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Estimates of the current and future burden of melanoma attributable to ultraviolet radiation in Canada

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ABSTRACT

Exposure to ultraviolet radiation (UVR) is an established cause of cutaneous melanoma. The purpose of this study was to estimate the current attributable and future avoidable burden of melanoma related to exposure to UVR and modifiable UVR risk behaviors (sunburn, sunbathing, and indoor tanning). The population attributable risk (PAR) associated with UVR in 2015 was estimated by comparing Canadian melanoma incidence rates in 2015 to estimated incidence rates of a 1920 birth cohort. Rates were adjusted for changes in reporting and ethnicity. We estimated PARs for modifiable UVR risk behaviors using Caucasian prevalence data from the Second National Sun Survey and relative risks that are generalizable to Canada from meta-analyses of relevant studies. Attributable cases apply to 98.9% of melanomas in Canada that occur in Caucasians. We also estimated the future burden of UVR risk behaviors using the potential impact fraction framework and potential reductions in prevalence of 10% to 50% from 2018 to 2042. Adult sunburn and sunbathing were associated with increased risks of melanoma of 1.28 (95% CI: 1.15, 1.43) and 1.44 (95% CI: 1.18, 1.76), respectively. In 2015, we estimate that 62.3% of melanomas in Canada were attributable to exposure to UVR and that 29.7% were attributable to the combination of sunburn (7.4%), sunbathing (17.8%), and indoor tanning (7.0%). A 50% reduction in modifiable UVR behaviors could avoid an estimated 11,980 melanoma cases by 2042. Prevention strategies aimed at modifiable UVR behaviors are crucial to reduce the growing burden of melanoma in Canada.

1. Introduction

Incidence rates of cutaneous malignant melanoma in Canada have increased steadily between 1970 and 2010 (Kachuri et al., 2013), and in 2017, an estimated 7323 new cases of melanoma were diagnosed (Canadian Cancer Society, 2018). While the overall relative increase in incidence during this time period has been larger for men than women, from 1992 to 2010 there have been greater relative increases for

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women (Kachuri et al., 2013). Exposure to ultraviolet radiation (UVR) from the sun is the primary risk factor for melanoma. The International Agency for Research on Cancer (IARC) has concluded that exposure to solar UVR is carcinogenic to humans and causes cutaneous malignant melanoma (International Agency for Research (IARC), 2010, 1992). More recently IARC recognized that artificial sources of UVR such as indoor tanning devices are also carcinogenic (International Agency for Research (IARC), 2012).

The classification of UVR as a human carcinogen draws on substantial epidemiological evidence. Ambient UVR is strongest at low latitudes and ecological studies of Caucasian populations show increased incidence of melanoma among those in close proximity to the equator (Armstrong and Kricker, 2001). Evidence from a large number of case–control studies is generally consistent, showing positive associations with residing in areas with high ambient UVR throughout life, in early life, and even for short periods in early adult life (Armstrong and Kricker, 2001). The body site distribution of melanoma favors sites usually exposed to the sun, such as the head and neck or the forearms (Elwood and Gallagher, 1998). The behavioral patterns of UVR exposure that are associated with melanoma are complex and in some cases divergent. Positive associations are consistently observed between a history of sunburn and measures of intermittent exposure to the sun (such as sunbathing) and melanoma at all latitudes (Chang et al., 2009; Gandini et al., 2005). Occupational and chronic patterns of exposure appear to be stronger risk factors at low latitudes, where ambient UVR is strongest (Chang et al., 2009; Gandini et al., 2005). However, the lack of an association at higher latitudes could be a product of the referent group including individuals with high levels of intermittent sun exposure and from the majority of this evidence coming from case-control studies that may be subject to recall bias (Armstrong and Kricker, 2001; Gandini et al., 2005).

Estimating the proportion of incident cases of melanoma that are attributable to UVR exposure is challenging, as solar UVR is a ubiquitous exposure and the carcinogenic effects are dependent on latitude and behavioral patterns (Chang et al., 2009; Gandini et al., 2005). It is therefore difficult to capture the risk and distribution of relevant types of exposure for a specific population. Given this challenge, previous population attributable risk (PAR) studies for Ontario (Cancer Care Ontario, 2016), the United Kingdom (Parkin et al., 2011), France (Arnold et al., 2018a,b; Boffetta et al., 2008), the United States (Schottenfeld et al., 2013), Australia (Armstrong and Kricker, 1993; Olsen et al., 2015), Columbia (de Vries et al., 2017) and worldwide (Arnold et al., 2018a,b) have relied on a method of estimation that calculates the difference between the melanoma incidence in the target population and a theoretical 'unexposed' population. The most commonly employed variant of this approach is to use the melanoma rates in an early birth cohort (with assumed greater skin coverage and lower UVR exposure) as the non-exposed group in a comparison with current melanoma rates. The method of PAR estimation based on prevalence of exposure and relative risk estimates for UVR risk factors is less frequently used since the measurement of exposure and the corresponding relative risk is difficult to capture. Additionally, these exposures merit specific methods in the estimation of PAR because of the high correlation between UVR risk factors (Ezzedine et al., 2008; Holman et al., 2014). However, this approach to PAR estimation is important, since it represents the proportion of melanoma cases that could be reduced by the modification of individual behaviors.

In this study, we estimated the proportion and number of incident cutaneous melanoma cases in the Canadian population in 2015 that were attributed to UVR and modifiable UVR risk behaviors, including indoor tanning, sunburn, and sunbathing. In addition, the potential impact fractions and number of melanoma cases that could be prevented up to 2042 under different scenarios of UVR risk behavior change were estimated.

2. Methods

2.1. Current burden – population attributable risk estimation

The general methodologic framework for this project has previously been published (Brenner et al., 2018) and a brief overview has been included in this special issue (Brenner et al., 2019). Given the unique nature of UVR exposure, a modified approach was used for this risk factor. To estimate the proportion of melanoma cases in Canada in 2015 that were attributable to UVR exposure, a birth cohort comparison was conducted. To estimate attributable cases to different UVR risk behaviors the traditional risk factor approach was employed. Joint prevalence distributions were used to estimate a combined UVR risk behavior PAR. Occupational exposure to UVR was not considered in the ComPARe Study.

2.1.1. Birth cohort comparison

To estimate an overall PAR for UVR exposure, we used the direct approach to PAR estimation:

$$PAR = \frac{Incidence_{population} - Incidence_{non-exposed}}{Incidence_{population}}$$

In this analysis, $\text{Incidence}_{\text{population}}$ was the incidence rate of melanoma in Canada in 2015, and $\text{Incidence}_{\text{non-exposed}}$ was the estimated incidence rate of melanoma for a 1920 birth cohort in Canada. Using melanoma incidence data from 1971 to 2015 a log normal age-cohort model was fit and used to predict incidence rates for a 1920 birth cohort. The 1920 birth cohort was selected to avoid predicting incidence far outside of the range of the data.

Given that melanoma is often treated outside of hospital settings, there is potential for under-reporting to Canadian cancer registries, and capture-recapture studies from Ontario provide evidence of this (Tran et al., 2013; Walter et al., 1994). To account for this, the annual number of melanoma cases were inflated by the proportion of cases not reported, using capture rates from Ontario in 1976 (Walter et al., 1994) and 1993–2009 (Tran et al., 2016). A logistic regression model was used to extrapolate these capture rates to years without these data. Years 2004 and 2005 were removed from the model, since the capture rates were unusually low (66.8% and 51.4% compared to 88.7% and 96.0% in 2003 and 2006, respectively) and therefore not representative of national capture rates.

Melanoma rates differ by ethnicity (in particular rates are 20 times lower among Blacks and Asians compared to Caucasians) (Erdei and Torres, 2010), and the ethnic distribution of the Canadian population has diversified in the most recent cohort. Given that the current evidence suggests that melanoma in Blacks and Asians is not attributable to UVR exposure to the same degree as in Caucasians, one method to account for the contemporary shift in ethnicity is to only apply this approach to Caucasians, Hispanics, and Aboriginals. The proportion of Blacks and Asians in years 1971 to 2015 was estimated using Canadian census data in five-year increments starting at 1971 and ending at 2016. Proportions between the census years were estimated by assuming a consistent increasing or decreasing trend. The numbers of melanoma cases in Blacks and Asians were estimated by applying the incidence rate from the US (SEER) to the number of Black and Asians in each year by age and sex. These melanoma cases were then subtracted from the total number of reported adjusted melanoma cases, which were then divided by the number of Caucasians, Hispanics, and Aboriginals in the cohort to derive a rate.

Age- and sex-specific PARs were estimated to account for changes in the population distribution of age and sex between the two cohorts. The numbers of attributable cases in 2015 were summed and divided by the total cases to estimate an overall PAR.

2.1.2. UVR risk factor approach

The proportion of melanoma cases in 2015 in Canada attributable to different UVR risk behaviors (indoor tanning, sunburn, and sunbathing) was estimated using the traditional risk factor approach that applies summary relative risks and population prevalence estimates to the Levin formula (Levin, 1953). The methods for estimating PARs for indoor tanning and the results for that analysis have been previously published (O'Sullivan et al., 2019).

2.1.2.1. Estimating relative risks relevant in Canada. Given that ambient UVR varies across countries, it is important to consider studies that are generalizable to Canada. To determine relative risks for each UVR risk behavior, a systematic review and meta-analysis was conducted to identify studies that were relevant to the Canadian population. A full-text review of all studies included in the most recent review for the risk of melanoma associated with solar UVR behaviors (International Agency for Research (IARC), 2010, 1992), as well as a systematic review of studies published after 2007 were conducted. The literature search was conducted in PubMed using the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). All studies published between January 2008 and August 2018 were reviewed using the following search terms: "sun" or "sunbathing" or "sunburn" or "sunlight" or "solar ultraviolet" or "sunbed" or "indoor tanning" or "artificial ultraviolet" and "melanoma". The latter terms relevant to indoor tanning were included to capture studies that include sunburn or sunbathing as secondary analyses. Abstract and title screening was conducted by DO'S, while full-text review was performed by two independent reviewers in a blinded review (DO'S and WDK). The final inclusion criteria for studies included in the quantitative meta-analysis were studies: 1) conducted at a northern latitude (> 39 N); 2) reported an effect estimate for adult or lifetime exposure; 3) adjusted for important confounders (host characteristics and other UVR risk behaviors in this study); 4) did not adjust for variables on the causal pathway (dysplastic nevi); 5) contained an appropriate control group (was not related to exposure to UVR); and 6) included all histological subtypes of melanoma. If two studies reported on the same population, the study with the largest sample size or with the most relevant exposure was included in the meta-analysis.

For studies that met our inclusion criteria we extracted the adjusted effect estimates for "ever" being exposed to the UVR risk factor. Some studies included in this analysis reported effect estimates for different levels of exposure rather than an overall estimate for "ever" being exposed. To obtain an "ever" exposed metric to match our prevalence estimates, effect estimates for exposure levels were combined using inverse variance weighting. The standard error for this estimate was computed using crude data to adjust for the degree of covariance among the exposure categories (Greenland and Longnecker, 1992). If a prospective study reported effect estimates for different periods of life, the period that best approximated lifetime exposure was used. This best lifetime exposure period was determined using the longest exposure window or exposure period closest to diagnosis that was not within the defined latency period.

For the purposes of this study, hazard ratios and odds ratios were treated as approximations of relative risk. DerSimonian and Laird random-effect models were used in all analyses (DerSimonian and Laird, 1986). The degree of heterogeneity was estimated using the Q-test and the I^2 statistics (Deeks et al., 2011). To assess publication bias we inspected funnel plots and employed both Egger's weighted linear regression (Egger et al., 1997) and Begg's rank correlation tests (Begg and Mazumdar, 1994). Where there was evidence of publication bias, the trim and fill approach was employed to obtain a summary relative risk estimate. All analyses were performed using the R computing framework (www.r-project.org).

2.1.2.2. Estimating prevalence of exposure. UVR risk behaviors are represented as "ever being exposed" and therefore we required prevalence estimates at the end of the relevant exposure period. A lag period of five-years between exposure prevalence and cancer incidence was used – requiring prevalence data from 2010. Prevalence was based on the 2006 National Sun Survey (NSS2) (Marrett et al., 2010) to represent the target year of 2010. Age-sex specific prevalence estimates of sunburn and sunbathing among Caucasians in the past year were obtained from the NSS2. Most studies assessing the association of UVR risk factors with melanoma derive relative risk estimates by comparing melanoma incidence rates among those who have "ever been exposed" to those who have not. Given this issue, conversion factors for each of the risk factors were estimated to convert "exposed in the past year" to "ever exposed". Conversion factors for adults were estimated by comparing ever exposure of the control group in a Canadian-specific study conducted in Ontario (Walter et al., 1999) to past year prevalence estimates for Ontario from the First National Sun Survey (Shoveller et al., 1998). These conversion factors were then applied to the prevalence of exposure for the two oldest age groups and sex reported in the NSS2. Conversion factors for the youngest age group were not estimated due to a lack of data and, therefore, it was assumed that past-year exposure represented ever exposure in this age-group.

Table 1
Melanoma cases diagnosed in 2015, estimated to be attributable to increases in UVR exposure in Canada.

Age	Melanoma			All cancers[a]	
	Obs.	PAR	AC	Obs.	PAR
Males					
20–34	105	70.5	74	845	8.8
35–49	405	74.3	301	5355	5.6
50–64	1135	72.0	817	27,920	2.9
65+	2165	60.7	1314	60,790	2.2
Total	3810	65.8	2506	94,910	2.6
Females					
20–34	225	68.0	153	1370	11.2
35–49	540	71.9	388	10,300	3.8
50–64	990	66.0	653	29,635	2.2
65+	1300	44.3	576	50,855	1.1
Total	3055	57.9	1770	92,160	1.9
Total	6865	62.3	4276	187,070	2.3

Abbreviations: AC = Attributable cases due, Obs. = Observed cases, PAR = Population attributable risk.

[a] Excludes cases of non-melanoma skin cancer.

2.1.2.3. Cancer incidence and target population. Melanoma incidence by age and sex in 2015 was obtained from the Canadian Cancer Registry. Given that the relative risks for UVR risk behaviors are primarily derived from studies that only include Caucasians, and that the majority of melanoma cases in Canada occur among Caucasians, our PAR estimates only apply to this subgroup. To apply our approach exclusively to Caucasians, UVR risk behavior prevalence for Caucasians was ascertained from the NSS2. To estimate the number of attributable cases, the Caucasian-specific PARs were then applied to 98.9% of melanoma cases in Canada.

2.1.2.4. Population attributable risk. Age- and sex-specific exposure prevalence and summary relative risk estimates from meta-analyses were applied to the Levin formula (Levin, 1953) to estimate age- and sex-specific PARs for each UVR risk factor. PAR estimates were applied to Canadian melanoma incidence data for each age and sex category, and the number of attributable cases was summed. The number of attributable cases was divided by the total incident cases in 2015 to obtain overall PARs associated with each UVR risk factor. Monte Carlo simulation methods were used to estimate 95% confidence intervals (CIs) around PAR estimates. The same methods were used to estimate PARs for Canadian provinces.

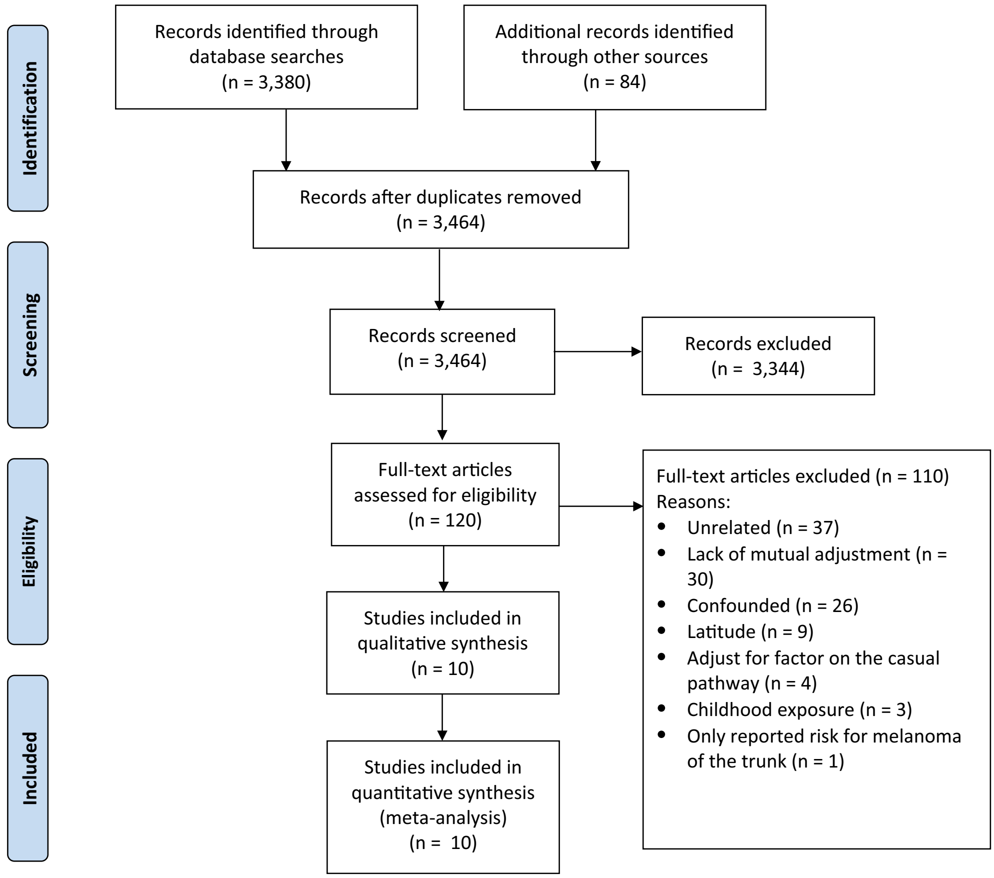

Fig. 1. Flow diagram of the selection procedure of studies relevant to Canada assessing the relationship of sunburn or sunbathing with the risk of melanoma.

Table 2
Characteristics of studies relevant to Canada investigating the association of sunburn and/or sunbathing with the risk of melanoma (n = 10).

Study and location	Design	Population	Age (range)	% Men	Exposure(s)
Autier, 1994 Europe	Population case-control 1991–1992	412 cases, 445 controls	20– > 60	45.0	Sunburn
Autier, 1998 Europe	Population case-control 1991–1992	412 cases, 445 controls	20– > 60	45.0	Sunbathing
Bataille, 2004 United Kingdom	Hospital based case-control 1989–1993	413 cases, 416 controls	16–75	Not reported	Sunburn
Chen, 1996 Connecticut, USA	Population case-control 1987–1989	512 cases, 624 controls	> 18	52.8	Sunburn
Han, 2006 USA (Nurses)	Nested case-control 1989–1998	200 cases, 804 controls	30–79	0.0	Sunbathing and sunburn
Kaskel, 2001 Germany	Hospital based case-control 1996–1997	271 cases, 271 controls	Not reported	Not reported	Sunbathing
Nielsen, 2012 Sweden	Prospective cohort 1990–1992	215 cases, 29,305 non-cases	25–64	0.0	Sunburn and sunbathing
Walter, 1999 Ontario, Canada	Population case-control 1984–1986	583 cases, 608 controls	20–69	47.1	Sunburn
Westerdahl, 1994 Sweden	Population case-control 1988–1990	400 cases, 640 controls	15–75	48.8	Sunbathing
Zaridze, 1992 Russia	Population case-control not reported	96 cases, 96 controls	Not reported	Not reported	Sunbathing

2.1.2.5. Combined UVR risk behavior PAR estimation. Given that UVR risk behaviors are strongly related (Ezzedine et al., 2008; Holman et al., 2014) and that combined PAR estimates can be underestimated when risk factors are dependent (Poirier et al., 2019b), joint exposure distributions of sunburn, sunbathing, and indoor tanning were used to estimate a combined PAR. To estimate a combined UVR risk behavior PAR, joint prevalence distributions of the UVR risk factors in the past year by age and sex were obtained from the NSS2. To obtain a measure of ever exposure within each joint distribution stratum, we used the relationships between the risk factors in the past year and the marginal totals to apply these relationships to our estimated "ever" exposures. Multiplicative relative risks were then applied to each joint distribution prevalence and PAR estimated for a multilevel exposure (Hanley, 2001).

2.2. Future burden – potential impact fraction estimation

2.2.1. Prevalence of exposure projections

Estimates of future PAR and PIF require an assumed exposure distribution. There are insufficient historical data on the prevalence of UVR risk behaviors necessary to project future trends. Therefore, we assumed stable prevalence of exposure in the future based on the NSS2.

2.2.2. Cancer incidence projections

The methodology for cancer incidence projections has been published previously (Poirier et al., 2019a). Briefly, a decision algorithm to choose the most appropriate model for the projection was used and face validity was evaluated independently of goodness-of-it. Sex-specific incidence for melanoma was projected using a negative-binomial based age-drift-period-cohort model (Moller et al., 2002).

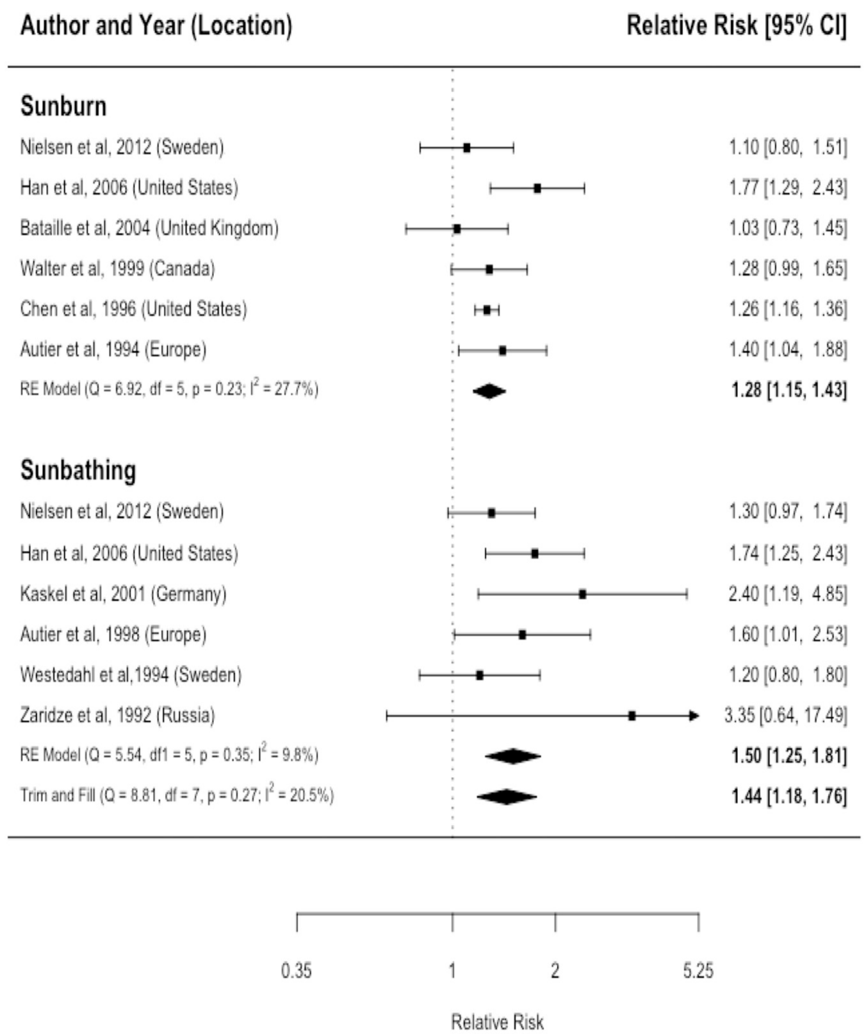

Fig. 2. Estimated relative risk of melanoma for sunburn and sunbathing that are generalizable to Canada.

Table 3
Estimated prevalence of exposure to sunburn and sunbathing among Caucasian Canadians.[a]

Age (years)	Prevalence (95% confidence interval)					
	Sunburn			Sunbathing		
	Past year (%)	Conversion factor[b]	Ever exposed (%)	Past year (%)	Conversion factor[b]	Ever exposed (%)
Men						
16–24	35.5 (30.1–41.3)	–	35.5 (30.1–41.3)	35.2 (29.9–41.0)	–	35.2 (29.9–41.0)
25–44	27.6 (24.8–30.7)	1.72	47.5 (42.7–52.8)	20.7 (18.1–23.5)	2.75	56.8 (49.8–64.6)
44+	18.1 (15.8–20.6)	1.72	31.1 (27.2–35.4)	15.4 (13.3–17.7)	2.75	42.3 (36.6–48.7)
Total	23.6 (21.8–25.5)	–	37.0 (34.2–40.0)	19.9 (18.3–21.6)	–	45.9 (42.2–49.8)
Women						
16–24	33.7 (28.9–38.9)	–	33.7 (28.9–38.9)	53.0 (47.8–58.2)	–	53.0 (47.8–58.2)
25–44	22.8 (20.5–25.3)	1.72	39.3 (35.2–43.5)	32.9 (30.3–35.6)	2.75	90.5 (83.3–97.9)
44+	11.1 (9.6–12.9)	1.72	19.2 (16.5–22.2)	18.2 (16.3–20.2)	2.75	50.0 (44.8–55.6)
Total	17.7 (16.4–19.1)	–	27.3 (25.3–29.5)	27.3 (25.7–28.9)	–	62.8 (59.1–66.5)
Overall	20.6 (19.5–21.7)	–	32.1 (30.4–33.8)	23.7 (22.6–24.9)	–	54.5 (52.0–57.3)

Note: Total and overall prevalence calculated by population weighted averages.
[a] Data from the Second National Sun Survey (2006).
[b] Conversion factors were estimated by comparing estimates from Walter et al. (1999) and The First National Sun Survey.

2.2.3. Counterfactuals

To estimate the proportion of melanoma cases associated with UVR risk behaviors that could be avoided in the future, we considered three counterfactual scenarios (10, 25, and 50% reductions by 2037 – assuming a 5 year latency period). These counterfactuals were applied to each UVR risk behavior, as well as to all UVR risk behaviors combined. For the latter, we assumed for each counterfactual scenario that the percentage reduction in exposure would occur equally across joint exposure categories. To estimate the cumulative cases that could be prevented by 2042, we assumed that a constant decrease from current

Table 4
Melanoma cases and proportions estimated to be attributable to sunburn, sunbathing and combined UVR risk behaviors in Canada in 2015.

Age at exposure	Age at diagnosis	Sunburn			Sunbathing		Combined[a]	
		Obs.	PAR	AC	PAR	AC	PAR	AC
Men								
16–24	20–29	40	10.0	4	12.5	5	27.2	11
25–44	30–49	470	11.7	55	19.8	93	34.7	163
45 +	≥50	3300	7.9	261	15.6	513	25.9	855
Total	Total	3810	8.4	320	16.0	611	27.0	1029
Women								
16–24	20–29	110	8.2	9	19.1	21	39.0	43
25–44	30–49	655	9.8	64	28.2	185	45.4	301
45 +	≥50	2290	5.1	116	17.8	408	28.8	667
Total	Total	3055	6.2	189	20.1	614	32.7	1011
Total								
16–24	20–29	150	8.7	13	17.3	26	36.0	54
25–44	30–49	1125	10.6	119	24.7	278	41.2	464
45 +	≥50	5590	6.7	377	16.4	921	27.2	1522
Total	Total	6865	7.4	509	17.8	1225	29.7	2040

Abbreviations: AC = Attributable cases, Obs. = Observed cases, PAR = Population attributable risk.
[a] Includes joint distributions for indoor tanning (O'Sullivan et al., 2019), sunburn, and sunbathing.

prevalence (2018) to the counterfactual scenario would be achieved by 2037.

Ethics approval was granted for this project by the Health Research Ethics Board of Alberta - Cancer Committee (HREBA.CC-14-0220_REN4) and the Queen's University Health Sciences Research Ethics Board (File # 6015362).

3. Results

3.1. Current attributable burden for ultraviolet radiation overall

The PARs and numbers of attributable melanoma cases by age and sex are presented in Table 1. In 2015, we estimated that 62.3% of all melanomas in Canada were attributable to increases in exposure to UVR compared to a 1920 cohort, accounting for 4276 cases and 2.3% of all cancers. The PAR estimates were higher in men than for women with PARs of 65.8% (2506 cases) and 57.9% (1770 cases), respectively. For both sexes, PAR estimates were greatest for the 35–49 age group and smallest for the 65+ age group. Age- and sex-specific PARs and attributable cases for Canadian provinces are presented in Supplemental Table 1.

3.2. Current attributable burden for sunburn, sunbathing, and combined modifiable UVR risk behaviors

3.2.1. Estimated risk of melanoma associated with sunburn and sunbathing relevant to Canada

We identified 3380 studies in the initial PubMed search (Fig. 1). Thirty-four studies from the PubMed search and 86 additional studies identified from previous reviews (Chang et al., 2009; Gandini et al., 2005; International Agency for Research (IARC), 2010, 1992) underwent full-text review. After full-text screening and applying our exclusion criteria, 10 studies examining the association of sunburn and/or sunbathing on the risk of melanoma were included in the quantitative analysis. The primary reasons for exclusion were a lack of an effect estimate for either of these exposures ($n = 37$), and a lack of mutual control for the other UVR behaviors included in this study ($n = 30$) or a lack of control for other important confounders ($n = 26$). The specific reasons of exclusion for each individual study during the full-text review are presented in Supplemental Table 2 and the characteristics of the included studies are presented in Table 2 (Autier et al., 1994, 1998; Bataille et al., 2004; Chen et al., 1996; Han et al., 2006; Kaskel et al., 2001; Nielsen et al., 2012; Walter et al., 1999; Westerdahl et al., 1994; Zaridze et al., 1992). Of the included studies, four studies each reported results for the relationship of sunburn or sunbathing with melanoma risk, while two studies reported risk estimates for both sunburn and sunbathing.

Random effect meta-analyses yielded a pooled relative risk of developing melanoma of 1.28 (95% CI: 1.15, 1.43) associated with ever having a severe sunburn and a relative risk of 1.50 (95% CI: 1.25, 1.81) associated with ever intentionally sunbathing (Fig. 2). There was little heterogeneity among relative risk estimates for both the sunburn ($Q = 0.23$; $I^2 = 27.7\%$) and sunbathing ($Q = 0.35$; $I^2 = 9.8\%$) meta-analyses. There was no statistical evidence of publication bias in the meta-analysis of relative risks for ever sunburn ($p = 0.93$). There was suggestion of publication bias for sunbathing ($p = 0.13$; Supplemental Fig. 1) and the trim and fill approach implied that there may be two unpublished studies among the sunbathing meta-analysis and yielded a summary relative risk of 1.44 (95% CI: 1.18, 1.76). The trim and fill relative risk estimate for sunbathing was used in all PAR and PIF analyses. In our previous publication (O'Sullivan et al., 2019) we estimated that a relative risk of 1.38 (1.22, 1.56) for the ever versus never use of an indoor tanning device.

3.2.2. Prevalence of UVR exposure behaviors

Based on the past-year prevalence estimates from the NSS2 survey and applying our conversion factors (Table 3), we estimate that 32.1% of Caucasian Canadians have had a severe sunburn in adulthood, and that 54.5% have intentionally sunbathed at least once in adulthood (Table 3). The prevalence of sunburn in adulthood was higher for men (37.0%) than for women (27.3%). In contrast, the prevalence of intentionally sunbathing in adulthood was higher for women (62.8%) than for men (45.9%) (Table 3). For both men and women the prevalence of ever sunburn and sunbathing was highest for those aged 25–44. The prevalence of sunburn and sunbathing overall and stratified by sex for Canadian provinces are presented in Supplemental Tables 3 and 4.

3.2.3. Current attributable burden for UVR behaviors

Estimated age- and sex-specific PARs for sunburn, sunbathing, and combined UVR risk behaviors (including indoor tanning) are presented in Table 4. In 2015, an estimated 29.7% of melanomas (2040 cases) were attributable to the combination of sunburn, sunbathing, and indoor tanning. Independently, 7.4% of melanomas (509 cases) were attributable to sunburn, while 17.8% (1225 cases) were attributable to intentional sunbathing. PARs for sunburn were higher for men than for women at all age groups. In contrast, the PARs for intentional sunbathing and for combined modifiable UVR risk behaviors were higher for women than for men in all age groups. The PARs for sunburn, sunbathing and combined modifiable UVR risk behaviors were highest for those aged 30–49 and lowest for those aged > 50. Measures of statistical uncertainty (95% CIs) are presented in Supplemental Table 5. PAR results for Canadian provinces overall and stratified by sex for sunburn, sunbathing, and combined UVR risk behaviors is presented in Supplemental Table 6.

3.3. Future avoidable burden of melanoma

We estimated that 10,349 melanoma cases will occur in 2042. If no reductions in modifiable UVR risk behaviors (indoor tanning, sunburn, or intentional sunbathing) occur, we estimate that 3032 cases will be attributed to these behaviors in 2042. The number of melanoma cases that could be prevented by changing the prevalence of modifiable UVR risk behaviors, both separately and combined are presented in Table 5. If a 50% reduction in the prevalence of these risk behaviors steadily occurs by 2037, 1242 melanoma cases could be prevented in 2042, with a cumulative total of 11,980 cases by 2042 (Fig. 3). If reduction of these

Table 5
Projected melanoma cases and proportions estimated to be attributable to modifiable UVR risk behaviors and proportion of melanoma cases that could be prevented in 2042 with various changes in the prevalence of modifiable UVR risk behaviors in Canada.

Sex	Statistic	CTF	Indoor tanning	Sunburn	Sunbathing	Combined
Men	Projected cases	Base	5299	5299	5299	5299
	PAR (%)		4.6	8.3	15.9	26.6
	AC		242	439	841	1409
Women	Projected cases		5050	5050	5050	5050
	PAR (%)		9.9	6.0	19.6	32.1
	AC		499	304	990	1623
Total	Projected cases		10,349	10,349	10,349	10,349
	PAR (%)		7.2	7.2	17.7	29.3
	AC		741	743	1831	3032
Men	Projected cases	50% reduction by 2037	5178	5079	4879	4704
	PIF (%)		2.3	4.2	7.9	11.2
	Prevented cases		121	220	420	595
	Cumulative cases		1187	2158	4133	5841
Women	Projected cases		4800	4898	4555	4403
	PIF (%)		5.0	3.0	9.8	12.8
	Prevented cases		250	152	495	647
	Cumulative cases		2401	1462	4759	6139
Total	Projected cases		9978	9977	9434	9107
	PIF (%)		3.6	3.6	8.8	12.0
	Prevented cases		371	372	915	1242
	Cumulative cases		3588	3620	8892	11,980
Men	Projected cases	25% reduction by 2037	5239	5189	5089	5023
	PIF (%)		1.1	2.1	4.0	5.2
	Prevented cases		60	110	210	276
	Cumulative cases		594	1079	2036	2779
Women	Projected cases		4925	4974	4802	4756
	PIF (%)		2.5	1.5	5.2	5.8
	Prevented cases		125	76	248	294
	Cumulative cases		1201	831	2380	2877
Total	Projected cases		10,164	10,163	9891	9779
	PIF (%)		1.8	1.8	4.4	5.5
	Prevented cases		185	186	458	570
	Cumulative cases		1795	1910	4416	5656
Men	Projected cases	10% reduction by 2037	5275	5255	5215	5193
	PIF (%)		0.5	0.8	1.6	2.0
	Prevented cases		24	44	84	106
	Cumulative cases		237	432	827	1081
Women	Projected cases		5000	5019	4951	4938
	PIF (%)		1.0	0.6	2.0	2.2
	Prevented cases		50	31	99	112
	Cumulative cases		480	292	952	1109
Total	Projected cases		10,275	10,274	10,166	10,131
	PIF (%)		0.7	0.7	1.8	2.1
	Prevented cases		74	75	183	218
	Cumulative cases		717	724	1779	2191

Abbreviations: AC = Attributable cases, CTF = Counterfactual scenario, PIF = Potential impact fraction.

behaviors were more modest (10–25%) by 2037, we would expect 218–570 cases to be prevented in 2042 and 2191–5656 cumulative melanoma cases could be prevented by 2042 (Fig. 3). Results for Canadian provinces stratified by sex are presented in Supplemental Tables 7 and 8.

4. Discussion

Incidence rates of melanoma in Canada have increased by over 50% in both males and females over the last three decades (Canadian Cancer Society, 2018). After adjusting for improvements in reporting and changes in the ethnic distribution of Canada, we estimated that 62.3% of melanomas (4276 cases) in 2015 were attributable to increases in UVR exposure. These estimates account for increases in exposure to solar UVR, but also for the use of indoor devices that were not available for earlier birth cohorts. In addition, we estimated that the combination of sunburn, intentional sunbathing, and indoor tanning accounted for 29.7% of melanomas, with sunburn, sunbathing, and indoor tanning accounting for 7.4%, 17.8%, and 7.0% (O'Sullivan et al., 2019) of melanoma cases, respectively. PAR estimates for UVR exposure and for sunburn were highest for men, while PARs for sunbathing and for UVR behaviors combined were highest for women. By reducing the prevalence of indoor tanning, adulthood sunburn, and intentional sunbathing by 50%, 12,089 cases of melanomas could be prevented by 2042.

Several studies have used a similar birth cohort comparison to estimate a PAR for UVR. Parkin employed this approach using incidence data from 1960 to 2010 and a 1903 birth cohort as the referent in a comparison with 2010 incidence data and estimated a PAR of 85.9% for the UK (Parkin et al., 2011). In 2010, Olsen and colleagues compared 2010 Australian melanoma rates to both the UK referent cohort and 1982 incidence data for Australia and estimated PARs of 63.3% and 45.1% respectively. Both the study for France and the world used the UK cohort as the referent and observed PARs of 83% for France and 90% for North America. The higher PAR for the UK, France, and North America is likely a product of not accounting for improvements in the reporting of melanoma, as capture rates for the UK have been historically low (Paterson et al., 2001), and to some extent the use of a referent population that was less exposed to UVR (earlier cohort). The higher PAR in comparison to Australia can be partly explained by our use of earlier incidence data, but also possibly due to changes in exposure as a result of population-wide sun behavior campaigns and the

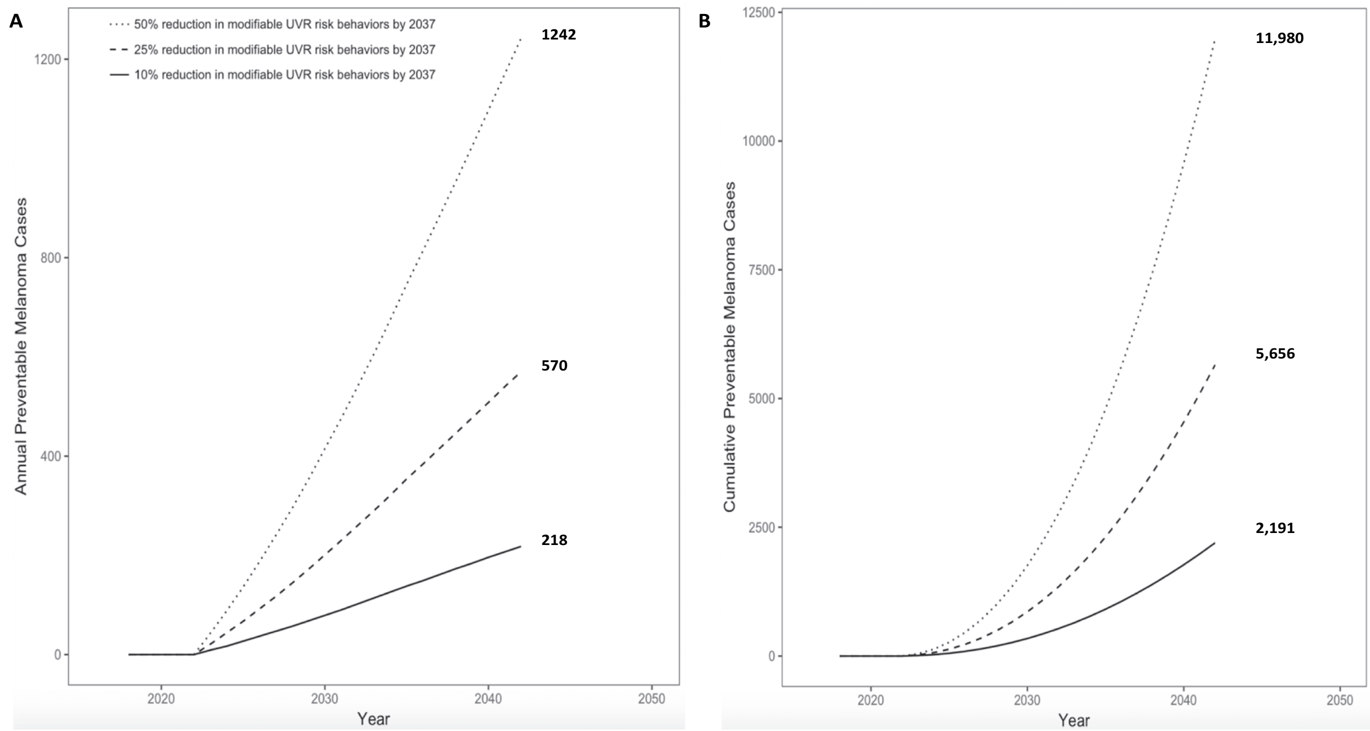

Fig. 3. A) Projected annual preventable melanoma cases attributable to modifiable UVR risk behaviors by applying 3 counterfactual scenarios; B) Projected cumulative preventable melanoma cases attributable UVR risk behaviors by applying 3 counterfactual scenarios.

banning of indoor tanning devices.

The method of PAR estimation based on the prevalence of exposure and relative risk estimates for UVR risk behaviors has been employed several times for indoor tanning (Arnold et al., 2018a,b; Boniol et al., 2012; Gandini et al., 2014), but has rarely been used for sun-related behaviors. Indeed, only one study has estimated a PAR for sun-related behaviors (Gandini et al., 2014) and no study has sought to quantify a combined PAR across multiple UVR risk behaviors. Gandini and colleagues estimated that 13% of melanoma cases in Italy were attributable to intentional sun exposure, defined as > 3 h in the sun per day. Our estimate of 17.8% of melanomas being attributable to intentional sunbathing is higher, but the estimates are difficult to compare given the disparate methods employed.

Strengths of our risk factor approach relate to estimates of relative risk, exposure estimation, and future burden under different counterfactual scenarios. First, we estimated relative risks for each UVR risk behavior that were generalizable to Canada and adjusted for important confounders. This method for PAR estimation is important given that ambient UVR varies by latitude. Second, we only included estimates that were mutually adjusted for the other UVR risk behaviors to ensure independent relative risks. Third, we used joint prevalence distributions due to the potential dependency of UVR risk behaviors. This point is important given that when risk factors are dependent, combining PARs with the Miettinen-Steenland and Armstrong approach (Miettinen, 1974; Steenland and Armstrong, 2006) can lead to an underestimation (Poirier et al., 2019b). In this analysis we did not observe a large difference with the two approaches; the combined PAR was 29.7% when accounting for joint distributions and 29.2% when using the Miettinen-Steenland and Armstrong formula. Finally, our incorporation of PIFs is important for future interventions and policy targeted at these behaviors, and this type of analysis for UVR risk behaviors has only been conducted once before (de Vries et al., 2012).

Our analysis of the prevalence of UVR risk behaviors among Caucasian Canadians show that yearly exposure is highest among the youngest age groups and decreases with age. From a cancer prevention standpoint, interventional strategies should be aimed at young adults, which if successful could lead to a considerably lower lifetime exposure to UVR if modification of behaviors can occur early in life. In addition, among this age group we observed that women were more likely to use indoor tanning devices (O'Sullivan et al., 2019) and sunbathe, while men were more likely to sunburn. These results suggest that prevention strategies should be sex-specific – focusing on reduction of tanning among young women, and on sun protection among young men.

While this study is the first application of the birth cohort approach that accounts for changes in ethnicity and reporting practices, our methods have some limitations. First, we generalized ethnic-specific melanoma incidence rates from the USA to Canada, which likely introduced some misclassification because of the potential differences in diagnosis and reporting. Second, the risk of melanoma associated with UVR exposure for Hispanics and Aboriginals is lower than that for Caucasians, however, the proportion of Hispanics and Aboriginals in Canada has only changed marginally. Third, we applied the rate of under-reporting equally across age groups and sex, which could lead to misclassification if under-reporting is more prevalent in a specific demographic group. Finally, we applied capture rates of Ontario to all of Canada, which may not be nationally representative.

Despite the strengths of our risk factor approach, our analysis has limitations that warrant acknowledgement. Our prevalence estimates were based on self-reported data and social desirability bias could have led to underestimations of exposure. In addition, there is a considerable amount of uncertainty involved in our conversion factor for past-year exposure to ever exposure that could possibly lead to inaccurate results. Third, age categories were collapsed because of the lack of reliable prevalence estimates from the NSS2 and an appropriate conversion factor for certain categories. Our analysis of modifiable UVR risk behaviors was limited to adult exposures, which could underestimate PARs given that exposure early in life, particularly sunburns have been shown to play a role in the development of melanoma. For our PIF analyses we were unable to include projections of UVR risk behaviors due to insufficient population-based data. Our cohort approach provides some evidence that UVR risk behaviors have decreased in recent cohorts, particularly among younger men, and therefore our PIF estimations could be slight overestimations. Finally, projections of cancer incidence involves several assumptions each of which are associated with some degree of uncertainty, which ultimately influence our estimates of preventable cases.

5. Conclusions

To our knowledge, this is the first attempt to estimate the current and future burden of melanoma in Canada attributable to UVR and modifiable UVR risk behaviors. In addition, the methods we have employed can be adapted to derive estimates in other contexts. Given that melanoma rates continue to increase in Canada, preventive strategies aimed at the modifiable UVR behaviors is crucial to reduce the growing burden of melanoma.

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Conflict of interest

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2019.03.012.

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