Catalogue no. 82-003-X
ISSN 1209-1367

Health Reports

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Release date: May 17, 2017

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^{p}	preliminary
^{r}	revised
x	suppressed to meet the confidentiality requirements of the *Statistics Act*
^{E}	use with caution
F	too unreliable to be published
*	significantly different from reference category ($p < 0.05$)

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The risk of melanoma associated with ambient summer ultraviolet radiation

by Lauren Pinault, Tracey Bushnik, Vitali Fioletov, Cheryl E. Peters, Will D. King and Michael Tjepkema

Abstract

Background: Depletion of the ozone layer has meant that ambient ultraviolet radiation (UVR) has increased in recent decades. At the same time, the incidence of skin cancers, including melanoma, has risen. The relatively few large-scale studies that linked ambient UVR to melanoma found a trend toward rising incidence closer to the equator, where UVR estimates are highest. Similar research has not been conducted in Canada, where ambient UVR is generally lower than in countries further south.

Data and methods: Modelled UVR data for the months of June through August during the 1980-to-1990 period were spatially linked in Geographic Information Systems to 2.4 million white members of the 1991 Canadian Census Health and Environment Cohort and tracked for melanoma diagnosis over an 18-year period (1992 to 2009). Standard Cox proportional hazards models were used to estimate melanoma risk associated with increases of ambient summer UVR, assigned by residence at baseline. Models were adjusted for age, sex and socioeconomic (SES) characteristics. Separate analyses by body site of melanoma were conducted. Effect modification of the association between ambient UVR and melanoma by sex, age, outdoor occupation and selected SES characteristics was evaluated.

Results: Differences of one standard deviation (446 J/m^2 or 7%) in average ambient summer UVR were associated with an increased hazard ratio (HR) for melanoma of 1.22 (95% CI: 1.19 to 1.25) when adjusting for sex, age and SES characteristics. The HR for melanoma in relative UVR (per 1 standard deviation) was larger for men (HR = 1.26; 95% CI: 1.21 to 1.30) than for women (HR = 1.17; 95% CI: 1.13 to 1.22).

Interpretation: Ambient summer UVR is associated with a greater risk of melanoma among the white population, even in a country where most people live within a narrow latitudinal belt. A stronger association between melanoma and ambient UVR was evident among men and among people of lower SES.

Key words: CanCHEC, census, medical record linkage, skin cancer, skin neoplasms, sunburn, sunlight

Ultraviolet radiation (UVR) is part of the total radiation that reaches the surface of the Earth. It can be modelled using geophysical characteristics, including ozone and cloud cover derived from satellite observations, and data from ground-based spectrophotometers.[1] Depletion of the ozone layer has increased the intensity of UVR, particularly in regions closer to the poles.[2-4]

UVR exposure has harmful effects on the skin, including sunburn, skin aging, and skin cancer development as either non-melanoma (basal and squamous cell carcinomas) or melanoma skin cancers.[5,6] Carcinogenesis in skin is influenced by DNA damage, gene mutation, immunosuppression, oxidative stress and inflammatory response, all of which can be attributed to UVR.[7]

Cutaneous melanoma (hereafter referred to as "melanoma") is among the 10 most common cancers diagnosed in Canada, with 6,800 new cases in 2015.[8,9] Between 1986 and 2010, incidence increased, on average, by 2% per year among men and by 1.5% per year among women.[8] Melanoma mortality also rose, especially among men, whose age-standardized mortality rate increased 1.2% per year between 1986 and 2009.[8]

UVR through sun exposure is the leading risk factor for melanoma.[10] Additional risk factors include the presence of nevi, fair skin and light hair, family or personal history of melanoma, immune suppression, older age, male sex and xeroderma pigmentosum.[6,8] A lower incidence among post-menopausal women suggests that differences in susceptibility between the sexes may be linked to hormones.[11] A study in the United Kingdom found a higher incidence of melanoma among more affluent socio-economic (SES) groups, possibly because of exposure to UVR through travel or other behavioural differences.[12]

The present study sought to determine if large-scale patterns of association between ambient UVR and melanoma incidence exist in Canada, even though most of the population lives within a narrow latitudinal range. Modelled UVR data were spatially linked to members of the 1991 Canadian Census Health and Environment Cohort (CanCHEC), a dataset comprising 2.6 million census respondents who were followed for melanoma diagnosis over an 18-year period. Owing to data limitations, the risk of developing melanoma attributed to ambient UVR was determined only for white cohort members. The effect modification of the strength of this association by sex, age and SES characteristics was also evaluated.

Non-melanoma skin cancers are more common than melanoma (an estimated 76,100 diagnoses in 2014[8]), but because incidence data are lacking in most provinces, they were not considered in this study.

Methods

Data sources

UVR data were derived from a statistical model developed by Environment Canada, which represented the mean erythemal and vitamin D action spectrum weighted UVR estimates for 1980 to 1990.[1] The model was based on measurements of

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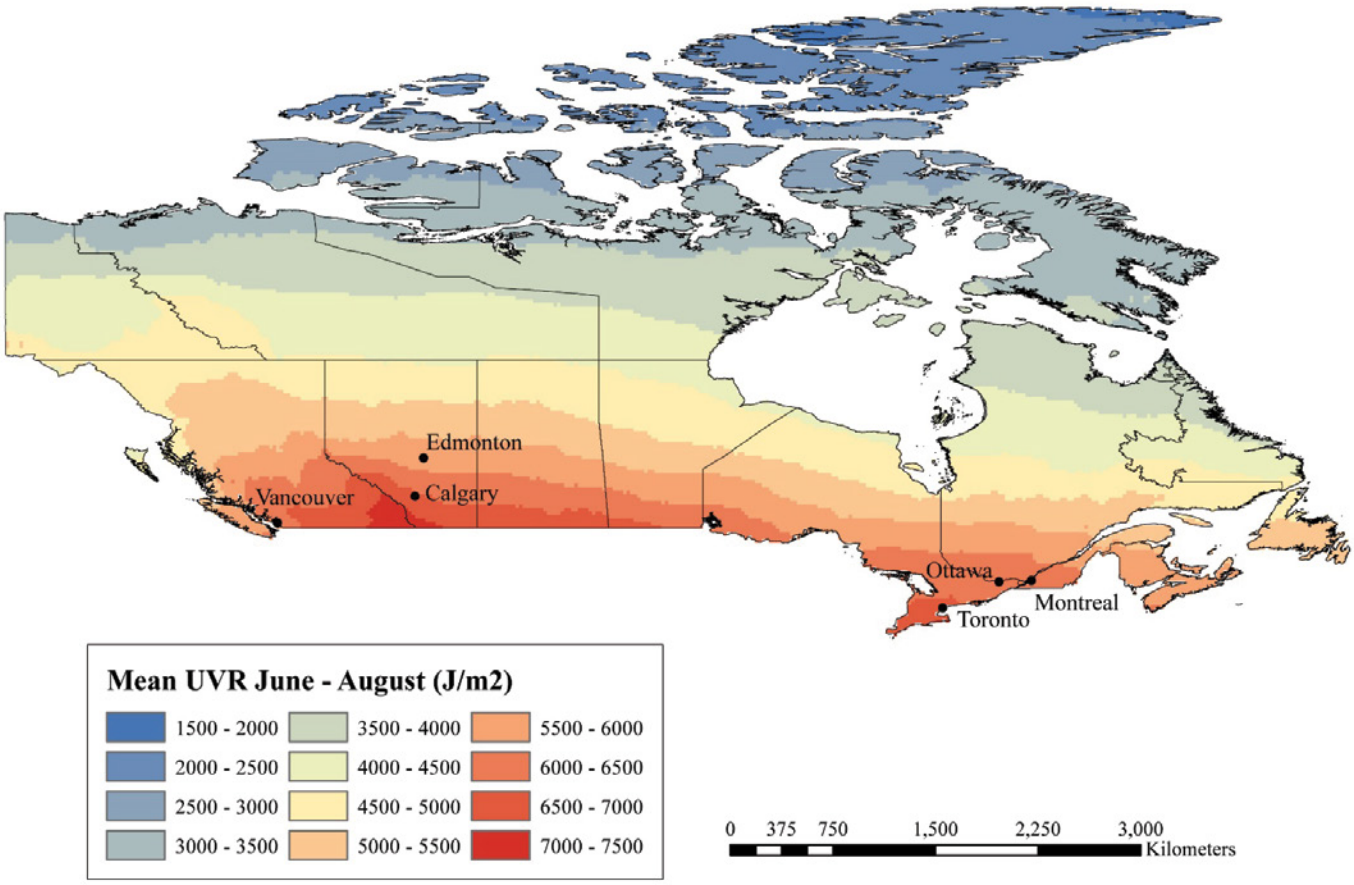
Map 1
Mean ultraviolet radiation (UVR) in Joules per metres squared (J/m²) for June through August, Canada, 1980 through 1990



Source: Environment Canada, modelled UVR data.

solar radiation by pyranometers and satellite observations (by Total Ozone Mapping Spectrometer) for ozone, with adjustments for snow cover, altitude and air pressure.[1] It was validated with ground-based measurements by Brewer spectrophotometers in Canada and the United States.[1]

The UVR model used was based on the vitamin D production action spectrum UV.[1] The action spectrum for melanoma is not well established. UVB (short wavelength: 320 to 290 nm) may play a stronger role in melanoma initiation than UVA (long wavelength: 400 to 320 nm),[13] although broad associations between UVA and melanoma have been described.[14] Because the vitamin D action spectrum is far less sensitive for UVA than the erythemal (skin reddening) action spectrum, it is more suitable as a proxy for a melanoma action spectrum. UV values weighted according to the erythemal and vitamin D action spectra are nearly proportional in summer.[15]

Ozone absorbs solar UVB and prevents approximately 97% of UVB from reaching the Earth's surface.[16] (Cloud cover can also block some UVR.[16]) The 1980-to-1990 decade was a period of increased UVR irradiance (for example, as much as 5% of summer UVB in Toronto) due to ozone depletion.[16] Since these long-term changes are relatively small compared with latitudinal differences, for this project, it was assumed that mean UVR from 1980 to 1990 also applied to the years after 1990. Given that most exposure to UVR in Canada is limited to summer months, the estimate used for this study was mean daily UVR for June through August (Map 1).

CanCHEC is a dataset formed through linkage of 2.6 million respondents to the 1991 Census long-form questionnaire with the Canadian Mortality Database (CMDB), the Canadian Cancer Registry (CCR), the Canadian Cancer Database (CCDB) and the Historical Tax Summary File (HTSF), using standard deterministic and probabilistic linkage techniques.[17] Respondents to the long-form questionnaire represented about 20% of Canadian households. Respondents were eligible for inclusion in CanCHEC if they consented to link their data, were aged 25 or older on census day (June 4, 1991), and were not residents of institutions.[17] Follow-up for death or cancer was until December 31, 2009.

The linkage has been documented elsewhere.[17] The cohort has been validated and used in other environmental health research.[18] The cohort is generally representative of the Canadian population, but contains larger percentages of people who are: working age, married or in a common-law relationship, urban residents, of higher education and income, labour force participants and not Aboriginal.[17]

Based on postal codes reported to the 1991 Census, respondent residences were mapped at baseline (census day) in a Geographic Information System (GIS) (ArcGIS v.10, ESRI 2010), using Statistics Canada's Postal Code Conversion File (PCCF+) version 5K.[19] The PCCF+ program employs a population-weighted random allocation algorithm to assign approximate postal code location (for example, a block face centroid), with a reported error rate of 1.4% in Census Metropolitan Areas.[19] UVR estimates (point values at baseline) were extracted for all respondent residence points using GIS.

The original 2,630,000 CanCHEC members (rounded to nearest 100) aged 25 to 89 were linked to UVR data. Recent immigrants (107,400 who arrived during the 10 years immediately before 1991) were excluded from this study because their UVR exposure history was unknown. To ensure similar risk among cohort members at the beginning of follow-up, an additional 2,300 who had been diagnosed with melanoma (recorded in the CCDB) during the 10-year washout period before cohort inception were excluded. As well, 122,700 people who were members of visible minorities were excluded, because fewer than 100 melanoma cases were found among this group. Visible minority status is derived from ethnic origin and other ethno-cultural information and is defined as persons (other than Aboriginal) who are non-Caucasian in race or non-white in colour.[20]

After exclusions, 2,397,600 respondents were included in this study (13.2% of the 1991 Canadian population aged 25 to 89).

Table 1
Mean ultraviolet radiation (UVR) exposure, number of melanoma cases diagnosed from 1992 through 2009 and hazard ratios for melanoma diagnosis, by selected characteristics, 1991 Canadian Census Health and Environment Cohort

Characteristic	Cohort members	UVR exposure‡ (Joules per metres squared) Mean	Standard deviation	Melanoma cases§	Hazard ratio††	95% confidence interval from	to
Total	2,397,600	6,176	453	8,900	...	...	...
Sex							
Men	1,187,300	6,163	458	4,900	1.33*	1.28	1.39
Women†	1,210,300	6,171	449	3,900	1.00	...	...
Age group (years)							
25 to 34†	664,900	6,135	492	1,400	1.00	...	...
35 to 44	620,200	6,145	471	2,000	1.62*	1.51	1.73
45 to 54	411,100	6,170	446	1,900	2.40*	2.24	2.57
55 to 64	315,500	6,207	414	1,800	3.26*	3.04	3.49
65 to 74	249,300	6,222	383	1,300	3.81*	3.53	4.11
75 to 84	115,700	6,220	372	400	3.70*	3.29	4.16
85 to 89	20,800	6,224	364	<100	3.79*	2.72	5.28
Immigrant status							
Not immigrant†	2,071,700	6,138	461	7,400	1.00	...	...
Immigrant	325,900	6,352	346	1,500	1.02	0.96	1.08
Marital status							
Married or common-law†	1,774,100	6,166	460	7,100	1.00	...	...
Separated, widowed, divorced	327,000	6,194	412	1,000	0.82*	0.77	0.88
Single	296,500	6,145	455	700	0.83*	0.77	0.90
Household income adequacy quintile							
1st (lowest)†	386,200	6,144	467	900	1.00	...	...
2nd	453,100	6,163	456	1,400	1.23*	1.13	1.34
3rd	498,500	6,169	451	1,600	1.35*	1.24	1.47
4th	522,400	6,174	448	2,100	1.63*	1.50	1.76
5th	537,300	6,179	448	2,800	1.94*	1.80	2.10
Educational attainment							
Less than secondary completion†	847,700	6,136	478	2,500	1.00	...	...
Secondary completion	879,200	6,170	448	3,200	1.41*	1.34	1.49
Postsecondary non-university	369,300	6,189	437	1,500	1.68*	1.58	1.80
University graduation	301,300	6,218	408	1,600	2.05*	1.93	2.19
Occupational group							
Management†	197,300	6,200	446	1,000	1.00	...	...
Professional	266,300	6,182	451	1,300	1.04	0.96	1.13
Skilled, technical, supervisory	578,800	6,155	467	2,100	0.76*	0.71	0.82
Semi-skilled	573,100	6,169	456	1,800	0.71*	0.66	0.77
Unskilled	180,400	6,115	512	500	0.55*	0.49	0.61
Not employed	601,700	6,175	418	2,200	0.61*	0.56	0.67
Outdoor occupation							
No†	2,187,600	6,175	446	8,200	1.00	...	...
Yes	207,100	6,080	516	600	0.78*	0.72	0.85

… not applicable
* significantly different from reference category ($p < 0.05$)
† reference category
‡ mean for June, July and August, 1980 through 1990
§ rounded to nearest hundred; may not add to totals because of rounding
†† stratified by age (5-year age groups) and sex, except sex (stratified only by age) and age (stratified only by sex)
Source: 1991 Canadian Census Health and Environment Cohort (CanCHEC) linked to UVR dataset.

Statistical analysis

Standard Cox proportional hazard models were used to examine associations between ambient UVR and SES characteristics and the incidence of melanoma.[21] Malignant melanoma was identified with variables for histology (ICD-O-3 codes 8720 to 8790), behaviour (ICD-O-3 code 3) and site (ICD-O-2/3 codes C440 to C449), consistent with methods used by the Canadian Cancer Society.[8] Respondents were followed for melanoma diagnosis from census day to the diagnosis date recorded in the CCR, the date of death recorded in the CMDB, or

the final date of follow-up (December 31, 2009). Only the first instance of a case of melanoma is recorded in the CCR; as a result, the dataset does not contain duplicate cases.

All models were stratified by age (5-year age groups) and sex, except for comparisons within age groups or by sex. Demographic and SES characteristics (at baseline) were: immigrant (immigrated more than 10 years before census day), marital status, household income adequacy quintile, educational attainment, occupational group and outdoor occupation (Table 1). Household income adequacy quintiles were calculated based on the ratio of household income to the low-income cut-off for their household and community size. Low-income cut-offs, adjusted for household size and community size/region,[17,20] identify households spending more than 20% of their income on food, shelter and clothing. A variable indicating occupations performed primarily outdoors (at least two hours a day) was developed from National Occupational Classification for Statistics (NOC-S 2006) and industry of work variables in the census, based on CAREX Canada job exposure matrices,[22] and verified by an industrial hygienist.

Separate analyses were conducted to examine associations between ambient UVR and melanoma by sex and by site (head or neck: ICD-O-2/3 topography codes C440 to C444; trunk: C445; upper limb or shoulder: C446; or lower limb or hip: C447). Effect modification of this association was examined by comparing sex (and sex by site of melanoma), broad age groups (younger than 65 versus 65 or older), outdoor occupation, household income adequacy quintile (lowest versus highest), and educational attainment (less than secondary completion versus university graduation). Cochran's Q was used to test for statistically significant differences between hazard ratios (HR).[23]

To examine the shape of the relationship between the risk of melanoma (HR) and ambient UVR, spline HR curves were fitted using the smoothing method in the R package, "smoothHR," on a fully adjusted HR model.[24]

To comply with disclosure guidelines, after analysis, sample sizes were rounded to the nearest 100.

Table 2
Adjusted hazard ratios for melanoma diagnosis from 1992 through 2009, by sex and selected characteristics, 1991 Canadian Census Health and Environment Cohort

	Total (n = 8,900)‡			Men (n = 4,900)§			Women (n = 3,900)§		
		95% confidence interval			95% confidence interval			95% confidence interval	
Characteristic	Hazard ratio	from	to	Hazard ratio	from	to	Hazard ratio	from	to
UV radiation Z-score	1.22*	1.19	1.25	1.26*	1.21	1.30	1.17*	1.13	1.22
Immigrant status									
Not immigrant†	1.00	…	…	1.00	…	…	1.00	…	…
Immigrant	0.93*	0.88	0.99	0.85*	0.79	0.92	1.07	0.98	1.17
Marital status									
Married or common-law†	1.00	…	…	1.00	…	…	1.00	…	…
Separated, widowed, divorced	0.92*	0.86	0.99	0.88*	0.79	0.99	0.94	0.85	1.03
Single	0.87*	0.80	0.94	0.89*	0.80	1.00	0.85*	0.75	0.95
Household income adequacy quintile									
1st (lowest)†	1.00	…	…	1.00	…	…	1.00	…	…
2nd	1.16*	1.06	1.26	1.14*	1.00	1.28	1.18*	1.05	1.33
3rd	1.21*	1.11	1.32	1.21*	1.07	1.36	1.22*	1.08	1.37
4th	1.39*	1.28	1.51	1.45*	1.29	1.63	1.32*	1.17	1.49
5th	1.52*	1.40	1.65	1.55*	1.38	1.74	1.48*	1.32	1.68
Educational attainment									
Less than secondary completion†	1.00	…	…	1.00	…	…	1.00	…	…
Secondary completion	1.29*	1.22	1.36	1.23*	1.14	1.32	1.37*	1.26	1.50
Postsecondary non-university	1.46*	1.36	1.56	1.34*	1.21	1.48	1.58*	1.43	1.74
University graduation	1.65*	1.53	1.79	1.66*	1.50	1.83	1.63*	1.44	1.84
Occupational group									
Management†	1.00	…	…	1.00	…	…	1.00	…	…
Professional	0.93	0.85	1.01	0.89*	0.79	0.99	1.01	0.86	1.17
Skilled, technical, supervisory	0.88*	0.82	0.95	0.87*	0.80	0.96	0.93	0.80	1.07
Semi-skilled	0.88*	0.81	0.96	0.83*	0.75	0.93	0.95	0.82	1.09
Unskilled	0.76*	0.68	0.85	0.80*	0.69	0.92	0.73*	0.60	0.89
Not employed	0.84*	0.77	0.92	0.91	0.81	1.02	0.82*	0.70	0.96
Outdoor occupation									
No†	1.00	…	…	1.00	…	…	1.00	…	…
Yes	0.95	0.87	1.03	0.94	0.85	1.04	1.06	0.87	1.29

… not applicable
* significantly different from reference category ($p < 0.05$)
† reference category
‡ stratified by sex and age (5-year age groups) and adjusted for all covariates in model
§ stratified by age (5-year age groups) and adjusted for all covariates in model
Source: 1991 Canadian Census Health and Environment Cohort (CanCHEC) linked to ultraviolet radiation (UVR) dataset.

Results

UVR exposure

In Canada, UVR was generally highest in southerly latitudes, although estimates for mountainous regions in the west surpassed those for regions further east, largely because of altitude and less cloud cover (Map 1). For example, the difference in mean June through August UVR exposure (Joules per metres squared, J/m^2, a unit of radiation) between Toronto and Montreal was 326 J/m^2 (5.3%), and between Calgary and Edmonton, 734 J/m^2 (12%).

Mean June-to-August UVR exposure among CanCHEC members was 6,176 J/m^2 and ranged from 2,678 J/m^2 to 7,290 J/m^2 (Table 1). UVR exposure varied little by demographic and SES characteristics, although immigrants' exposure was 214 J/m^2 higher than that of non-immigrants ($p < 0.0001$). The UVR exposure estimate for cohort members diagnosed with melanoma was slightly below the mean: 6,133.6 J/m^2 (data not shown in tables).

Table 3
Adjusted hazard ratios for melanoma diagnosis from 1992 through 2009, by melanoma site and selected characteristics, 1991 Canadian Census Health and Environment Cohort

	Head or neck (n = 1,600)			Trunk (n = 2,800)			Upper limb or shoulder (n = 2,000)			Lower limb or hip (n = 1,800)		
		95% confidence interval			95% confidence interval			95% confidence interval			95% confidence interval	
Characteristic	Hazard ratio	from	to	Hazard ratio	from	to	Hazard ratio	from	to	Hazard ratio	from	to
UV radiation Z-score	1.11*	1.05	1.17	1.31*	1.25	1.37	1.29*	1.22	1.36	1.21*	1.15	1.28
Immigrant status												
Not immigrant†	1.00	…	…	1.00	…	…	1.00	…	…	1.00	…	…
Immigrant	0.92	0.81	1.05	0.88*	0.79	0.98	0.87*	0.77	0.98	1.14*	1.00	1.29
Marital status												
Married or common-law†	1.00	…	…	1.00	…	…	1.00	…	…	1.00	…	…
Separated, widowed, divorced	0.87	0.74	1.02	0.97	0.85	1.11	0.97	0.83	1.12	0.78*	0.67	0.91
Single	0.84	0.69	1.02	0.87*	0.75	1.00	0.88	0.74	1.04	0.83*	0.70	0.98
Household income adequacy quintile												
1st (lowest)†	1.00	…	…	1.00	…	…	1.00	…	…	1.00	…	…
2nd	1.19	0.99	1.43	1.34*	1.14	1.58	1.02	0.85	1.23	1.04	0.87	1.26
3rd	1.25*	1.03	1.50	1.48*	1.26	1.74	1.08	0.91	1.29	1.04	0.86	1.25
4th	1.33*	1.10	1.60	1.62*	1.38	1.90	1.38*	1.16	1.63	1.22*	1.01	1.46
5th	1.38*	1.14	1.66	1.85*	1.58	2.17	1.53*	1.29	1.82	1.36*	1.14	1.64
Educational attainment												
Less than secondary completion†	1.00	…	…	1.00	…	…	1.00	…	…	1.00	…	…
Secondary completion	1.18*	1.04	1.33	1.34*	1.21	1.47	1.28*	1.14	1.43	1.53*	1.34	1.74
Postsecondary non-university	1.49*	1.28	1.75	1.34*	1.18	1.52	1.39*	1.20	1.60	1.88*	1.61	2.19
University graduation	1.68*	1.40	2.00	1.48*	1.29	1.70	1.71*	1.46	2.01	2.12*	1.77	2.52
Occupational group												
Management†	1.00	…	…	1.00	…	…	1.00	…	…	1.00	…	…
Professional	0.88	0.70	1.10	0.96	0.83	1.11	0.84	0.71	1.01	0.94	0.78	1.14
Skilled, technical, supervisory	1.07	0.88	1.30	0.82*	0.72	0.93	0.82*	0.70	0.96	0.86	0.72	1.04
Semi-skilled	0.94	0.76	1.16	0.88	0.77	1.01	0.82*	0.69	0.97	0.85	0.70	1.02
Unskilled	0.92	0.70	1.21	0.69*	0.57	0.85	0.82	0.66	1.03	0.53*	0.39	0.71
Not employed	0.97	0.79	1.21	0.91	0.77	1.07	0.73*	0.60	0.88	0.78*	0.63	0.96
Outdoor occupation												
No†	1.00	…	…	1.00	…	…	1.00	…	…	1.00	…	…
Yes	1.02	0.85	1.22	1.03	0.90	1.18	1.05	0.90	1.24	1.13	0.96	1.33

… not applicable
* significantly different from reference category ($p < 0.05$)
† reference category
Note: All models stratified by age (5-year age groups) and sex, and adjusted for all covariates in model.
Source: 1991 Canadian Census Health and Environment Cohort (CanCHEC) linked to ultraviolet radiation (UVR) dataset.

Table 4
Number of melanoma cases diagnosed from 1992 through 2009 and adjusted hazard ratios for effect modification of association between ambient ultraviolet radiation (UVR) and melanoma diagnosis, by melanoma site and selected characteristics, 1991 Canadian Census Health and Environment Cohort

			95% confidence interval					95% confidence interval		Cochran's Q	
Category 1	Melanoma cases	Hazard ratio	from	to	Category 2	Melanoma cases	Hazard ratio	from	to	Q	p
Men (all sites)	4,900	1.26	1.21	1.30	**Women (all sites)**	3,900	1.17	1.13	1.22	7.22	0.007
Head or neck	1,100	1.13	1.05	1.20	Head or neck	500	1.08	0.98	1.19	0.57	0.452
Trunk	2,000	1.32	1.25	1.39	Trunk	800	1.28	1.18	1.39	0.38	0.537
Upper limb or shoulder	1,000	1.37	1.27	1.48	Upper limb or shoulder	1,000	1.21	1.12	1.30	5.19	0.023
Lower limb or hip	500	1.19	1.07	1.32	Lower limb or hip	1,300	1.22	1.15	1.30	0.16	0.688
Younger than 65	7,200	1.21	1.18	1.24	**65 or older**	1,700	1.26	1.18	1.34	1.23	0.267
Outdoor occupation	600	1.37	1.26	1.49	**Other/No occupation**	8,200	1.23	1.20	1.26	5.76	0.016
Lowest household income adequacy quintile	900	1.27	1.18	1.37	**Highest household income adequacy quintile**	2,800	1.16	1.11	1.21	3.92	0.048
Less than secondary completion	2,500	1.30	1.24	1.36	**University graduation**	1,600	1.13	1.06	1.20	13.75	<0.001

Notes: All models stratified by age (5-year age groups) and sex, and adjusted for immigrant status, marital status, household income adequacy quintile, educational attainment, occupational group, and outdoor occupation, except for covariate used for comparison.
Source: 1991 Canadian Census Health and Environment Cohort (CanCHEC) linked to UVR dataset.

Melanoma cases

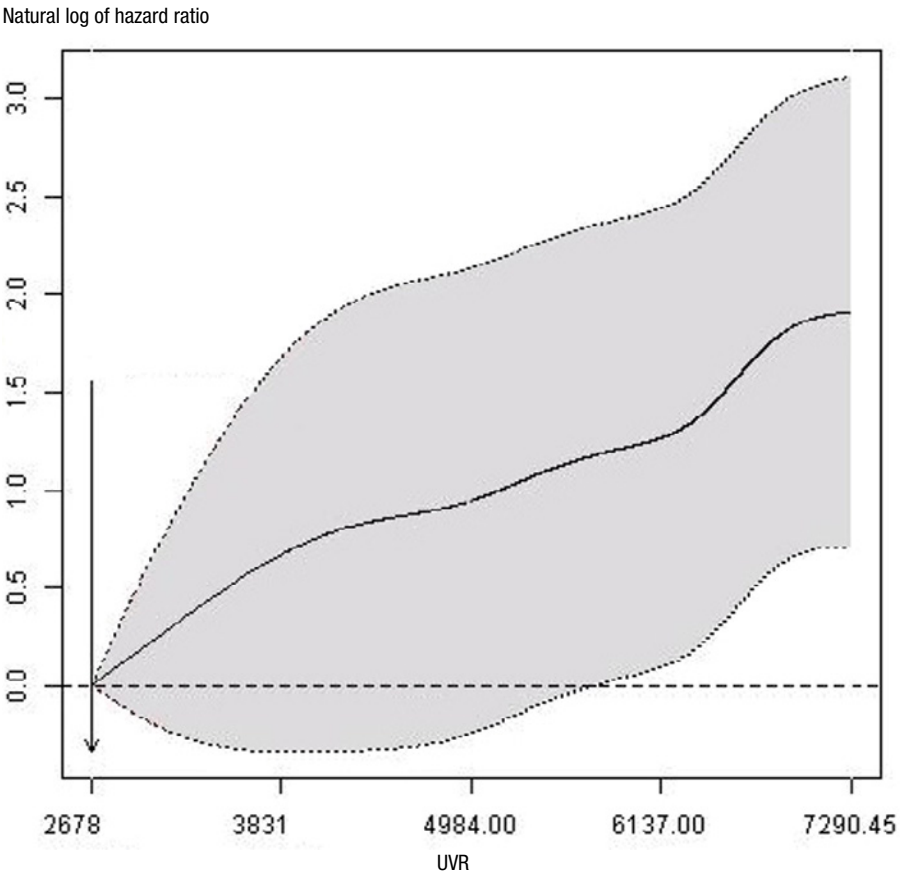
During the 18-year follow-up, 8,900 cases of melanoma were diagnosed among CanCHEC members: 4,900 among men and 3,900 among women (Table 1). When considered separately, most covariates were associated with an increased or decreased risk of melanoma. Greater risk was associated with male sex, older age, higher household income adequacy quintile, and higher educational attainment; lower risk was associated with unmarried marital status, occupations other than those designated management or professional, and outdoor occupations.

The sites where melanoma tended to be diagnosed differed for men and women. Compared with women, men had a greater risk of melanoma of the head or neck (HR = 2.25; 95% CI: 2.03 to 2.49) and trunk (HR = 2.53; 95% CI: 2.34 to 2.75), no significant difference for the upper limb or shoulder (HR = 1.08; 95% CI: 0.99 to 1.18), and a lower risk for the lower limb or hip (HR = 0.36; 95% CI: 0.33 to 0.40) (models stratified by 5-year age group) (data not shown in tables).

Ambient UVR and melanoma

UVR was transformed to a z-score for analysis, where 1 unit of the z-score (and the unit used for HRs) corresponded to 1 standard deviation (S.D.) of UVR—an increase of 446 J/m^2, or about 7% of the mean. The HR for melanoma associated with a 1 S.D. increase in the z-score of ambient UVR was 1.22 (95% CI: 1.19 to 1.25) for both sexes when adjusting for all covariates (Table 2). For men, the HR for melanoma associated with ambient UVR was 1.26 (95% CI: 1.21 to 1.30), which was statistically greater than that for women (HR = 1.17; 95% 1.13 to 1.22) (Cochran's Q = 7.22; $p < 0.01$) (Table 2). When these HRs were scaled to a real-world example, the HR for melanoma comparing the difference in UVR between Toronto and Montreal was 1.16 (95% CI: 1.13 to 1.18); the difference between Calgary and Edmonton was 1.38 (95% CI: 1.33 to 1.44) (data not shown in tables).

Figure 1
Nonparametric estimates of association between melanoma diagnosis from 1992 through 2009 and summer-month ultraviolet radiation (UVR) exposure, 1991 Canadian Census Health and Environment Cohort



Note: Model stratified by age and sex and adjusted for all covariates in Table 1.

Associations between ambient UVR and melanoma differed by site of diagnosis. The HR for melanoma per increase of 1 S.D. in z-score was 1.31 (95% CI: 1.25 to 1.37) for the trunk, which was significantly greater than the HR for the head or neck (Cochran's Q = 20.97; $p < 0.001$) or for the lower limb or hip (Cochran's Q = 4.88; p = 0.027) (Table 3).

The association between ambient UVR and melanoma was significantly elevated among men, people with outdoor occupations, those in the lowest household income adequacy quintile (versus the highest), and those who had less than secondary completion (versus university graduation) (Table 4). Although lower-income and less-educated respondents had a lower overall risk of melanoma, the association with ambient UVR was stronger among these groups, especially outdoor workers (versus those who did not work outside). Significantly weaker associations between ambient UVR and melanoma were observed among people in the highest income adequacy quintile (versus the lowest) and the highest educational attainment group (versus the lowest).

The relationship between ambient UVR and the HR for melanoma can be depicted as an increasing exponential curve. As a result, the model of best fit (based on Akaike Information Criterion and Bayesian Information Criterion) was an approximately linear relationship between the natural log (ln) of the HR and increasing UVR (Figure 1).

Discussion

This analysis was based on linkage of a large, nationally representative cohort of census respondents to a model of summertime UVR exposure. Among the white population, rising ambient UVR was associated with an increased risk of melanoma diagnosis. The overall adjusted HR for melanoma was 1.22 per increase of summertime UVR of 446 J/m^2 (about 7% of the mean daily summertime UVR dose).

By site of diagnosis, HRs for melanoma per increase in UVR were greater for the trunk than for the head, lower limb or hip. Greater melanoma risk associated with ambient summertime UVR was observed for men, people in the lowest household income adequacy quintile, and people who had not completed secondary school.

A strength of this study was the large size of CanCHEC, among whom 8,900 cases of melanoma were diagnosed during the 18-year follow-up. The large sample size permitted examination of effect modification of melanoma risk by sex and SES, and made it possible to adjust risk estimates for a variety of SES characteristics.

Another strength of this study was the ability to adjust estimates for immigrant status, and remove recent immigrants from the analytical cohort, thereby excluding people whose recent UVR exposure was largely unknown.

The association between ambient UVR and melanoma described in the present analysis was generally consistent with results for the United States and Europe,[25-29] even though methodologies differed. In the United States, geographic associations between UVR and skin cancer (and melanoma) incidence and mortality, particularly among the non-Hispanic white population, have been reported.[25-27] In Europe, increased melanoma incidence in southerly latitudes has been observed.[28,29] Although statistics indicate a higher incidence of melanoma in several northern European countries where UVR is low (Norway, the Netherlands, Denmark, Sweden), these statistics do not account for differences in susceptibility due to skin colour or behaviour.[30]

The identification of increased melanoma risk related to recent ambient UVR exposure in this analysis is relatively novel. An international case-control study found significantly increased risk for ambient UVR exposure only during childhood (highest versus lowest exposure quartile: OR = 2.10, 95% CI: 1.43 to 3.08), and weak or non-significant associations with exposure during adulthood.[31] Similarly, a prospective study of American women reported an increased melanoma risk for UVR exposure estimated at birth and at age 15, but no association with UVR exposure during adulthood (age 30).[32]

Men's risk of melanoma was greater than women's, and the relationship between ambient UVR and melanoma risk was stronger among men. Data from the 2006 Second National Sun Survey indicated that men spend more time in the sun—in excess of 2 hours a day for 35% of men, compared with 19% of women.[33] Men are also less likely to use sun protection.[33] In the present study, men had a greater risk of melanoma of the trunk and upper limb or shoulder; women had a greater risk of melanoma of the lower limb or hip. Previous studies suggested that this may be due to behaviour (for example, clothing).[34] Differences in associations between ambient UVR and melanoma by site may be attributable to the likelihood of chronic versus sporadic exposure and to the risk of sunburn of different sites—according to the National Sun Survey, in 47% of cases of serious sunburn, the trunk was the main body part affected.[34]

In this analysis, overall melanoma risk was associated with higher household income, higher educational attainment and higher status occupations. This is consistent with a 2008 study in England that reported reduced melanoma risk among people of lower SES.[12] However, despite the greater risk of melanoma among among higher SES people in Canada, the association between ambient UVR and melanoma was significantly weaker in these groups. The elevated overall risk among higher SES groups might be influenced less by ambient UVR exposure and more by exposures such as sun vacations, leisure-time activities, and differences in sun protection. For example, higher SES adults are more likely to report sunburn[35] and less likely to wear protective clothing or seek shade.[36]

The stronger association between ambient UVR and melanoma among people in lower income adequacy quintiles, outdoor workers and those who had not completed secondary school sug-

What is already known on this subject?

- Exposure to ultraviolet radiation (UVR) is a major risk factor for melanoma skin cancer.
- In other countries, latitudinal gradients in melanoma incidence and mortality have been attributed to differences in ambient UVR.
- Similar research has not been conducted in Canada where most people live within a narrow latitudinal belt.

What does this study add?

- When adjusting for age, sex and socioeconomic status, differences of one standard deviation (446 J/m^2 or 7%) in average ambient summer UVR exposure were associated a melanoma hazard ratio (HR) of 1.22.
- HRs for melanoma overall were greater for men than for women.
- Melanoma HRs were greater for men on the head or neck and trunk, but greater for women on the lower limb or hip.
- Higher melanoma risk associated with ambient summer UVR was observed for men, people in the lowest household income adequacy quintile (versus highest), and those with the lowest (versus highest) educational attainment.

gests greater everyday exposure in the summer, and a weaker role for exposures such as sun vacations and tanning.

Limitations

The small number of melanoma cases (fewer than 100) among visible minority cohort members prevented extending this study to the non-white population. As well, it was not possible to account for differences in intermittent or chronic exposure to UVR such as the use of tanning equipment, sun vacations and early life sunburns.[5,30,37] Skin pigmentation, the presence of nevi, diet, immune suppression, exposure to other carcinogens, genetic susceptibility, family history of melanoma and other risk factors[6,8] could not be taken into account.

UVR exposure was estimated from a static, three-month average model, and did not adjust for personal exposure to UVR. It is possible that exposure might be confounded with UVR if persons in high-UVR environments also spend more time outdoors.

Several sources of error were introduced through either the UVR model or the cohort. The UVR model was based on action spectra for vitamin D production. However, the actual action spectrum for melanoma carcinogenesis is not known. And as noted, the UVR model was based on the years 1980 to 1990 and on the assumption that modelled UVR would be similar during follow-up. But because UVR increased during this period,[2-4] the model likely underestimated actual exposure, although the underestimate would affect all cohort members equally.

UVR estimates were assigned at baseline from residence geocoded using the postal code and PCCF+ program. In urban settings where postal code areas are small (typically, a few city blocks), the PCCF+ program is accurate.[19] However, in rural locales where postal code areas can be large, estimates of ambient UVR are less likely to have been assigned accurately. This inaccuracy may be partially mitigated by relatively low spatial variability in the UVR model.

The use of baseline residence also increases the possibility of exposure misclassification because of residential moves. Nonetheless, previous air pollution research using CanCHEC indicated that assigning exposures using mobility rather than at baseline had little effect on hazard ratios. Few respondents moved far enough during follow-up to experience substantially different exposure.[38] By 2007, only 7.4% of cohort members had moved to a different province. However, it is likely that baseline estimates for UVR differ to some degree from those that would be derived from mobility, and that use of the latter would reduce exposure misclassification.

Conclusion

This analysis highlights the role of ambient UVR during the summer as an important predictive factor in melanoma incidence in Canada. The association between ambient UVR and melanoma was modified by sex and by SES characteristics. Although the overall risk was less among people of lower SES, a stronger association was observed between ambient UVR and melanoma among these groups. Additional research is necessary to include the role of personal behaviours in ambient UVR exposure to determine their combined influence on melanoma risk. ■

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