years of exposure among white male participants: range=0.58 to 43.70, mean=10.02, median=8.04; years of exposure among black male participants: range=0.12 to 58.88, mean=9.38, median=7.55.

Years of exposure for only low intensity jobs for male participants: range=0.12 to 58.88, mean=8.49, median=7.31; years of exposure for only low intensity jobs among white male participants: range=0.78 to 43.70, mean=8.72, median=7.54; years of exposure for only low intensity jobs among black male participants: range=0.12 to 58.88, mean=8.01, median=6.76.

Years of exposure for any high intensity jobs for male participants: range=0.58 to 41.83, mean=15.17, median=13.06; years of exposure for any high intensity jobs among white male participants: range=0.58 to 41.12, mean=15.59, median=13.07; years of exposure for any high intensity jobs among black male participants: range=3.44 to 41.83, mean=14.43, median=12.58.