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Indoor tanning and skin cancer in Canada: A meta-analysis and attributable burden estimation

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ABSTRACT

Background: Consistent epidemiologic and experimental studies have demonstrated that UV-emitting tanning devices cause melanoma and non-melanoma skin cancer. The purpose of this study was to estimate the relative risk of skin cancer associated with the use of indoor tanning devices relevant to Canada, to estimate the proportion and number of skin cancers in Canada in 2015 that were attributable to indoor tanning, and to explore differences by age and sex.

Methods: Skin cancer cases attributable to the use of an indoor tanning devices were estimated using Levin's population attributable risk (PAR) formula. Relative risks for skin cancer subtypes that were relevant to Canada were estimated through meta-analyses and prevalence of indoor tanning was estimated from the 2006 National Sun Survey. Age- and sex-specific melanoma data for 2015 were obtained from the Canadian Cancer Registry, while estimated NMSC incidence data were obtained from the 2015 Canadian Cancer Statistics report.

Results: Ever use of indoor tanning devices was associated with relative risks of 1.38 (95% CI 1.22–1.58) for melanoma, 1.39 (1.10–1.76) for basal cell carcinoma (BCC), and 1.49 (1.23–1.80) for squamous cell carcinoma (SCC). Overall, 7.0% of melanomas, 5.2% of BCCs, and 7.5% of SCCs in 2015 were attributable to ever of indoor tanning devices. PARs were higher for women and decreased with age.

Conclusion: Indoor tanning contributes to a considerable burden of skin cancer in Canada. Strategies aimed at reducing use should be increased and a total ban or restrictions on use and UV-intensity should be considered by health regulators.

Abbreviations: BCC, basal cell carcinoma; CI, confidence interval; AC, attributable cases; NMSC, non-melanoma skin cancer; NSS2, The Second National Sun Survey; PAR, population attributable risk; PRISMA, preferred reporting items for systematic reviews and meta-analyses; RR, relative risk; SCC, squamous cell carcinoma; UVA, ultraviolet A; UVB, ultraviolet B; UVR, ultraviolet radiation

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1. Introduction

Incidence rates of cutaneous malignant melanoma and non-melanoma skin cancer (NMSC) in Canada have been steadily increasing between 1986 and 2010 [1]. The estimated age standardized incidence rate for melanoma in 2017 was 18.5 cases per 100,000 (7300 cases) [2] and 198.4 for NMSC (78,300 cases) in 2015 [3]. Melanoma is the most deadly form of skin cancer, and has become one of the most common cancers among young adults in Canada, particularly for females [1]. Of NMSC cases, approximately 77% are basal cell carcinoma (BCC) and 23% are squamous cell carcinoma (SCC) [1]. Although rarely fatal, the high incidence of NMSC represents a significant burden of disease in terms of morbidity, quality of life, social impact, and health care costs [4].

There is consistent epidemiologic evidence that indoor tanning causes melanoma and non-melanoma skin cancer (NMSC) and in 2012 the International Agency for Research on Cancer (IARC) classified artificial sources of ultraviolet radiation as carcinogenic (class 1) to humans [5]. Indoor tanning is similar to sun exposure for ultraviolet B (UVB) radiation exposure, but is 10–15 times stronger than sun exposure for ultraviolet A (UVA) radiation [6]. With longer wavelengths than UVB radiation, UVA rays penetrate more deeply into the skin than UVB, and can cause mutations in tumor suppressor genes or other oncogenes, both directly through DNA damage and indirectly through oxidative stress [7]. Moreover, UVA has been shown to be relatively ineffective at inducing pigmentation changes that can attenuate the potentially damaging effects of future exposure to UVR, as UVB does [8]. Additionally, indoor tanning devices have been shown to induce harmful burns, which an estimated two-thirds of users experience at least once [9]. While indoor tanning devices in Europe are limited in intensity to an ultraviolet index of 12, Canada and the USA do not place restrictions on owners or users [10]. In addition, there is some evidence that the risk of skin cancer associated with ever use of indoor tanning devices is greater in North America than in Europe [11], which could be a reflection of varying use patterns and device restrictions.

Population attributable risks (PAR) for skin cancer associated with indoor tanning have previously been estimated for Europe [12,13], France [14], Australia [13], and the United States [13], but not for Canada. Two main limitations of these previous studies is that they did not restrict the studies included in the PAR estimates for ever use of indoor tanning devices to those with a relevant exposure distribution to their own population, and they included studies that did not control for confounding from exposure to solar UVR exposure. Therefore, not only does a Canadian estimate require an exposure distribution for Canada, but it also requires a relative risk estimate that is applicable to the types of devices and usage patterns which represent Canadian indoor tanning exposure.

While Brazil and Australia have banned indoor tanning devices [10], Canada only restricts use to those over the age of 18 [15]. In addition, indoor tanning users in Canada are required to wear protective glasses and all commercial equipment must display labels that detail the health risks of indoor tanning, including that it can cause cancer [15]. However, minors can still use tanning devices with signed consent from a guardian, and restriction in terms of intensity, frequency, or duration of use are not mandated in Canada [15]. Therefore, attributable burden estimates have important implications for policy and preventive initiatives aimed at reducing the burden of skin cancer in Canada. Thus, the objective of this study was to estimate the risk of skin cancer associated with the ever use of indoor tanning devices that is relevant to Canada and to quantify the proportion and number of skin cancer cases in Canada that could be attributed to indoor tanning in 2015. A secondary objective included exploring the extent to which PAR estimates varied by age, sex, and province.

2. Materials and methods

This manuscript is part of The Canadian Population Attributable Risk of Cancer (ComPARe) study – a project aimed at quantifying the number and proportion of cancer cases in Canada, now and in the future, that could be prevented through changes in the prevalence of modifiable exposures associated with cancer. The methods for this study have previously been described [16].

The proportion and number of skin cancer cases in Canada that occurred in 2015 that were attributable to the use of indoor tanning devices (tanning bed, sunlamp or tanning light) was estimated using summary relative risks relevant to Canada derived from our own meta-analyses and were applied in combination with estimates of the prevalence of ever use of indoor tanning devices in Canada with the traditional PAR method [17].

2.1. Estimating relative risks

The most common exposure metric used for indoor tanning in epidemiologic studies is the ever use of an indoor tanning device (tanning bed, sunlamp or tanning light). In different parts of the world the duration and lifetime frequency of exposure for individuals with ever use of an indoor tanning device can vary considerably and therefore it is necessary to consider studies that reflect the reality of use in Canada. To identify these appropriate studies, we restricted our inclusion to studies with a frequency of use distribution similar to Canada or a similar overall prevalence if the former was not reported. Additionally, individuals who use indoor tanning devices tend to spend more time in the sun, which implies the need for estimates of risk that control for exposure to solar ultraviolet radiation to determine the independent contribution of indoor tanning to the development of skin cancer.

To quantify the risk of developing each of the three types of skin cancer associated with ever use of indoor tanning devices, we conducted a systematic review using the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The literature search was conducted in PubMed, including all studies published up to August 2018 on the relationship of indoor tanning and the risk of skin cancer. The search terms used were as follows: "artificial UV" or "artificial ultraviolet" or "artificial light" or "indoor tanning" or "non-solar ultraviolet", "solaria" or "solarium" or "sunbathing" or "sunbed" or "sunlamp" or "tanning bed" or "tanning booth" or "tanning parlour" or "tanning salon" and "melanoma" or "basal cell carcinoma" or "BCC" or "squamous cell carcinoma" or "SCC" or "non-melanoma skin cancer" or "NMSC." Abstract and title screening was performed by DO'S. In the initial screening process, articles were deemed suitable for full-text review if they had been performed in adult humans, involved a skin cancer outcome, and were of relevance to the research question (assessed some measure of artificial UVR) or assessed solar UVR – to capture studies that include indoor tanning as a secondary analysis. Full-text review was conducted by two independent reviewers (DO'S and WDK). Reviews and meta-analyses were excluded from this study and we made no restriction on the language of studies assessed for inclusion. Reference lists and other secondary sources were examined for additional relevant articles. The final inclusion criteria for studies included in the quantitative meta-analysis were studies: 1) reporting an effect estimate that was adjusted for important confounding variables (including host characteristics and an adequate measure of exposure to solar UVR); 2) that did not adjust for variables on the causal pathway (dysplastic nevi); contained an appropriate control group (was not related to exposure to UVR); 3) that had a summary of the exposure distribution (for example, approximately 30–50% of users had greater than ten times of use) or overall prevalence (for example, 8–28% ever use) of indoor tanning similar to the largest Canadian study (Walter et al. [18]). If multiple papers reported results on the same study population, we used the paper with the longest follow-up that reported an effect estimate of "ever" use of an indoor tanning device – or could be

derived from what was reported. If a prospective study reported effect estimates for different periods of life, the period that best approximated lifetime exposure was used.

For the purposes of this study, hazard ratios and odds ratios were treated as approximations of relative risk. Relative risk estimates were weighted using the inverse variance method assuming a fixed effects model given our strict inclusion criteria. Heterogeneity among studies was investigated with the Q-test and the I^2 statistics [19]. To assess publication bias we visually reviewed funnel plots and employed both Egger's weighted linear regression [20] and Begg's rank correlation tests [21]. Given that the Begg's and Egger's tests are underpowered in meta-analyses with few studies [22], in the presence of statistically insignificant publication bias, we also employed the trim and fill approach to ensure the validity of our results. All analyses were performed using the R computing framework (www.r-project.org).

2.2. Estimating prevalence of exposure

The temporal relation between exposure and cancer diagnosis follows a sequence of relevant exposure period, induction period, latency period, and cancer diagnosis. The exposure prevalence of consequence to cancer incidence in a given year is that occurring during the relevant exposure period. In the majority of epidemiologic studies of this relationship, use of indoor tanning devices has been represented as "ever" exposed and therefore the prevalence of exposure in the target population at the end of the relevant exposure period is desired. The range of exposure, induction, and latency periods are difficult to establish for the indoor tanning-skin cancer association. We targeted a five-year lag between exposure prevalence and cancer incidence, hence requiring prevalence data from 2010. Prevalence was based on the 2006 National Sun Survey (NSS2) [23] to represent the target year of 2010.

To estimate PARs, the same exposure metric must be used for both the risk of skin cancer and for the prevalence of exposure in the population. Prevalence estimates for the ever use of indoor tanning devices are not available in Canada and therefore the prevalence of ever use was estimated by applying a conversion factor to past year exposure. Estimates of the prevalence of use of indoor tanning devices among Caucasians in the past year by age and sex were extracted from the 2006 NSS2. Prevalence data was restricted to Caucasians, since a small proportion of non-Caucasians use indoor tanning devices, but studies assessing skin cancer risk restrict to Caucasians and therefore relative risks are not generalizable to these individuals. The specific question in the NSS2 asked participants: "During the past 12 months, have you used any artificial tanning equipment such as tanning bed, sunlamp, or tanning light for any reason including medical reasons." Age-specific conversion factors were estimated to convert "use in the past year" to "ever use" using a meta-analysis on the international prevalence of indoor tanning, which summarized the differences in prevalence of exposure for "ever exposed" and "exposed in the past year" [24]. Within that meta-analysis, we used the results of a subgroup analysis that restricted to studies from North America. Using this study, we divided the prevalence of use in the past five years or ever use by the prevalence of use in the past year for each age group and derived conversion factors to apply to the past year prevalence from the NSS2.

2.3. Cancer incidence and target population

Melanoma incidence data by age and sex in 2015 were obtained from the Canadian Cancer Registry. The overall number of estimated NMSC cases in 2015 were obtained from the Canadian Cancer Statistics report [3]. These estimates were based on incidence data from four provincial registries (Alberta, Manitoba, New Brunswick and Newfoundland) and extrapolated to the rest of Canada. Age, sex, and histological subtype distributions were estimated from NMSC data obtained from the Manitoba Cancer registry and were applied to the number of NMSC cases estimated by the Canadian Cancer Statistics report.

Given that the relative risks for indoor tanning are primarily derived from studies that only include Caucasians, and that the majority of melanoma cases in Canada occur in Caucasian populations (98.9%) [25], our PAR estimates only apply to the Caucasian population of Canada. To estimate the number of attributable cases, the Caucasian-specific PARs were applied to 98.9% of the skin cancer cases in Canada.

2.4. Population attributable fraction estimations

Age- and sex-specific exposure prevalence and summary relative risk estimates were used with Levin's formula [17] to estimate age- and sex-specific PARs:

$$PAR = \frac{Pe\,(RR - 1)}{1 + [Pe\,(RR - 1)]}$$

PAR = Population attributable risk
Pe = Prevalence of exposure in the general population
RR = Relative Risk

To estimate the excess attributable cases we multiplied the age- and sex-specific PARs by the skin cancer incidence data for each age and sex category and the numbers of attributable cases were summed. The total number of attributable cases was then divided by the total incident cases in that year to derive overall PARs associated with indoor tanning. The same methods were used to estimate PARs for specific Canadian provinces.

To estimate 95% confidence intervals for PAR estimates, Monte Carlo simulation methods were used where the relative risk values were drawn from a log-normal distribution derived from the RR and its associated variance estimated from 95% Cis, while prevalence values were drawn from a binomial distribution with parameter n as the number of survey participants and parameter p as the prevalence of exposure estimated from the survey. We simulated 10,000 samples and used the 2.5th and 97.5th percentiles of the resulting PAR distribution as the lower and upper limits of its 95% CI [26,27].

3. Results

3.1. Estimated risk of skin cancer associated with indoor tanning

We identified 759 unique studies in the initial PubMed search (Fig. 1). Thirty-nine studies from the PubMed search and 18 additional studies identified from reference lists and secondary sources underwent full-text review. After full-text screening and applying our exclusion criteria, 11 studies examining the association of indoor tanning with at least one of the skin cancer subtypes were included in the quantitative analysis. The primary reasons for exclusion were a lack of control for confounding (n = 21) and a non-Canadian specific exposure distribution or prevalence (n = 10). The specific reasons of exclusion for each individual study in the full-text review is presented in Supplemental Table 1.

Characteristics of the 11 studies investigating the association of indoor tanning and the risk of skin cancer that were relevant to Canada are presented in Table 1 [18,28–37]. A total of 3315 melanoma cases, 6335 basal cell carcinoma cases, 583 squamous cell carcinoma cases, and 78,809 healthy individuals were examined in these studies. The majority of the included studies were conducted in North America (n = 7), while three studies were conducted in Europe and one in Australia.

There was little evidence of heterogeneity in the relative risk estimates for any of the skin cancer subtypes (I^2 = 26%, 0%, 0% for melanoma, BCC, and SCC, respectively) and therefore fixed effect meta-analyses were conducted for each subtype for the ever use of indoor tanning devices. The meta-analysis for melanoma yielded a relative risk of 1.38 (95% CI 1.22–1.58; Fig. 2). There was some statistical evidence of publication bias for melanoma (p = 0.06), but the trim and fill

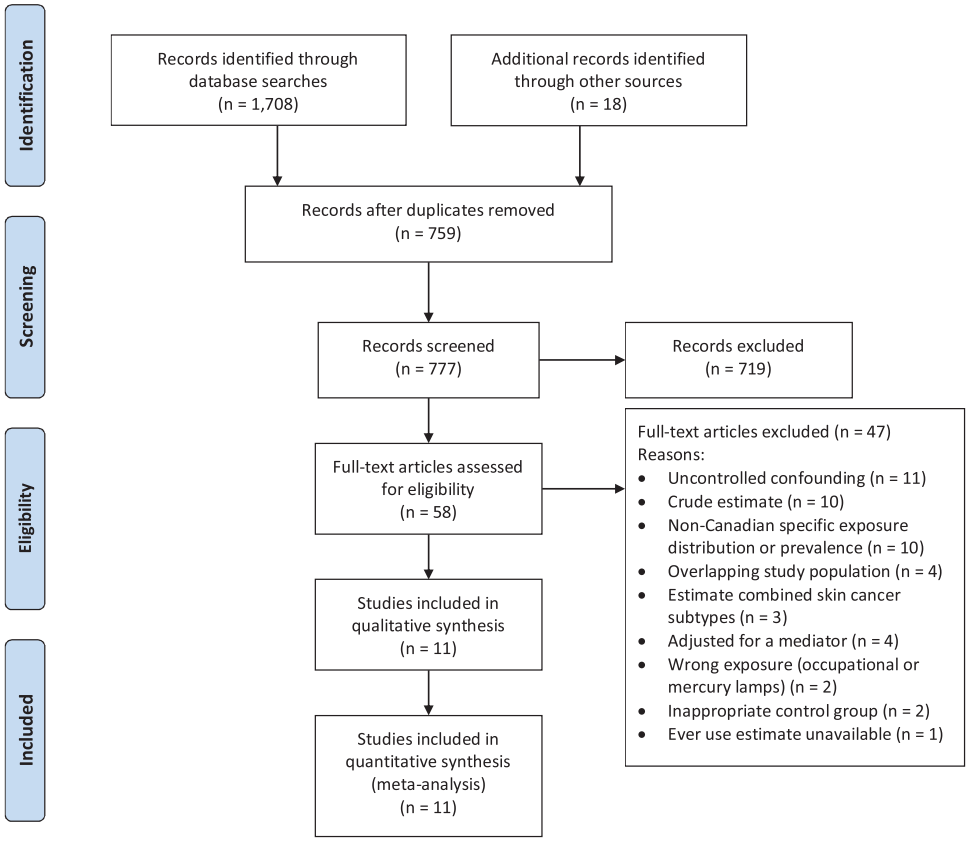

Fig. 1. Flow diagram of the selection procedure of studies relevant to Canada assessing the relationship of indoor tanning with the risk of melanoma and non-melanoma skin cancers. Description: A PRISMA flow diagram that details the inclusion and exclusion of studies considered for this meta-analysis.

approach did not identify any unpublished studies. There was no evidence of publication bias for BCC (p = 0.5) or SCC (p = 0.8) and meta-analysis relative risks were 1.39 (95% CI 1.10–1.76) for BCC and 1.49 (95% CI 1.23–1.80) for SCC, respectively (Fig. 2).

3.2. Estimated prevalence of indoor tanning in Canada

The 2006 past year prevalence of indoor tanning and the estimated prevalence of ever using an indoor tanning device by age and sex among Canadian Caucasians are shown in Table 2. Based on data from the NSS2 and the application of our conversion factors it was estimated that, among Caucasian Canadians over the age of 16, 10.6% used an indoor tanning device in the past year and 26.3% had used an indoor tanning device at least once in their lifetime. Women had higher ever and past year use of indoor tanning devices than men in all age groups. Among women, both past year and ever use of indoor tanning devices was highest among young adults (16–24 years) and decreased with age. Among men, the youngest age groups (16–24 and 25–44 years) had similar past year use of indoor tanning devices, while the oldest age group (45+ years) had considerably lower use. The middle age group (25–44 years) had greater ever use of indoor tanning devices than both the youngest (16–24 years) and oldest age groups (45+ years). Provincial-specific prevalence estimates are presented in Supplemental Table 2.

3.3. Estimated population attributable risk of melanoma and non-melanoma skin cancer in Canada in 2015

Estimated age- and sex-specific PARs for indoor tanning and each skin cancer subtype are presented in Table 3. In 2015, 7.0% of

Table 1
Characteristics of studies relevant to Canada investigating the association of indoor tanning with the risk of melanoma and non-melanoma skin cancers (n = 11).

Study and Location	Study design and Years of accrual	Population	Age (range)	Indoor tanning prevalence distribution
Badjik, 1996 Alberta, Canada (Males)	Population Case-control 1983-1984	226 BCCs, 180 SCCs, 406 controls	25-79	8% ever
Bataille, 2004 United Kingdom	Hospital Based Case-control 1989-1993	413 melanomas, 416 controls	16-75	25% ever 43% > 30 lifetime uses
Chen, 1998 Conneticut, USA	Population Case-control 1987-1989	512 melanomas, 624 controls	> 18	19% ever 42% > 10 lifetime uses
Clough-Gorr, 2008 New Hampshire, USA	Population Case-control 1995-1998	423 melanomas, 678 controls	20-69	33% ever 45% > 10 lifetime uses
Cust, 2011 Australia	Population Case-control 2000-2002	604 melanomas, 479 controls	18-39	17.5% ever 32% > 10 lifetime uses
Han, 2006 USA (Nurses)	Nested Case-control 1989-1998	200 melanomas, 804 controls	30-79	12% ever
Karagas, 2002 New Hampshire, USA	Population Case-control 1993-1995	603 BCCs, 540 controls	25-74	14% ever
Swerdlow, 1988 Scotland	Hospital Based Case-control 1979-1984	180 melanomas,120 controls	15-84	8% ever
Walter, 1999 Ontario, Canada	Population Case-control 1984-1986	583 melanomas, 608 controls	20-69	18% ever 43% > 10 lifetime uses
Westerdahl, 1994 Sweden	Population Case-control 1988-1990	400 melanomas, 640 controls	15-75	24% ever
Zhang, 2012 USA (Female Nurses)	Prospective Cohort 1989-2009	5506 BCCs, 403 SCCs, 73,494 controls	25-62	12% ever

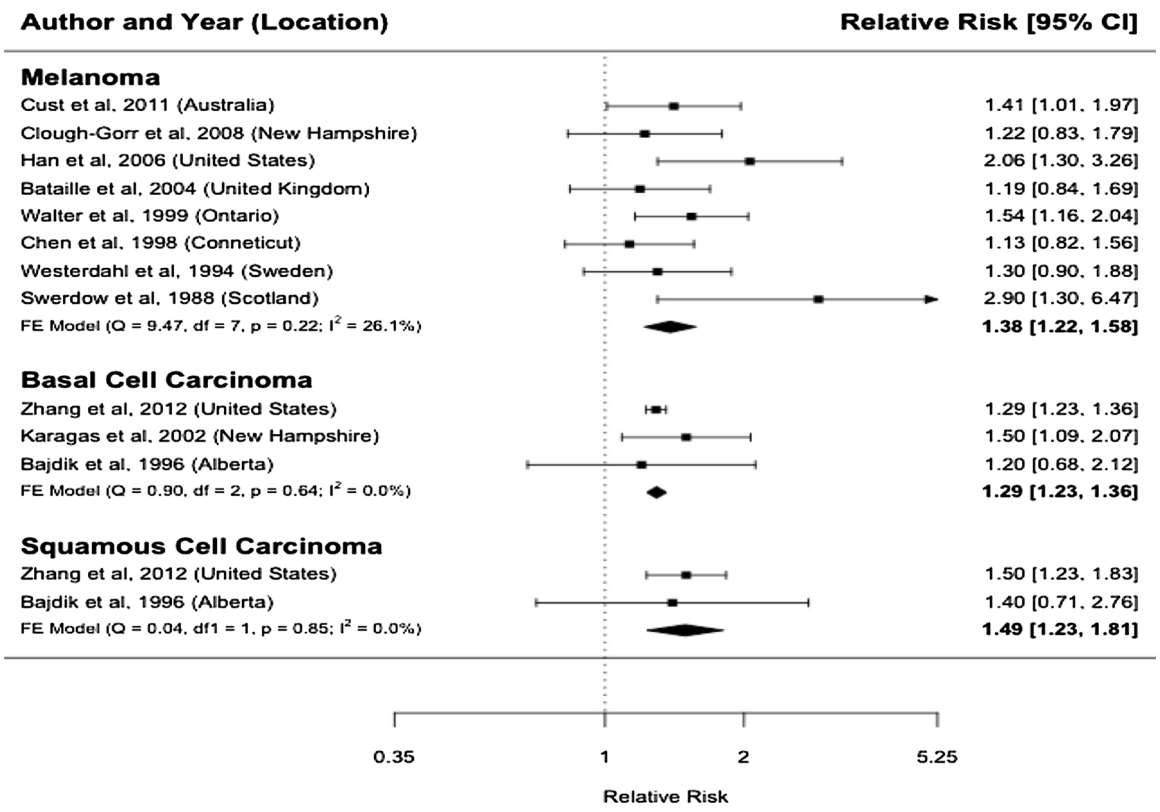

Fig. 2. Estimated relative risks of skin cancer subtypes comparing ever users of indoor tanning devices to non-users that are generalizable to Canada. Description. A forest plot that presents skin cancer subtype-specific relative risks from investigation of ever use of indoor tanning devices and skin cancer risk that are generalizable to use patterns in Canada.

Table 2
Estimated prevalence of indoor tanning among Caucasian Canadians.

	Prevalence (95% confidence interval)		
Age (years)	**Past year (%)**	**Conversion Factor****	**Ever use (%)**
Men			
16-24	8.5 (5.8-12.4)	1.92	16.3 (11.1-23.8)
25-44	8.0 (6.4-10.0)	2.69	21.6 (17.2-26.9)
44 +	4.4 (3.3-5.9)	2.69	11.8 (8.9-15.9)
Total	6.1 (5.2-7.2)	–	15.6 (13.3-18.4)
Women			
16-24	30.4 (25.7-35.4)	1.92	58.3 (49.3-68.0)
25-44	18.9 (16.7-21.2)	2.69	50.7 (44.9-57.0)
44 +	9.0 (7.6-10.5)	2.69	24.2 (20.4-28.2)
Total	14.9 (13.7-16.2)	–	36.8 (33.8-40.0)
Overall	10.6 (9.8-11.5)	–	26.3 (24.3-28.5)

Note: Total and overall prevalence calculated by population weighted Average.
*Data from the Second National Sun Survey (2006).
**Conversion factor (past year vs. ever) derived from Wehner et al., 2014.

melanomas (482 cases), 5.2% of BCCs (3025 cases), and 7.5% of SCCs (1524 cases) were attributable to indoor tanning, accounting for 5.9% of all skin cancer in Canada (5031 cases). For each of the subtypes, the PARs were higher for women than for men. While for women the PAR estimates decreased with age, the highest PAR for men occurred in the middle age group (30–49). Measures of uncertainty (95% Cis) are presented in Supplemental Table 3. Sex-specific PARs for Canadian provinces are presented in Supplemental Table 4. Overall, Alberta had the highest proportion of melanoma and non-melanoma skin cancer cases attributable to indoor tanning, while British Columbia had the lowest burden.

4. Discussion

In this study, patterns of indoor tanning use relevant to Canada were associated with a relative risk of 1.38 for melanoma, 1.39 for basal cell carcinoma, and 1.49 for squamous cell carcinoma. Overall, we estimated that 7.0% of melanomas, 5.2% of BCCs, and 7.5% of SCCs in Canada in 2015 were attributable to the use of indoor tanning devices. In addition, we found that there were considerable differences in PAR estimates by age, sex, and province. In particular, PAR estimates were highest for women in all age groups, particularly among the youngest age group. In contrast, the largest PAR for men occurred in the middle age group, which could be evidence of a reduction of indoor tanning among the most recent cohorts of men.

The most recent meta-analyses on indoor tanning and the risk of melanoma and NMSC have observed relative risks for the ever use of an indoor tanning devices of 1.16 for melanoma [11], 1.29 for BCC [13] and 1.67 for SCC [13]. Differences in summary relative risk estimates in this study may be attributable to our stringent exclusion criteria, where distinct from previous studies were criteria based on control for confounding and an exposure distribution similar to Canada. If we removed these criteria we observe relative risks closer to those reported in previous meta-analysis, 1.23 (95% CI 1.11 to 1.37) for melanoma, 1.28 (0.84 to 1.37) for BCC and 1.72 (95% CI 1.48 to 2.00). Our confounding exclusion criteria were aimed at obtaining an unbiased effect estimate, in particular with respect to not controlling for factors in the causal pathway and controlling for sun exposure behaviours. The rationale behind the exposure distribution criteria was that "ever exposed" might be associated with disparate frequency of exposure in different studies. We sought to obtain a relative risk estimate for an exposure that was similar to what we could expect in Canada.

In a previous analysis, Wehner [13] estimated that the proportion of melanoma cases in the United States, Europe, and Australia attributable to indoor tanning were 8.1%, 9.4%, and 2.6%, respectively. In an

Table 3
Melanoma and non-melanoma skin cancer cases and proportions attributable to indoor tanning in Canada in 2015.

Age at Exposure	Age at Diagnosis	Melanoma			Basal cell carcinoma			Squamous cell carcinoma		
		Obs.	PAR	AC	Obs.	PAR	AC	Obs.	PAR	AC
Men										
16-24	20-29	40	5.0	2	170	4.7	8	8	12.5	1
25-44	30-49	470	7.5	35	2626	5.8	153	286	9.4	27
44+	> =50	3300	4.2	137	28429	3.3	935	12781	5.4	694
Total	Total	3810	4.6	174	31225	3.5	1096	13075	5.5	722
Women										
16-24	20-29	110	18.2	20	223	14.4	32	19	21.1	4
25-44	30-49	655	15.6	102	3004	12.7	381	318	19.8	63
44+	> =50	2290	8.1	186	23420	6.5	1516	7017	10.5	735
Total	Total	3055	10.1	308	26647	7.2	1929	7354	10.9	802
Total										
16-24	20-29	150	14.7	22	393	10.2	40	27	18.5	5
25-44	30-49	1125	12.2	137	5630	9.5	534	604	14.9	90
44+	> =50	5590	5.8	323	51849	4.7	2451	19798	7.2	1429
Total	Total	6865	7.0	482	57872	5.2	3025	20429	7.5	1524

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

earlier analysis, Boniol [12] estimated that 5.6% of melanomas in Europe were attributable to indoor tanning, after calculating country-specific PARs and then pooling the results. The proportions estimated for the US and Europe by Wehner [13] are slightly higher than estimated for Canada. While this higher estimate may reflect a true difference in PAR, it is likely that the estimates are inflated because of the use of an overall exposure, rather than age- and sex-specific estimates, as we have done here. This is because the youngest age groups tend to contribute to a higher prevalence, but to a lower number of attributable cases, given the rarity of skin cancer in younger age groups. Indeed, in a sensitivity analysis that we conducted using an overall exposure prevalence for Canada resulted in considerably greater PAR estimates with 8.9% for melanoma, 7.1% for BCC, and 11.4% for SCC. Wehner et al. [23] in a subsequent study are the only previous investigators to have estimated PARs for NMSC in relation to indoor tanning. They estimated for the US and Europe that 9.3% and 10.8% BCCs, and 19.2% and 21.8% SCCs are attributable to indoor tanning use, which are substantially higher than those reported herein. In addition to the points previously raised, the difference in PAR estimates primarily reflects the difference in relative risk estimates used for SCC. Finally, our incorporation of ethnicity in our methods is novel and an important consideration, particularly in countries with considerable ethnic diversity.

Despite a dose-response relation between cumulative use of indoor tanning devices and skin cancer development, the most common exposure metric used in epidemiologic studies is the ever use of an indoor tanning device. While collapsing the data into a dichotomous exposure variable does not affect the PAR for a single study [38], it does in a meta-analysis if the exposure distribution varies among the included studies. Given this issue, we selected studies that had an exposure distribution that was relevant to Canada which was a novel approach. Since patterns of indoor tanning in North America confer a greater risk of melanoma development than in Europe [11], the studies conducted by Wehner [13,24] and Boniol [13] for Europe were likely inflated by not restricting to studies with exposures relevant to Europe. In addition, we accounted for ethnicity in our estimations, and provide estimates of statistical uncertainty through a Monte Carlo approach – both of which are novel for PAR studies on indoor tanning and skin cancer.

The uncertainty involved in our conversion factor for past-year exposure to ever exposure is a limitation. Past year exposure is likely to be highly variable and susceptible to many different factors – rendering the conversion to ever exposure extremely difficult. A limited evaluation of the validity of our conversion factors comes from a study conducted in the Canadian province of Quebec that reports use in the past-year and the past 5-years [39]. Conversion factors were generally lower (as expected) but of a similar magnitude to our lifetime conversion factors. For example, for the age group 16–24 the past-year to 5-year ratio was 1.7 compared to our conversion of 1.9. For those aged 25–54 the past-year to 5-year ratio was 1.9 compared to our conversion factor of 2.7. The past-year to 5-year ratio, particularly for older adults, does not capture individuals that no longer indoor tan, but that did in their younger years. The decrease in past-year year prevalence by age provides evidence that this is common and that our conversion factor likely results in prevalence that is within a reasonable range of the true prevalence.

We have other limitations that must be acknowledged. The oldest age category (65+) had to be grouped because of the lack of reliable prevalence estimates from the NSS2 and an appropriate conversion factor for this age category. In addition, prevalence estimates from the NSS2 were based on self-reported behaviours, which could be susceptible to social desirability bias. For the meta-analysis component, we based the Canadian relevant exposure distribution on only one Canadian study, which may have led to misclassified inclusion or exclusion of some studies. Additionally, our meta-analyses for BCC and SCCincluded a small number of studies resulting in a large degree of uncertainty in the relative risk estimates. In addition, we relied on some older studies, however, a sensitivity analysis by publication date (before 2000 vs. in 2000 or after) found no difference in relative risk. Canada does not have a national surveillance system for NMSC and, consequently, many cases treated at clinics without confirmatory biopsies are not reported. This situation led to an underestimation of the number of NMSC cases attributable to indoor tanning. Moreover, because only the first NMSC occurring on each individual is reported and multiple NMSCs on the same individual may be caused by indoor tanning, our PAR estimates for NMSC would similarly be underestimated. Finally, Miettinen's formula [40] is typically preferred when confounder adjusted relative risk estimates are used in the calculation of a PAR, but it was not possible to use this formula since it requires the availability of exposure distribution data among skin cancer cases.

While there is emerging evidence that moderate exposure to solar UVR may be protective against the risk of developing some non-cutaneous cancers [41], there is no evidence that a similar beneficial effect exists for indoor tanning. Indeed, it has previously been shown that the use of indoor tanning devices does not protect against solid non-cutaneous cancers and may even increase the risk of developing some hematologic malignancies [42]. Given the lack of benefit of indoor tanning and the large burden of skin cancer attributable to it, efforts to reduce use are required or a total ban should be considered, as already been implemented in Australia and Brazil.

5. Conclusion

The rates of skin cancer in Canada have been consistently increasing over time and in this study we estimate that 7.0% of melanomas, 5.2% of BCCs, and 7.5% of SCCs in Canada in 2015 are attributable to indoor tanning. Given that indoor tanning is one of the risk factors for skin cancer that is most amenable to change through policies that limit or restrict use, strategies aimed at reducing use should be increased and a total ban or restrictions on use and UV-intensity should be considered by health regulators.

Authorship contribution statement

DO'S, DRB, PAD, PJV, CMF, and WDK were responsible for the study conception and contributed substantially to the study design. DO'S, DRB, and WDK drafted the manuscript. DO'S, DRB, PAD, PJV, CMF, and WDK revised the draft paper and gave final approval of this version to be accountable for all aspects of the work in ensuring that questions related to accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflicts of interest

No conflicts of interest exist.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2019.01.004.

References

[1] Canadian Cancer Society's Advisory Committee on Canacer Statistics, Canadian Cancer Statistics 2014, Canadian Cancer Society, Toronto, ON, 2014.
[2] Canadian Cancer Society's Advisory Committee on Canacer Statistics, Canadian Cancer Statistics 2017, Canadian Cancer Society, Toronto, ON, 2017.
[3] Canadian Cancer Society's Advisory Committee on Cancer Statistics, Canadian Cancer Statistics 2015, Canadian Cancer Society, Toronto, ON, 2015.
[4] H. Krueger, D. Williams, M. Chomiak, L. Trenaman, The Economic Burden of Skin Cancer in Canada: Current and Projected, Final Report, Canadian Partnership against Cancer, Toronto, ON, Canada, 2010 26.
[5] IARC Working Group on the Evaluation of Carcinogenic Risk to Humans, A Review of Human Carcinogens, IARC Monographs - Radiation, World Health Organisation, 100D. Lyon (France), 2012.
[6] B. Gerber, P. Mathys, M. Moser, D. Bressoud, C. Braun-Fahrländer, Ultraviolet emission spectra of sunbeds, Photochem. Photobiol. 76 (6) (2002) 664–668.
[7] S.E. Whitmore, W.L. Morison, C.S. Potten, Tanning salon exposure and molecular alterations, J. Am. Acad. Dermatol. 44 (5) (2001) 775–780.
[8] Y. Miyamura, S.G. Coelho, K. Schlenz, J. Batzer, C. Smuda, W. Choi, M. Brenner, T. Passeron, G. Zhang, L. Kolbe, The deceptive nature of UVA tanning versus the modest protective effects of UVB tanning on human skin, Pigment Cell Melanoma Res. 24 (1) (2011) 136–147.
[9] J.L. Stapleton, J. Hillhouse, R. Turrisi, J.K. Robinson, K. Baker, S.L. Manne, E.J. Coups, Erythema and ultraviolet indoor tanning: findings from a diary study, Transl. Behav. Med. 3 (1) (2012) 10–16.
[10] P. Gies, J. Javorniczky, S. Henderson, A. McLennan, C. Roy, J. Lock, C. Lynga, A. Melbourne, L. Gordon, UVR emissions from solaria in Australia and implications for the regulation process, Photochem. Photobiol. 87 (1) (2011) 184–190.
[11] S. Colantonio, M.B. Bracken, J. Beecker, The association of indoor tanning and melanoma in adults: systematic review and meta-analysis, J. Am. Acad. Dermatol. 70 (5) (2014) 847–857 e18.
[12] M. Boniol, P. Autier, P. Boyle, S. Gandini, Cutaneous melanoma attributable to sunbed use: systematic review and meta-analysis, Bmj 345 (2012) e4757.
[13] M.R. Wehner, M.L. Shive, M.-M. Chren, J. Han, A.A. Qureshi, E. Linos, Indoor tanning and non-melanoma skin cancer: systematic review and meta-analysis, Bmj 345 (2012) e5909.
[14] M. Arnold, M. Kvaskoff, A. Thuret, P. Guénel, F. Bray, I. Soerjomataram, Cutaneous melanoma in France in 2015 attributable to solar ultraviolet radiation and the use of sunbeds, J. Eur. Acad. Dermatol. Venereol. (2018).
[15] Department of Justice Canada, Radiation Emitting Devices Regulations (C.R.C., c. 1370), Available at: (2019) http://laws-lois.justice.gc.ca/eng/regulations/C.R.C.,_c._1370/index.html.
[16] D.R. Brenner, A.E. Poirier, S.D. Walter, W.D. King, E.L. Franco, P.A. Demers, P.J. Villeneuve, Y. Ruan, F. Khandwala, X. Grevers, Estimating the current and future cancer burden in Canada: methodological framework of the Canadian population attributable risk of cancer (ComPARe) study, BMJ Open 8 (7) (2018) e022378.
[17] M.L. Levin, The occurrence of lung cancer in man, Acta-Unio Internationalis Contra Cancrum 9 (3) (1953) 531–541.
[18] S. Walter, W. King, L. Marrett, Association of cutaneous malignant melanoma with intermittent exposure to ultraviolet radiation: results of a case-control study in Ontario, Canada, Int. J. Epidemiol. 28 (3) (1999) 418–427.
[19] J.J. Deeks, J.P. Higgins, D. Altman, 9.5. 2 Identifying and measuring heterogeneity, The Cochrane handbook for systematic reviews of interventions, Version 5(0) (2011).
[20] M. Egger, G.D. Smith, M. Schneider, C. Minder, Bias in meta-analysis detected by a simple, graphical test, Bmj 315 (7109) (1997) 629–634.
[21] C.B. Begg, M. Mazumdar, Operating characteristics of a rank correlation test for publication bias, Biometrics (1994) 1088–1101.
[22] J.A.C. Sterne, D. Gavaghan, M. Egger, Publication and related bias in meta-analysis: power of statistical tests and prevalence in the literature, J. Clin. Epidemiol. 53 (11) (2000) 1119–1129.
[23] L.D. Marrett, D.A. Northrup, E.C. Pichora, M.T. Spinks, C.F. Rosen, The second national sun survey: overview and methods, Can. J. Public Health 101 (4) (2010) 10–13.
[24] M.R. Wehner, M.-M. Chren, D. Nameth, A. Choudhry, M. Gaskins, K.T. Nead, W.J. Boscardin, E. Linos, International prevalence of indoor tanning: a systematic review and meta-analysis, JAMA Dermatol. 150 (4) (2014) 390–400.
[25] L. Pinault, T. Bushnik, V. Fioletov, C.E. Peters, W.D. King, M. Tjepkema, The risk of melanoma associated with ambient summer ultraviolet radiation, Health Rep. 28 (5) (2017) 3.
[26] I.-M. Lee, E.J. Shiroma, F. Lobelo, P. Puska, S.N. Blair, P.T. Katzmarzyk, L.P.A.S.W. Group, Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy, Lancet 380 (9838) (2012) 219–229.
[27] A.G. Renehan, I. Soerjomataram, M. Tyson, M. Egger, M. Zwahlen, J.W. Coebergh, I. Buchan, Incident cancer burden attributable to excess body mass index in 30 European countries, Int. J. Cancer 126 (3) (2010) 692–702.
[28] C. Bajdik, R. Gallagher, G. Astrakianakis, G. Hill, S. Fincham, D. McLean, Non-solar ultraviolet radiation and the risk of basal and squamous cell skin cancer, Br. J. Cancer 73 (12) (1996) 1612.
[29] V. Bataille, A. Winnett, P. Sasieni, J.N. Bishop, J. Cuzick, Exposure to the sun and sunbeds and the risk of cutaneous melanoma in the UK: a case–control study, Eur. J. Cancer 40 (3) (2004) 429–435.
[30] Y.-T. Chen, R. Dubrow, T. Zheng, R.L. Barnhill, J. Fine, M. Berwick, Sunlamp use and the risk of cutaneous malignant melanoma: a population-based case-control study in Connecticut, USA, Int. J. Epidemiol. 27 (5) (1998) 758–765.
[31] K.M. Clough-Gorr, L. Titus-Ernstoff, A.E. Perry, S.K. Spencer, M.S. Ernstoff, Exposure to sunlamps, tanning beds, and melanoma risk, Cancer Causes Control 19 (7) (2008) 659–669.
[32] A.E. Cust, B.K. Armstrong, C. Goumas, M.A. Jenkins, H. Schmid, J.L. Hopper, R.F. Kefford, G.G. Giles, J.F. Aitken, G.J. Mann, Sunbed use during adolescence and early adulthood is associated with increased risk of early-onset melanoma, Int. J. Cancer 128 (10) (2011) 2425–2435.
[33] J. Han, G.A. Colditz, D.J. Hunter, Risk factors for skin cancers: a nested case–control study within the Nurses' Health Study, Int. J. Epidemiol. 35 (6) (2006) 1514–1521.
[34] M.R. Karagas, V.A. Stannard, L.A. Mott, M.J. Slattery, S.K. Spencer, M.A. Weinstock, Use of tanning devices and risk of basal cell and squamous cell skin cancers, J. Natl. Cancer Inst. 94 (3) (2002) 224–226.
[35] A. Swerdlow, J. English, R. MacKie, C. O'Doherty, J. Hunter, J. Clark, D. Hole, Fluorescent lights, ultraviolet lamps, and risk of cutaneous melanoma, Bmj 297 (6649) (1988) 647–650.
[36] J. Westerdahl, H. Olsson, A. Måsbäck, C. Ingvar, N. Jonsson, L. Brandt, P.-E. Jönsson, T. Möller, Use of sunbeds or sunlamps and malignant melanoma in southern Sweden, Am. J. Epidemiol. 140 (8) (1994) 691–699.
[37] M. Zhang, A.A. Qureshi, A.C. Geller, L. Frazier, D.J. Hunter, J. Han, Use of tanning beds and incidence of skin cancer, J. Clin. Oncol. 30 (14) (2012) 1588.
[38] S.D. Walter, Calculation of attributable risks from epidemiological data, Int. J. Epidemiol. 7 (2) (1978) 175–182.
[39] M. Rhainds, L. De Guire, J. Claveau, A population-based survey on the use of artificial tanning devices in the province of Quebec, Canada, J. Am. Acad. Dermatol. 40 (4) (1999) 572–576.
[40] O.S. Miettinen, Proportion of disease caused or prevented by a given exposure, trait or intervention, Am. J. Epidemiol. 99 (5) (1974) 325–332.
[41] H. van der Rhee, J.W. Coebergh, E. de Vries, Is prevention of cancer by sun exposure more than just the effect of vitamin D? A systematic review of epidemiological studies, Eur. J. Cancer 49 (6) (2013) 1422–1436.
[42] D.E. O'Sullivan, T.W. Hillier, D.R. Brenner, C.E. Peters, W.D. King, Indoor tanning and the risk of developing non-cutaneous cancers: a systematic review and meta-analysis, Cancer Causes Control (2018) 1–14.