Reference:

Authors:
Richard Gallagher is an environmental epidemiologist with a major research interest in risk factors for cutaneous malignant melanoma, basal and squamous cell cancers. His research output includes more than 200 peer-reviewed articles, chapters, and books, some 70 of which are on sun sensitivity, pigmentary factors, solar and artificial UV radiation, and risk of the 3 major forms of skin cancer. He is currently Scientist Emeritus, Cancer Control Research Program at the BC Cancer Research Centre in Vancouver, and Clinical Professor, School of Population and Public Health at the University of British Columbia. He is the Principal of Alpine Epidemiology Limited (alpine.epi@shaw.ca), a consulting company incorporated in BC in 1996 specializing in cancer risk assessment for public bodies and corporations.

John McLaughlin is a cancer epidemiologist who has established and directed large scale population-based cancer research and prevention programs across Ontario. He recently completed a term as a Vice-President at Cancer Care Ontario where he launched the Ontario Health Study, a large-scale prospective research program which will be used by investigators across the province and across Canada to identify causes of major diseases. His current primary appointments are Senior Investigator, Prosserman Centre for Health Research, Samuel Lunenfeld Research Institute, Toronto, and Professor, Dalla Lana School of Public Health, University of Toronto. He has published more than 160 peer-reviewed scientific papers, chapters and books and has acted as a scientific consultant to many organizations and community groups.

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Dr. Loraine Marrett, Ph.D.
Director, Prevention and Surveillance and Senior Scientist, Prevention and Cancer Control, Cancer Care Ontario; Professor, Dalla Lana School of Public Health, University of Toronto

Dr. DeAnn Lazovich, Ph.D.
Associate Professor, Division of Epidemiology and Community Health, School of Public Health; and Prevention and Etiology Program Co-Leader, Masonic Cancer Center, University of Minnesota

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For further information:
Healthy Public Policy Directorate
Toronto Public Health
277 Victoria Street, 7th Floor
Toronto, Ontario
Canada M5B 1W2

Tel: 416-338-7030
About this Report:

Toronto Public Health commissioned Richard Gallagher and John McLaughlin to undertake this independent review of the evidence on ultraviolet radiation and skin cancer to inform a Toronto Public Health staff report on reducing skin cancer risk from indoor tanning. Toronto Public Health has a mandate under the Chronic Disease Prevention Standard of The Ontario Public Health Standards to support the development of healthy public policy to reduce exposure to ultraviolet radiation.

The Toronto Public Health staff report Reducing Skin Cancer Risk from Indoor Tanning provides information regarding: the health risks of indoor tanning, indoor tanning use in Toronto and Ontario, Toronto indoor tanning facilities’ practices, and legislation and policies related to indoor tanning equipment use. It commends the Ontario government for introducing legislation to help prevent skin cancer and protect the public, especially young people, from the harmful effects of indoor tanning.

The staff report, this technical report and a report summarising A Review of Toronto Indoor Tanning Facilities’ Websites were presented to the Toronto Board of Health at its meeting on March 25, 2013.

Copies of the three reports can be found at:

http://www.toronto.ca/health
# Table of Contents

Table of Contents ................................................................................................................................. iv
List of Tables ............................................................................................................................................... vi
List of Figures ............................................................................................................................................ vii
Executive Summary ................................................................................................................................... viii
Introduction .................................................................................................................................................. 1
Purpose of the Report ................................................................................................................................ 2
Methods ........................................................................................................................................................ 3
Types of Skin Cancers .................................................................................................................................. 5
  Cutaneous Malignant Melanoma (CMM) ............................................................................................. 5
  Second Primary CMM .......................................................................................................................... 5
  Basal Cell Carcinoma (BCC) ................................................................................................................ 5
  Squamous Cell Carcinoma (SCC) ......................................................................................................... 5
  Second Primary BCC and SCC ............................................................................................................. 5
Patterns and Trends in Skin Cancer Incidence and Mortality ....................................................................... 6
  CMM Incidence and Mortality Trends ................................................................................................. 6
  Age and Sex Distribution of Melanoma in Toronto and the Rest of Ontario...................................... 10
  Estimates of the Relative Frequency of BCC, SCC and CMM in Toronto and the Rest of Ontario .. 12
  Ethnicity-Adjusted Incidence Rates for Melanoma ............................................................................ 15
The Burden of Illness Associated with Skin Cancer ................................................................................... 18
Risk Factors Associated with Skin Cancer ................................................................................................. 19
  Individual Susceptibility Factors for Skin Cancer (Host Factors) ...................................................... 19
    Pigmentation, Ethnicity and Family History ....................................................................................... 19
    Sun Sensitivity ..................................................................................................................................... 20
    Freckling ........................................................................................................................................... 21
    Nevi (Skin Moles) ........................................................................................................................... 21
    Indicators of Sun Damage ............................................................................................................. 22
Ultraviolet Radiation ................................................................................................................................... 22
  Sun Exposure ....................................................................................................................................... 23
    Melanoma ......................................................................................................................................... 23
    Basal Cell Carcinoma ....................................................................................................................... 24
    Squamous Cell Carcinoma ............................................................................................................... 25
Indoor Tanning

Background

UVR Emission of Modern Sunbeds

Prevalence and Correlates of Indoor Tanning

Indoor Tanning and Risk of Skin Cancer

Melanoma

Basal Cell Carcinoma

Squamous Cell Carcinoma

Indoor Tanning and Risk of Other Cancers

Non Hodgkin Lymphoma (NHL)

Breast Cancer

Other Cancers

Summary – Indoor Tanning and Risk of Other Cancers

Vitamin D

Health Effects of Vitamin D

Indoor Tanning, Oral Supplementation, and Vitamin D Levels

Oral Supplementation and Vitamin D Levels

Supplementation vs. Artificial UV Radiation and Vitamin D Levels

Summary – Vitamin D and Skin Cancer

Overall Summary and Conclusions

References

Appendix 1: Skin Cancer Statistical Tables Used for Figures, and Supplementary Figure

Appendix 2: The Economic Burden of Skin Cancer
# List of Tables

Table 1: New Cases of Melanoma by Sex and Age Group for Toronto and the Rest of Ontario, 1999-2008.........................................................................................................................10

Table 2: Incidence Rates and Rate Ratios (RR) for Skin Cancer in British Columbia by Cancer Type, BCC, SCC, and CMM, by Sex and Year, 1973-2003 .................................................................................12

Table 3: Indoor Tanning and Cutaneous Malignant Melanoma: Ever vs. Never Exposed (Case-Control Studies)..........................................................................................................................32

Table 4: Indoor Tanning and Cutaneous Malignant Melanoma: Ever vs. Never Exposed (Cohort Studies).................................................................................................................................36

Table 5: Indoor Tanning and Cutaneous Malignant Melanoma: First Exposure Early in Life (Case-Control Studies).........................................................................................................................37

Table 6: Indoor Tanning and Cutaneous Malignant Melanoma: First Exposure Early in Life (Cohort Studies).................................................................................................................................39

Table 7: Indoor Tanning and Cutaneous Malignant Melanoma: Longest Duration or Highest Frequency of Use (Case-Control Studies)...................................................................................40

Table 8: Indoor Tanning and Cutaneous Malignant Melanoma: Longest Duration or Highest Frequency of Use (Cohort Studies)........................................................................................................42

Table 9: Indoor Tanning and Basal Cell Carcinoma: Ever vs. Never Exposed (Case Control Studies).... 51

Table 10: Indoor Tanning and Basal Cell Carcinoma: Ever vs. Never Exposed (Cohort Studies).............52

Table 11: Indoor Tanning and Squamous Cell Carcinoma: Ever vs. Never Exposed (Case-Control Studies).................................................................................................................................56

Table 12: Indoor Tanning and Squamous Cell Carcinoma: Ever vs. Never Exposed (Cohort Studies)..... 57

Appendix 1 Table 1.1: Melanoma Age-Standardized Incidence and Mortality Rates and Counts, Toronto and the Rest of Ontario, by Sex, 1986–2008.................................................................84

Appendix 1 Table 1.2: Incidence and Mortality Rates, Confidence Intervals, and Rate Ratios for Toronto Compared to the Rest of Ontario, for Specific Periods, by Sex, 1989-2008 .........................................................86

Appendix 1 Table 1.3: Estimation of Race-Specific and Race-Adjusted Incidence Rates for Melanoma of the Skin, Rest of Ontario and Toronto, by Sex and Year, 1991-2006 .................87

Appendix 1 Table 1.4: Data Points for Appendix Figure 1.1 (ASIRs per 100,000) ..................................89
List of Figures

Figure 1: Incidence and Mortality Trends for Cutaneous Malignant Melanoma for Toronto and the Rest of Ontario, by Sex, 1986-2008 .......................................................... 8

Figure 2: Incidence and Mortality Rate Ratios for Cutaneous Malignant Melanoma in Toronto Compared to the Rest of Ontario, for Specific Periods, by Sex, 1989-2008............. 9

Figure 3: Age Distribution of the Number of Incident Cases of Cutaneous Malignant Melanoma for Toronto and the Rest of Ontario, by Sex, 1999-2008 .................................................. 11

Figure 4: Estimates of Age Standardized Incidence Rates for Skin Cancer [Basal Cell Carcinoma (BCC), Squamous Cell Carcinoma (SCC) and Cutaneous Malignant Melanoma (CMM)] for Toronto and the Rest of Ontario, by Sex, 1993 and 2003 ................................................................. 14

Figure 5: Age Standardized Incidence Rates (ASIRs) and Race-Adjusted Incidence Rates for Melanoma (3-Year Moving Averages) for Toronto and the Rest of Ontario, by Sex, 1991-2006 ................................................................. 17

Appendix 1 Figure 1.1: Age Standardized Incidence Rates for Cutaneous Malignant Melanoma, for Canada and Ontario, by Year, both Sexes Combined, 1992-2009 (with 95% confidence limits, per 100,000, standardized to 1991 Canadian population) .... 88
Executive Summary

This report was commissioned by Toronto Public Health in order to bring together information on risk factors for skin cancer and in particular to summarize the current state of scientific knowledge on the relationship between use of sunbeds and sunlamps and the risk of the three major types of skin cancer: cutaneous malignant melanoma (CMM), basal cell carcinoma (BCC), and squamous cell carcinoma (SCC) of the skin. In addition, the authors conducted a comprehensive analysis of skin cancer incidence and mortality rates in Ontario. The report examines temporal trends in the incidence and mortality rates of melanoma in Toronto compared to the rest of Ontario over the past 20 years, as well as temporal trends in the incidence of melanoma in Canada overall.

The authors also conducted exhaustive searches of the scientific and medical literature published in peer reviewed journals on factors that alter the risk of developing skin cancer, including those inherent in individuals (i.e., susceptibility factors) such as skin and hair colour, sensitivity to sunburn and others, as well the major known ‘environmental’ factor - ultraviolet radiation (UVR) from the sun or from indoor tanning equipment. Peer reviewed scientific papers are those that are critically examined by other scientists prior to publication to determine that the study was carried out with scientific rigour and that the conclusions the authors reached were justified by the data the study produced. Studies of susceptibility factors and sun exposure in relation to skin cancer number in the hundreds, and the authors of the current report selected a group of well conducted investigations to summarize information on these issues. The numbers of studies of indoor tanning and its relationship to risk of the three skin cancers is less voluminous, and so the authors have endeavoured to bring together information from all peer reviewed investigations for presentation in the report. After review of information on indoor tanning and each of the three skin cancer types, a summary conclusion is offered on the extent to which the scientific evidence supports public health action to restrict access to indoor tanning equipment.

Skin cancer is the most common type of cancer among Caucasians of European origin (whites), and the most common cancer in Canada. Reliable estimates for melanoma, the most dangerous type of skin cancer, are easily determined as cancer registries around the world record this malignancy. GLOBOCAN 2008, a worldwide summary of the frequencies and rates of cancer throughout the world conducted by the International Agency for Research on Cancer (IARC), gives a figure of 199,627 cases of cutaneous melanoma in 2008 (Ferlay et al., 2010).

Estimates of non-melanocytic skin cancers (BCC and SCC) by country and by province are more difficult to obtain as cancer registries do not, in general, record these types of cancer. Canadian estimates for 2011 give an expected number of non-melanocytic skin cancers (NMSC) of about 74,000 and cutaneous malignant melanoma (CMM) of about 5500 (Canadian Cancer Society's Steering Committee on Cancer Statistics, 2011). Applying the ratio of NMSC/CMM from the Canadian estimate, there were an estimated 2.7 million new NMSCs worldwide in 2011, with lung cancer the next most common cancer worldwide at slightly over 1.6 million new cases annually (Ferlay et al., 2010).

In Ontario in 2011 an estimated 2500 new melanomas were diagnosed (Canadian Cancer Society's Steering Committee on Cancer Statistics, 2011) and based on national figures in the Canadian Cancer Society statistics publication the authors of this report estimate that about 33,660 NMSCs were diagnosed in the province. Ontario is a multi-ethnic province with a population estimated at 12.8 million in 2011, of which 22.8% (according to the 2006 Census) are visible minorities at lower risk of skin cancer than Caucasians of European origin (whites) (Statistics Canada, 2010). Toronto is one of the two most multiethnic cities in Canada with a population estimated at 2.6 million in 2011. According to the 2006
Census, almost half of Torontonians (47%) are members of a visible minority group (City of Toronto, n.d.), with a lower risk of skin cancer. Applying the Canadian Cancer Society’s data for Canada, the authors of this report estimated that there were approximately 310 new melanomas and 4270 new cases of NMSC diagnosed in Toronto residents in 2011, for a total of approximately 4580 newly diagnosed cases of skin cancer.

Skin cancer does not take as many lives, proportionally, as other cancers but the economic burden on society from the disease is very high. A recent investigation commissioned by the Canadian Partnership Against Cancer projected that by 2031 skin cancer costs due to direct medical expenditures as well as indirect costs due to lost productivity will approach $922 million annually (Krueger et al., 2010) assuming skin cancer rates are driven largely by population growth and aging. The direct costs of treatment of skin cancer plus the indirect cost of lost wages and productivity were estimated to be about $296 million for Ontario alone in 2011 (Krueger et al., 2010).

The principal risk factors for all three forms of skin cancer fall into two categories: individual susceptibility factors and environmental factors. Individual susceptibility factors include fair skin, light coloured hair and eyes, sun sensitivity, and a family history of skin cancer, all of which increase the risk of each of the three major types of skin cancer. In addition, moderate or pronounced freckling and a large number of benign nevi (skin moles) also increase the risk of cutaneous melanoma, the most dangerous form of skin cancer.

The principal environmental risk factor for skin cancer is exposure to solar (sunlight) and artificial ultraviolet radiation. Intermittent sun exposure (largely through recreational activities), especially early in life, increases the risk for both CMM and BCC. Cumulative lifetime exposure appears to be less important in these cancers. Risk of SCC appears to be more closely related to degree of chronic (through outdoor occupation) or cumulative solar exposure. An assessment of the evidence from many studies of sunlight and the risk of skin cancer carried out by the International Agency for Research on Cancer in 1992, determined solar UVR exposure to be a Group 1 carcinogen - that is, an agent known to cause skin cancer.

Skin cancer prevention programs appear to be a cost effective method of preventing cancer due to solar UVR exposure. Economic evaluation of programs such as the Australian population-based SunSmart program, and the United States Environmental Protection Agency's (EPA) SunWise program in schools, indicate that $2-$4 is saved due to reduced cancer incidence for every $1 invested (Shih et al., 2009; Kyle et al., 2008), although the savings take some time to materialize because of the long lag period between sun exposure and development of skin cancer. The prevention programs are aimed primarily at reducing UVR exposure through use of clothing and shifting outdoor activity to times of low solar UVR at the individual level and provision of adequate shade at the community level (Montague et al., 2001).

Exposure to artificial UVR in the general population in Canada occurs largely through use of indoor tanning equipment such as sunbeds, sunlamps, and tanning booths for the purposes of indoor tanning. Exposure to artificial UVR for the purpose of indoor tanning has come under scientific scrutiny as a potential cause of skin cancer. A number of high quality epidemiologic studies have been conducted in addition to several meta-analyses. Meta-analyses of data from studies of indoor tanning equipment indicate that use of such devices raises the risk of CMM (Gallagher et al., 2005; IARC, 2007, Boniol et al., 2012).

The latest summary of available evidence (Boniol et al., 2012) indicates that users of indoor tanning devices increase their risk of developing CMM by 20% compared to those who do not indoor tan.
(Relative Risk [RR] =1.20; 95% Confidence Interval [CI]=1.08-1.34). Furthermore the meta-analysis showed that among users, each additional tanning session increases risk of CMM by 1.8%. This is known as a dose-response relationship and is one of the strongest indicators that indoor tanning is not simply associated with melanoma, but causes it. The meta-analysis also showed that first use of tanning equipment before age 35 increases the risk of melanoma by 59% (RR=1.59; 95%CI=1.36-1.87).

Although studies of SCC and indoor tanning are less common than melanoma, the Boniol et al. (2012) meta-analysis based on five studies showed that use of indoor tanning devices more than doubled the risk of developing this cancer (RR=2.23; 95%CI=1.39-3.57). For BCC, users had a 9% increased risk (RR=1.09; 95%CI=1.01-1.18). A recent study (Zhang et al., 2012), based on information on 403 cases of SCC and 5506 cases of BCC diagnosed in a cohort of more than 73,000 female nurses followed for many years, showed that indoor tanning increased the risk of both BCC and SCC. More importantly, among sunbed users a dose-response relationship was seen - each incremental increase in exposure of four sunbed sessions per year increased the risk of BCC by 15% (Hazard ratio [HR]=1.15; 95%CI=1.11-1.19) and SCC by 15% (HR=1.15; 95%CI=1.01-1.31).

All of the estimates of increased risk quoted above include statistical adjustment to control for individual susceptibility factors as well as exposure to ultraviolet radiation from sun exposure. Such adjustment means that the findings of increased risk of skin cancer in users of indoor tanning devices are very unlikely to have resulted from confounding due to sun exposure. The International Agency for Research on Cancer has classified indoor tanning as a Group 1 carcinogen – that is, an exposure known to cause cancer (El Ghissassi et al., 2009; IARC, 2012).

Evidence that indoor tanning is carcinogenic is of significant public health concern as surveys conducted since 2006 show that in many municipalities across Ontario, at least 20% of Ontario adults age 18-24 used sunbeds or sunlamps in the year prior to the survey. An Ipsos Reid poll of 1476 Ontario students age 12-17 conducted in April 2012 on behalf of the Canadian Cancer Society revealed that 21% of grade 12 students reported ever having used tanning beds (Ipsos Reid, 2012).

The World Health Organization has recommended that use of sunbeds and other indoor tanning devices be restricted to those age 18 and over. In North America, five Canadian provinces--Nova Scotia (ban for under 19), Manitoba (parental consent for under 18), Quebec (ban for under 18), Newfoundland and Labrador (ban for under 19), and British Columbia (ban for under 18)--and over 30 states in the US have some form of restricted access to indoor tanning for young people. Several European countries, including France, Germany, the UK and most Australian states have comprehensive sunbed use laws, all of which include age-based bans.

The evidence from recent scientific studies suggests that regulations restricting the use of indoor tanning equipment in commercial salons to those aged 18 and over would be a prudent first step to consider for public health agencies in the Province of Ontario and other Canadian provinces.

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1 The 95% confidence interval indicates that there is a 95% probability that the relative risk of melanoma associated with indoor tanning (versus no indoor tanning) is between 1.08 and 1.34 (95%CI =1.08-1.34). That is, if the study were repeated many times, 95 times out of 100 the true increased risk of melanoma in the population would be between 8% and 34%.
Introduction

Skin cancer is the most common cancer in Canada in Caucasians of European origin (whites), but it also occurs at lower rates in other ethnic groups. Canadian estimates of numbers of newly diagnosed skin cancers in 2011 stand at about 74,000 for non-melanocytic skin cancers (NMSC), which includes basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) of the skin, and 5500 for melanoma (Canadian Cancer Society's Steering Committee on Cancer Statistics, 2011). Based on the national figures, in Ontario in 2011 an estimated 33,660 NMSCs and 2500 new melanomas were diagnosed (Canadian Cancer Society's Steering Committee on Cancer Statistics, 2011). The current report, using methods described below, estimates that approximately 4270 new cases of NMSC (3510 BCCs and 760 SCCs) and 310 new melanomas were diagnosed in Toronto residents in 2011, for a total of 4580 newly diagnosed skin cancers.

Cutaneous malignant melanoma is a life-threatening cancer. In 2011 an estimated 420 deaths in Ontario were attributed to this cancer (Canadian Cancer Society's Steering Committee on Cancer Statistics 2011). The primary method of treatment for melanoma is surgery, which is frequently successful. However, if the melanoma metastasizes there are presently no recognized second line curative treatments for the disease. Fortunately, survival rates for BCC and SCC are very good; however, there is a significant social impact on individuals who develop these cancers including fear and anxiety, surgical scars from removal, as well as a burden for family caregivers who look after those recuperating from treatment. In total, treatment of skin cancer and lost productivity were estimated to have cost Ontario about $296 million in 2011 (Krueger et al., 2010).

Skin cancer is preventable through reducing sun exposure by clothing choice, seeking shade, and shifting outdoor activities away from times when the UV index is high (Shih et al., 2009; Kyle et al., 2008). Use of sunscreen reduces the risk of SCC (Thompson et al., 1993; Green et al., 1999), but research indicating that sunscreens are effective at preventing CMM or BCC is more scanty (Green et al., 2011; Ulrich et al., 2009; Gallagher et al., 2000). Studies carried out in Australia and the United States indicate that prevention programs are highly cost effective (Shih et al., 2009; Kyle et al., 2008), although because of the known lag-time between solar exposure and skin cancer diagnosis, time will pass before the cost savings are seen at the population level.

Recently concerns have surfaced about the adverse effects on risk of skin cancer due to exposure to artificial UV radiation. Studies conducted internationally have shown that use of sunbeds and sunlamps for the purposes of indoor tanning increase the risk of all three skin cancers: CMM, BCC, and SCC. The strength of the evidence is such that recently the International Agency for Research on Cancer (El Ghissassi et al., 2009; IARC, 2012) declared the use of UV tanning devices to be carcinogenic to humans.

Recent surveys conducted in many municipalities across Ontario show that use of indoor tanning devices is common with at least 20% of Ontarians age 18-24 reporting use in the previous 12 months. In addition a survey carried out among school students in Ontario show significant use by minors with 21% of grade 12 students polled having ever used indoor tanning devices.

Skin cancer has become a major public health issue in Toronto, in Ontario and across Canada. This report will provide a clear picture of the scientific evidence concerning causes of the disease that can be used by public health organizations to craft interventions to reduce the incidence, mortality, and financial burden of skin cancer.

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2 The authors of this report estimated the number of cases of NMSC in Ontario in 2011 (33,660) based on the estimated number of cases of NMSC reported for Canada overall in the Canadian Cancer Statistics 2011 Report (Canadian Cancer Society's Steering Committee on Cancer Statistics, 2011).
Purpose of the Report

Toronto Public Health commissioned an in-depth review of the latest scientific information on skin cancer, with an emphasis on the contribution of indoor tanning to the burden of skin cancer. This report therefore consists of a review of the epidemiological literature on all aspects of skin cancer and its relationship with solar UVR and indoor tanning, as well as data on trends in skin cancer in Canada, Ontario, and in Toronto. A specific focus of this review is the epidemiologic literature examining the relationship between use of indoor tanning equipment and risk of skin cancer - with particular emphasis on the studies that appeared after a systematic analysis (IARC, 2007) which combined published data available from the early 1980s to 2006 on sunbed and sunlamp use and the three major types of skin cancer, and suggested that use of indoor tanning devices increased risk of CMM and SCC.

The current report contains the following sections:

1. Description of the methods employed
2. Description of the three types of skin cancer
3. Patterns and trends in the incidence and mortality rates of skin cancer (with a focus on Toronto, but placed in the context of Ontario and Canada)
4. Brief description of the economic and social burden of skin cancer
5. Review of risk factors associated with skin cancer, including a critical analysis of the contribution of indoor tanning
6. Prevalence and correlates of use of indoor tanning equipment
7. Vitamin D in relation to indoor tanning and oral supplementation
8. Summary and Conclusions
Methods

The descriptive epidemiology of skin cancer in Toronto and the rest of Ontario was based primarily on analyses of data provided by the Ontario Cancer Registry (OCR). A request for statistical data was submitted to the Surveillance Unit at Cancer Care Ontario (CCO), and statistics were retrieved from the OCR and provided in spreadsheet form. Within the OCR, skin cancer data within the geographic area covered by the Toronto Public Health unit were extracted and compared to skin cancer data from all other public health units in Ontario combined (i.e., the rest of Ontario). The geographic identifier in the OCR (i.e., public health unit) describes the area of residence of cases based on their home address postal code. Detailed methods are presented below each figure or table. The overall purpose and methods to characterize the frequency and patterns of skin cancer are described below.

- Melanoma incidence and mortality statistics are presented for 1986-2008. This period is the most recent period for which reliable skin cancer data are available (as recommended by the Surveillance Unit analysts at the OCR). It is noteworthy that although we are fortunate in Canada to have access to population-based cancer registries, the numbers reported by the OCR are likely to represent minimal estimates due in part to incompleteness of source data provided to the OCR, and because people who are affected may have multiple primary diagnoses.

- As basal and squamous cell skin cancers are not recorded by the OCR, estimation procedures were employed to determine the incidence of these cell skin cancers. Using standard procedures that have been used widely across Canada (Canadian Cancer Society’s Steering Committee on Cancer Statistics, 2011), these rates were estimated by applying weights to the melanoma rates, where the weights were derived from the relative frequency of basal and squamous cell cancers as observed in British Columbia in 2003 and reported in a recent paper (McLean et al., 2012).

- The geographic units of interest varied, and although the primary focus of this report is Toronto, certain analyses were also done for Ontario and Canada to provide comparators to the Toronto experience. CCO was able to provide melanoma incidence and mortality data for the population covered by the Toronto Public Health unit, which was compared to the rest of Ontario (i.e., all other public health units in Ontario combined). To place Toronto and Ontario rates and trends in context, information for Canada was obtained from the Canadian Cancer Registry at Statistics Canada (via the @Cansim” system at www5.statcan.gc.ca/cansim).

- Analyses of cancer statistics included:
  1. Assessment of trends in melanoma incidence and mortality rates over the past two decades (by sex). Using procedures that are widely used for Canadian cancer statistics and to provide a standard comparator, rates were age-standardized using the 1991 Canadian population. Because the risk of skin cancer increases with age, age standardization is used to adjust for changes over time in the age of the population. Therefore, any trends that are observed in skin cancer rates over time will be due to factors other than changes in the age of the population.
  2. Assessment of whether melanoma incidence rates in Toronto differ from those of the rest of Ontario. Age-standardized rates were also used for this analysis to adjust for any differences between Toronto and the rest of Ontario in the age of the populations.
  3. A description of the variation in melanoma incidence by age, for males and females, and an assessment of whether this pattern differs between Toronto and the rest of Ontario.

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3 Incidence rates describe the risk of developing a disease (e.g., melanoma) over a specific period of time (e.g., a one-year period). Mortality rates describe the risk of dying from a disease over a specific period of time. In this report, skin cancer incidence and mortality rates are expressed as the number of people diagnosed with skin cancer and the number of people who die from skin cancer, respectively, per 100,000 people in the population.
4. An estimate of the frequency of basal cell and squamous cell skin cancer in Toronto and the rest of Ontario.
5. Assessment of the extent to which the trend in melanoma incidence in Toronto is due to changes in the population’s ethnicity.
6. A comparison of melanoma rates between Canada and Ontario from 1992-2009 (as plotted in Appendix 1 Figure 1.1).

The critical review of the scientific literature was based on a systematic search for studies published in the peer-reviewed journals and indexed in PubMed and EBSCO from 1980 through January 2012 using keyword groups or terms including:

- Skin cancer, malignant melanoma, basal cell carcinoma, squamous cell carcinoma of the skin
- Latitude, epidemiology, incidence, mortality, prevalence, risk factor, economic impact, social impact, cost of treatment
- Fitzpatrick skin type, sun sensitivity, skin color, hair color, eye color, pigmentation, freckling, nevus, skin moles
- Sun exposure, sunlight, recreational sunlight exposure, intermittent sunlight exposure, occupational sunlight exposure, cumulative sunlight exposure, solar ultraviolet radiation, sunburn, reported sun exposure
- Indoor tanning, sunlamp, sunbed, tanning booth, tanning salon, tanning prevalence

By cross linking these terms using the word ‘AND’ peer-reviewed papers were accessed in abstract form. Review of the abstracts provided the key studies retrieved and referenced in this review. Bibliographic references in systematic review papers were scanned to identify papers not found by the methods noted above.

Due to volume of publications on most topics related to skin cancer it was not feasible to reference every paper. For instance, in the evaluation of one issue - the relationship between recreational sunlight exposure and subsequent malignant melanoma - more than 40 papers have been published. Where possible the authors referenced systematic reviews which produced summary evaluations, along with the key original papers in each area.
Types of Skin Cancers

Cutaneous Malignant Melanoma (CMM)
Cutaneous malignant melanoma is the least common of the three major types of skin cancer in Canada, but is the cause of the most mortality (Canadian Cancer Society’s Steering Committee on Cancer Statistics, 2011). In Canada, CMM incidence has been rising for many years, most recently (1998-2007) showing an annual percent increase of about 1.4% in both sexes. There are indications however, that rates in younger age cohorts (age 25-44) in Canada are stabilizing or declining (Erdmann et al., 2013). By comparison with other cancers such as lung and colorectal cancer, CMM five-year survival is excellent at 90%, but survival falls to around 78% in patients with lesions greater than 4.00 mm in depth (Canadian Cancer Society's Steering Committee on Cancer Statistics, 2011; Balch et al., 2009; Elsaesser et al., 2012). Mortality from CMM is significant, with a total of 950 deaths across Canada in 2011, including 420 in Ontario (Canadian Cancer Society's Steering Committee on Cancer Statistics, 2011), from which we estimate that more than 50 deaths would have occurred in Toronto alone.

Second Primary CMM
Survivors of a first primary melanoma are at much higher risk of a second new melanoma than persons of the same age in the general population. The risk varies from about 5.5% to 7.7% depending on length of follow-up (Nashan et al., 2003; Brobeil et al., 1997; Goggins and Tsao, 2003). A recent study carried out among patients diagnosed at New York University between 2002 and 2008 estimated the risk to be as high as 8.7% in the five years after diagnosis (Hwa et al., 2012).

Basal Cell Carcinoma (BCC)
Basal cell carcinoma is the most common type of skin cancer. It accounts for about 80% of non-melanocytic skin cancers in British Columbia (McLean et al., 2012), and likely, by extension, in Canada, Ontario and Toronto. The largest proportions of these cancers occur on sun exposed anatomic sites such as the face, ears, and other parts of the head and neck. Basal cell carcinoma also occurs fairly frequently on intermittently sun-exposed sites such as the trunk, particularly in males. For the most part, BCC is treated by surgical removal.

Squamous Cell Carcinoma (SCC)
Squamous cell carcinoma is the second most common type of skin cancer, comprising about 20% of non-melanocytic skin cancers (McLean et al., 2012). Squamous cell carcinoma can spread to distant sites, although, at most, only about 4% of these lesions reach the point of metastasis (spread to distant organs or sites) (LeBoeuf and Schmults, 2011). Squamous cell carcinomas (and occasionally BCC) on the face may be treated with Moh’s surgery, a process of iterative resection with immediate pathologic examination which helps to minimize any disfigurement. Moh’s procedures are effective in minimizing surgical scars (Rowe et al., 1992), but are significantly more expensive than standard surgical excision.

Second Primary BCC and SCC
Diagnosis of a first BCC or SCC increases the risk for a second non-melanocytic skin cancer (Marcil and Stern 2000; Efird et al., 2002). In addition, a meta-analysis of studies evaluating second cancers after an initial diagnosis of SCC or BCC indicated a relative risk of 2.74 for a subsequent melanoma and a 2.38-fold increased risk for cancer of the lip (Wheless et al., 2010).
Patterns and Trends in Skin Cancer Incidence and Mortality

CMM Incidence and Mortality Trends

Melanoma incidence and mortality trends were examined using data obtained from the Ontario Cancer Registry. Rates for Toronto were compared to those in the rest of Ontario using incidence rate ratios and mortality rate ratios\(^4\).

Incidence rates for CMM in the population served by Toronto Public Health in 2007 (the most recent year with data available) were 13.3 and 10.7 per 100,000 for males and females, respectively (age standardized, 3-year moving average\(^5\)). Mortality rates for CMM in Toronto were 3.2 and 1.5 per 100,000 for males and females, respectively. Detailed source data are provided in Appendix 1, Table 1.1, and the trends and patterns are summarized in Figure 1.

**Gender differences in CMM incidence and mortality rates**

Overall melanoma rates are consistently higher for males than females (Figure 1). Incidence rates for males are about 25% higher than for females (M:F incidence rate ratios in 2007 are 1.2 for Toronto and 1.3 for the rest of Ontario). Mortality rates among males are twice those of females in both Toronto and the rest of Ontario. The mortality rate ratios (M:F) using the 3-year moving average in 2007 are 2.2 for Toronto and 2.0 for the rest of Ontario. These data also demonstrate that the relative difference between the sexes is similar for Toronto and the rest of Ontario.


**CMM incidence and mortality rates in Toronto versus the rest of Ontario**

Melanoma incidence and mortality rates are lower for Toronto compared to the rest of Ontario, with incidence and mortality rate ratios of the 3-year moving average for 2007 (Toronto over the rest of Ontario)\(^6\) being:

- Incidence rate ratios (2007) (Toronto:Rest of Ont): Males = 0.69, Females = 0.72
- Mortality rate ratios (2007) (Toronto:Rest of Ont): Males = 0.85, Females = 0.78

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\(^4\) Incidence rate ratios are calculated by dividing the incidence rate in one group by the incidence rate in another group (e.g., males vs. females; Toronto vs. the rest of Ontario). Similarly, mortality rate ratios are calculated by dividing the mortality rate in one group by the mortality rate in another group. Rate ratios that are equal to 1.0 indicate no difference in the rates between the groups. Rate ratios greater than 1.0 or less than 1.0 indicate that the rates differ between the groups. For example, an incidence rate ratio (comparing groups A:B) of 1.8 indicates that group A has an 80 percent higher risk of the disease compared to group B. An incidence rate ratio of 0.8 indicates that group A has a 20 percent lower risk of the disease compared to group B.

\(^5\) A 3-year moving average for a specific year (e.g., 2007) is calculated by using data from 2006, 2007, and 2008 to estimate an average rate for these years. Moving averages are used to stabilize or smooth year-to-year fluctuations in rates so that long-term trends can be more easily observed.
These results suggest that the incidence rate of CMM is 31% lower in Toronto than in the rest of Ontario for males and 28% lower for females. The mortality rate from melanoma is also lower in Toronto compared to the rest of Ontario. For males, the mortality rate is about 15% lower in Toronto than in the rest of Ontario and for females it is about 22% lower in Toronto.

Trends over time in CMM incidence and mortality rate trend analyses were performed on the annual rates to examine whether there was a consistent trend across all years (1986-2008). These ‘join-point’ analyses assess whether there is a time point when the slope of the trend line changes, and it was found that a single trend parameter for all years provided the best-fitting model (i.e., there were no significant join points).

Figure 1 shows that for the rest of Ontario (excluding Toronto), CMM incidence rates for males and females have increased steadily and steeply between 1986-2008, whereas Toronto rates have increased only slightly. This can be expressed numerically by the average annual percent change (AAPC\(^6\)) and its level of statistical significance, where \(\text{ns}\) indicates that the trend was not statistically significant (i.e., no significant change over time in melanoma rates) and \(p<5\%\) indicates a statistically significant trend (i.e., there was a significant change over time in melanoma rates).

For the rest of Ontario (excluding Toronto), between 1986 and 2008 the incidence rate of melanoma increased on average 2.2% a year for males and 1.8% a year for females. In Toronto, melanoma rates increased significantly for females but not for males. In Toronto, melanoma rates among females increased by an average of 0.8% a year between 1986 and 2008.

- Toronto AAPC (Incidence Rates): Males = 0.6 (ns), Females = 0.8 (p<5\%)
- Rest of Ontario AAPC (Incidence Rates): Males = 2.2 (p<5\%), Females = 1.8 (p<5\%)

For males, the AAPC reported above for 1986 to 2008 is more than three-fold greater in the rest of Ontario compared to Toronto (2.2 vs. 0.6), whereas for females, the AAPC is more than two-fold greater in the rest of Ontario than in Toronto (1.8 vs. 0.8).

Melanoma mortality rates over the past two decades have increased only slightly. The greatest increase in CMM mortality rates occurred among males in the rest of Ontario, where the mortality rates from melanoma increased an average of 1.3% a year between 1986 and 2008. Melanoma mortality rates did not significantly increase for females in the rest of Ontario or for females and males in Toronto during this period. Among males, CMM mortality rates increased to a much greater extent in the rest of Ontario than in Toronto (1.3 vs. 0.2). For females however, the slight increase in mortality rates was the same for Toronto and the rest of Ontario:

- Toronto AAPC (Mortality Rates): Males = 0.2 (ns), Females = 0.4 (ns)
- Rest of Ontario AAPC (Mortality Rates): Males = 1.3 (p<5\%), Females = 0.4 (ns)

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\(^6\) The estimated average annual percent change describes the change in the rate of new cases of melanoma (incidence) or deaths from melanoma (mortality) over a one-year period.
To assess whether the difference between Toronto and the rest of Ontario in CMM rates was consistent over time, period-specific incidence and mortality rate ratios are plotted in Figure 2 (for source data see Appendix Table 1.2). For all 5-year periods, and for both males and females, incidence and mortality rates were lower in Toronto than for the rest of Ontario (i.e., the rate ratios are less than 1.0 across all periods).

These results also show that over the past two decades, the difference between the CMM incidence and mortality rates in Toronto and the rest of Ontario has increased, particularly for males. In 1989-1993, the incidence rate ratio comparing Toronto to the Rest of Ontario for males was 0.90, suggesting that the incidence of melanoma was 10% lower for males in Toronto than for males in the rest of Ontario. By 2004-2008, the incidence rate ratio decreased to 0.72, suggesting that the incidence rate of melanoma was 28% lower for males in Toronto than for males in the rest of Ontario. The mortality ratios for 2004-2008 show that the rates are also lower in Toronto than the rest of Ontario, and the pattern is similar for males and females. Thus, in the most recent period (2004-2008) the degree of difference in melanoma rates between Toronto and the rest of Ontario (as indicated by the rate ratios) is now similar in both sexes.
Figure 2: Incidence and Mortality Rate Ratios for Cutaneous Malignant Melanoma in Toronto Compared to the Rest of Ontario, for Specific Periods, by Sex, 1989-2008

Incidence Rate Ratios (Toronto / the rest of Ontario), by sex and period

* - Denotes significantly different from 1.0 (p < 5%)

Mortality Rate Ratios (Toronto / the rest of Ontario), by sex and period

* - Denotes significantly different from 1.0 (p < 5%)

Source: Cancer Care Ontario (Ontario Cancer Registry, 2011)
Notes: Rates by period, place and sex were prepared by Cancer Care Ontario, Prevention and Cancer Control (Surveillance), and age-standardized to the 1991 Canadian population.
- A ratio noted as significantly lower (p<5%) than 1.0 indicates that it is unlikely that the lower Toronto rate is due to chance.
- The rest of Ontario includes all other Health Units combined, but excludes cases/deaths with unknown residence.
Age and Sex Distribution of Melanoma in Toronto and the Rest of Ontario

Over the 10-year period, 1999-2008 there were 20,369 cases of incident CMM across Ontario (males and females combined), with 3317 (16%) occurring in Toronto and 17,052 occurring in the rest of Ontario (Table 1). The age- and sex-specific patterns in incident cases of melanoma are also depicted in Figure 3.

Prior to age 50, melanoma is more common among women, and after age 50 it is more common in men. Overall, however, in both sexes most melanomas occur after age 50 (for males about 75% and for females about 65%), with similar fractions in Toronto and the rest of Ontario. The proportion occurring at age 50 or over during 1999-2008 are:

- For males (% 50 and older): Toronto = 76%, Rest of Ontario = 77%
- For females (% 50 and older): Toronto = 68%, Rest of Ontario = 64%

For males, about half of all CMM cases in 1999-2008 occurred among those age 65 years and over. For females, the proportion of cases occurring after age 65 is lower than for males. Overall, the proportion of cases among those age 65 years and over is 5-7% higher in Toronto than in the rest of Ontario, among both males (a difference of 5%) and females (difference of 7%):

- For males (% 65 and older): Rest of Ontario = 45%, Toronto = 50%
- For females (% 65 and older): Rest of Ontario = 35%, Toronto = 42%

Table 1: New Cases of Melanoma by Sex and Age Group for Toronto and the Rest of Ontario, 1999-2008

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Rest of Ontario</th>
<th>Toronto</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–29</td>
<td>309</td>
<td>3.4%</td>
<td>66</td>
</tr>
<tr>
<td>30–49</td>
<td>1,846</td>
<td>20.0%</td>
<td>361</td>
</tr>
<tr>
<td>50–64</td>
<td>2,873</td>
<td>31.2%</td>
<td>459</td>
</tr>
<tr>
<td>65–79</td>
<td>3,108</td>
<td>33.7%</td>
<td>602</td>
</tr>
<tr>
<td>80+</td>
<td>1,074</td>
<td>11.7%</td>
<td>275</td>
</tr>
<tr>
<td>All ages</td>
<td>9,210</td>
<td>100%</td>
<td>1,763</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–29</td>
<td>472</td>
<td>6.0%</td>
<td>102</td>
</tr>
<tr>
<td>30–49</td>
<td>2,381</td>
<td>30.4%</td>
<td>400</td>
</tr>
<tr>
<td>50–64</td>
<td>2,224</td>
<td>28.4%</td>
<td>398</td>
</tr>
<tr>
<td>65–79</td>
<td>1,849</td>
<td>23.6%</td>
<td>405</td>
</tr>
<tr>
<td>80+</td>
<td>916</td>
<td>11.7%</td>
<td>249</td>
</tr>
<tr>
<td>All ages</td>
<td>7,842</td>
<td>100%</td>
<td>1,554</td>
</tr>
</tbody>
</table>

Source: Cancer Care Ontario (Ontario Cancer Registry, 2011)
Prepared by: Cancer Care Ontario, Prevention and Cancer Control (Surveillance)
Note: All other Health Units combined (rest of Ontario) excludes cases with unknown residence.
Melanoma (ICD-O-3 C44)
Figure 3: Age Distribution of the Number of Incident Cases of Cutaneous Malignant Melanoma for Toronto and the Rest of Ontario, by Sex, 1999-2008

Age distribution of Melanoma Cases in Toronto vs. the Rest of Ontario, 1999-2008

Source: Cancer Care Ontario (Ontario Cancer Registry, 2011) provided by Prevention and Cancer Control (Surveillance)
Notes: All other Health Units combined (rest of Ontario) excludes cases with unknown residence.
Melanoma (ICD-O-3 C44)
Estimates of the Relative Frequency of BCC, SCC and CMM in Toronto and the Rest of Ontario

Although NMSC (i.e., BCC and SCC) is the most common malignancy diagnosed among Canadians, most cancer registries do not routinely collect information on these cases. This is because the very high frequency of these tumours would result in unacceptably high workloads in registries, and also because they carry an excellent prognosis. Both BCC and SCC are usually detected readily and cured by surgical excision such that few deaths are attributed to NMSC.

In Ontario, the only type of skin cancer recorded by the Ontario Cancer Registry is CMM, thus patterns and trends for BCC and SCC for Toronto or the rest of Ontario can only be estimated using indirect and inferential methods. For this report, the approach used for many years to estimate NMSC frequency for Canada was adapted for the Ontario and Toronto populations. For the annual publication of Canadian Cancer Statistics (Canadian Cancer Society’s Steering Committee on Cancer Statistics, 2011), the total number of NMSC cases for all of Canada was estimated by first examining incidence rate trends in the three provinces that have collected NMSC data in the past (British Columbia, Manitoba, New Brunswick), and then applying these rates to the Canadian population projection for each year. Although this approach provides one approximation for all NMSCs, it does not distinguish between BCC and SCC. For example, this approach estimated that 74,000 new cases of NMSC were expected across Canada in 2011 (males and females together). To these are added the 5,500 new cases of CMM, which constituted 7% of all skin cancers combined.

The recent publication by McLean et al. (2012) is the single recent source of Canadian data on the relative frequency and trends of the specific types of skin cancer. This report provides Canadian data on which to base calculations of the approximate number of BCC and SCC cases in Toronto and the rest of Ontario. Using data collected by the British Columbia Cancer Registry from 1973 to 2003, McLean et al. examined the secular patterns of CMM, BCC and SCC. Incidence rates for all ages combined for each type of skin cancer increased steadily and substantially over the 30 year period (Table 2), and rates were consistently higher for males than females.

The calculated rate ratios indicated that in 2003, the BCC rate was more than 10-fold greater than the CMM rate for both males and females. Among males, the SCC rate was 3-fold greater than the CMM rate in 2003, whereas among females, the SCC rate was 1.5-fold greater than the CMM rate.

Table 2: Incidence Rates and Rate Ratios (RR) for Skin Cancer in British Columbia by Cancer Type, BCC, SCC, and CMM, by Sex and Year, 1973-2003

<table>
<thead>
<tr>
<th>Year</th>
<th>Incidence Rates*</th>
<th>Rate Ratios</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BCC</td>
<td>SCC</td>
</tr>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td></td>
<td>BCC</td>
<td>SCC</td>
</tr>
<tr>
<td>1973</td>
<td>95.1</td>
<td>24.4</td>
</tr>
<tr>
<td>1983</td>
<td>129.2</td>
<td>35.6</td>
</tr>
<tr>
<td>1993</td>
<td>180.2</td>
<td>56.8</td>
</tr>
<tr>
<td>2003</td>
<td>216.8</td>
<td>60.3</td>
</tr>
</tbody>
</table>

Source: McLean et al., 2012
* Incidence rates (per 100,000) are age standardized to the 1991 Canadian population and adjusted for BC ethnic composition.
With the British Columbia rates in Table 2 serving as a guide of the frequency of BCC and SCC relative to CMM, estimates were produced for Toronto and the rest of Ontario using the following methods:

- Age-standardized incidence rates for CMM presented in Figure 1 (and Appendix Table 1.1), which are 3-year moving averages, were multiplied by the rate ratios (of BCC:CMM and SCC:CMM) presented in Table 2, to approximate incidence rates for BCC and SCC in Toronto and the rest of Ontario. All rates were age standardized to the 1991 Canadian population.
- Calculations were done separately for males and females.
- This was done for each year that was included in both the report by McLean et al. (2012) and in the dataset obtained from the Ontario Cancer Registry (1993 and 2003).

One of the assumptions underlying these calculations is that the rate ratios observed in British Columbia are relevant to Toronto and the rest of Ontario however, there are several ways by which biases could arise, such as through differences in the source populations. For example with visible minorities having a lower risk of skin cancer, if they make up a larger proportion of the population in Toronto than BC this could bias the estimated Toronto rates (hence, see next section regarding ethnicity adjustment). If under ascertainment of CMM is greater in one or the other province this could also bias the estimates of BCC and SCC. In addition, the accuracy of the ratio SCC to BCC depends on the degree of completeness of reporting of each cancer type in British Columbia. It is known that reported BCC and SCC rates from cancer registries always underestimate true incidence as found when population-based skin cancer surveys are conducted (Gallagher and Lee, 1998). Thus all estimates in this report for both BCC and SCC should be understood to represent minimal incidence rates.

Accordingly, the BCC and SCC estimates produced in this way must be interpreted cautiously, and they cannot replace actual counts and rates that could be obtained directly if cancer registries across Canada collected the source data. These approximations are provided only to serve as a general indicator of relative frequency for the three types of skin cancer, and of the overall burden of skin cancer in Toronto and the rest of Ontario.

Figure 4 depicts the final results of this estimation procedure, by showing the relative contribution of each type of skin cancer, in Toronto versus the rest of Ontario. Figure 4 shows that rates of BCC and SCC are higher in males than females in the two years examined (1993 and 2003). Figure 4 also shows that rates of BCC and SCC are higher in the rest of Ontario than Toronto.

BCC is by far the most common form of skin cancer, with estimates that it accounted for 73% of skin cancers among males and 81% among females in 2003 in Toronto. Briefly, as shown in Figure 4, the age standardized incidence rates (ASIR per 100,000) and percentages of all skin cancers (%SC) for Toronto in 2003 were estimated to be:

- BCC: Males – ASIR = 145 (%SC=73%), Females – ASIR = 104 (%SC=81%)
- SCC: Males – ASIR = 40 (%SC=20%), Females – ASIR = 14 (%SC=11%)
- CMM: Males – ASIR = 12 (%SC=6.3%), Females – ASIR = 10 (%SC=7.5%)

It is noteworthy that the estimate of the relative contribution of melanoma to the total burden of skin cancers (6.3% for males and 7.5% for females) obtained by this method is equivalent to the 7% figure (for both sexes combined) noted above as derived in Canadian Cancer Statistics (Canadian Cancer Society's Steering Committee on Cancer Statistics, 2011).
The estimated increase in incidence rates of all three types of skin cancer from 1993 to 2003 was less for Toronto than the rest of Ontario, and within Toronto, was greater for females (16.6%) than males (4.8%). The ASIRs for all skin cancers combined, as plotted in Figure 4 were:

- Toronto: Males - 1993=189, 2003 = 197, Percentage increase from 1993 to 2003 = 4.8%
- Toronto: Females - 1993=110, 2003 = 128, Percentage increase from 1993 to 2003 = 16.6%

Figure 4: Estimates of Age Standardized Incidence Rates for Skin Cancer [Basal Cell Carcinoma (BCC), Squamous Cell Carcinoma (SCC) and Cutaneous Malignant Melanoma (CMM)] for Toronto and the Rest of Ontario, by Sex, 1993 and 2003*

Source: These estimates were produced in the current report, based on calculations that use data from multiple sources (see text for details).
* The data presented in these graphs show the 2 years for which British Columbia data published by McLean et al. (2012) overlap with the melanoma trend data presented in Figure 1 for the rest of Ontario and Toronto.
- Incidence rates (per 100,000) are age standardized to the 1991 Canadian population.
The above results were extended further to approximate the total number of skin cancer cases in 2011 in the Toronto population. This was done by multiplying population estimates for Toronto in 2011 by the incidence rates depicted in Figure 4. The data for this calculation were:

- ASIRs for 2003:  
  - CMM: Males = 12.4, Females = 9.7  
  - SCC: Males = 40.3, Females = 14.4  
  - BCC: Males = 144.9, Females = 104.6

- Assume ASIRs increased 1% annually as reported above for melanoma in Toronto, for 8 years (from 2003 to 2011)

- 2011 Census population for Toronto = 2,615,060 (1,255,585 males; 1,359,475 females)

Resultant estimates (rounded) for the number of incident cases in Toronto for 2011 are:

- CMM: Males = 170, Females = 140, Total = 310 (7% of total)
- SCC: Males = 550, Females = 210, Total = 760 (16% of total)
- BCC: Males = 1970, Females = 1540, Total = 3510 (77% of total)
- All Skin Cancers: Males = 2690, Females = 1890, Total = 4580

Thus, in Toronto in 2011, it is estimated that there were 4580 newly diagnosed cases of skin cancer, the majority of which were BCC (3510 cases, or 77%), followed by SCC (760 cases, or 16%) and CMM (310 cases, or 7%).

Ethnicity-Adjusted Incidence Rates for Melanoma

While the incidence trends presented above provide a useful indication of the overall occurrence of melanoma within the Toronto population, to understand the reasons and implications of these data, consideration must also be given to the changes in ethnic diversity. For example, given that skin cancer rates vary markedly by race, changes in the ethno-cultural make-up of a population could influence reported cancer rates. To assess the extent to which the observed trend in melanoma incidence rates for Toronto was due to changes in the population’s ethnicity, race-adjusted incidence rates were estimated for Toronto and the rest of Ontario.

Given that cancer registries in Canada do not collect information on race or ethnicity, the adjustment procedure relied on published estimates of differences in CMM risk by ethnic or racial group found in the international literature. As outlined above, it is well established that CMM incidence rates are much higher for Caucasians than for other races, being at least 6-fold greater even when contrasted with a mixed race comparison group (Curado et al., 2007, Moss, 1984, Pathak et al., 1982). As listed in Appendix 1, Table 1.3, census-based estimates of the prevalence of visible minorities in Toronto versus the rest of Ontario were combined with relative risks from the literature (e.g., RR=6 for melanoma risk in whites compared to visible minorities) to estimate race-specific melanoma incidence, which then permitted race-adjustment. In this way, race-adjusted incidence rates (standardized to the 1991 population) were obtained for the census-years for which all necessary source data were available.

Figure 5 contrasts ASIRs to race-adjusted values for Toronto and the rest of Ontario during census years (with the ASIRs being the same as shown in Figure 1). For Toronto, there has been a larger increase in the proportion of the population that is part of a visible minority (from 5% in 1991 to 9% in 2006 for the rest of Ontario, compared with 27% to 42% for Toronto – see Appendix 1, Table 1.3). In estimating race-specific rates, as an example, ASIRs for males in Toronto in 2006 were 20 (per 100,000) for whites and 3 (per 100,000) for visible minorities.
Figure 5 (and Appendix 1, Table 1.3) show that the impact of racial variation has been greater for Toronto than the rest of Ontario, as is demonstrated in the plotted differences between the traditional ASIR and the race-adjusted ASIR (Race adj-ASIR), which for 2006 were:

- For Toronto, Males: ASIR = 13.0, Race adj-ASIR = 15.5 (a 19% increase)
- For Toronto, Females: ASIR = 10.9, Race adj-ASIR = 13.0 (a 19% increase)
- For rest of Ontario, Males: ASIR = 18.7, Race adj-ASIR = 19.4 (a 4% increase)
- For rest of Ontario, Females: ASIR = 14.6, Race adj-ASIR = 15.2 (a 4% increase)

Implications of these results include:

- The process of race-adjustment shows that the CMM incidence rate trends over time are affected by changes in the population’s ethno-racial composition.
- With the influx of a relatively large number of people representing visible minorities (who have a lower CMM risk) the unadjusted CMM rates in 2006 were lower than they would have been if the populations’ racial distributions remained the same as in 1991.
- This occurred for both Toronto and the rest of Ontario. However, with Toronto having a larger influx of visible minorities, the impact of race-adjustment on the rates was greater for Toronto than the rest of Ontario (e.g., for Toronto, race-adjusted rates were 19% higher than the standard ASIRs, which was much larger than the 4% difference seen for the rest of Ontario in which the population is more stable and has a much larger fraction of Caucasians).
- Figure 5 demonstrates that the impact of race-adjustment increases over time, as the population continues to change after the year of standardization (1991). This would result in a slight under-estimation of the trend over time, again with Toronto being affected more than the rest of Ontario.
- These results demonstrate that changes in ethno-cultural composition is a partial explanation for why CMM rates are lower in Toronto than for the rest of Ontario, but even after such adjustment, rates in Toronto are still slightly lower.
- Even so, the overall patterns and trends for skin cancer incidence as outlined above remained unaltered after adjusting for race.
Figure 5: Age Standardized Incidence Rates (ASIRs) and Race-Adjusted Incidence Rates for Melanoma (3-Year Moving Averages) for Toronto and the Rest of Ontario, by Sex, 1991-2006*

Source: These estimates were produced in the current report, based on calculations that use data from multiple sources (see text for details).

* The graph shows the impact of adjusting for the increasing contribution of visible minorities in the population. The trend lines represent the usual ASIRs for melanoma. Black circles (for males) and black squares (for females) show ASIRs adjusted for race-ethnicity, with 1991 set as the standard for comparison.
The Burden of Illness Associated with Skin Cancer

Although survival from melanoma is good by comparison with other life-threatening cancers, and mortality from non-melanocytic skin cancer is quite low, people with skin cancer experience a heavy personal and social burden. Surveys indicate that a significant proportion of patients diagnosed with melanoma suffer anxiety, depression and other clinically relevant psychological distress with diagnosis (Newton-Bishop et al., 2004; Kasparian et al., 2009). Further, the presence of a significant scar after surgery for removal was noted to be associated with difficulties in domestic social and sexual roles, particularly in young individuals and especially women (Newton-Bishop et al., 2004). Interestingly, poor perception of the scar was present in some cases even where the scar was covered by clothing. Presence of co-morbid conditions in patients with skin cancer is reported to increase quality of life-related problems (Schlesinger-Raab et al., 2010). In addition to the personal burden experienced by patients, caregiver time and effort is significant even in cases with only localized disease. In a study of caregiver effort for a variety of cancers, caregivers spent an average of 8.3 hours per day for 13.7 months in direct patient care (Yabroff and Kim, 2010). Melanoma was grouped in this study with bladder and uterine cancer, both of which, like melanoma, have more favourable mortality than other cancers under investigation. Even so, caregivers for these three cancers spent an average of 6.8 hours per day for a total of 12.1 months with the patient.

In addition to the social costs associated with skin cancers, the financial burden on the Canadian health system is significant. A detailed analysis of costs carried out by Krueger et al. (2010) for the Canadian Partnership Against Cancer estimated that in 2004 direct medical costs for treatment of skin cancer were about $66 million and the indirect cost such as lost earnings and lost productivity costs came to $465 million.

Krueger and colleagues (2010) estimated that for Ontario alone, in 2011 direct and indirect costs for skin cancer were about $296 million. Further details on estimating the economic burden of skin cancer are presented in Appendix 2.
Risk Factors Associated with Skin Cancer

The three principal types of skin cancer have common susceptibility factors such as fair skin, light coloured hair, and sensitivity to ultraviolet radiation, whether solar or artificial. However, there are several other host characteristics such as freckling and number or density of nevi (skin moles), which are important for some, but not all skin cancers. Although the risk of skin cancer is increased in individuals who undergo kidney and other organ transplantation (Kovach and Stasko, 2009), and potentially in individuals who are exposed to occupational carcinogens (Fortes and deVries, 2008), the principal external or environmental risk factor is exposure to sunlight and to artificial UV radiation. However, the nature of the relationship between ultraviolet radiation exposure and each of the three types of skin cancer differs somewhat. This section will summarize research on host susceptibility factors and solar UV radiation and each of the types of skin cancer. In addition, the relationship between indoor tanning and each of the skin cancers will be critically reviewed.

Individual Susceptibility Factors for Skin Cancer (Host Factors)

Pigmentation, Ethnicity and Family History

Skin cancer is primarily a disease of Caucasians of European origin (Whites), and because of this most epidemiologic studies of CMM, BCC, and SCC have been conducted in white populations. Skin cancer occurs in all ethnic groups, but the incidence rates of CMM - the only skin cancer uniformly recorded by cancer registries - are much higher in Whites than in Africans, South and East Asians in their home countries (Curado et al., 2007). The lower risks in Asians and in blacks are also seen in comparison with whites in American data, as indicated by rates from the US Surveillance Epidemiology and End Results program whose comprehensive cancer registries represent nearly 10% of the American population. Rates of melanoma in the US are highest in whites (19.4/100,000) and lowest in Asians (1.0/100,000) and blacks (0.9/100,000). Latinos in the US appear to have intermediate rates (3.0/100,000), although they are closer to those of more heavily pigmented populations than Whites. A similar difference in rates by ethnicity is likely in Canada, although US data is commonly used to document ethnic differences in North America as Canadian cancer registries do not collect and publish information on ethnicity. Racial or ethnic differences in the incidence rates of BCC and SCC are likely to be very similar to those seen for melanoma.

Indicators of pale phenotype such as light skin colour (Elwood et al., 1984; Naldi et al., 2000a; Gallagher et al., 1995a,b; Armstrong and Kricker, 2001; Zanetti et al., 1996), light hair colour (Holman and Armstrong, 1984; Walther et al., 2004); and light (blue or grey) eye colour (Naldi et al., 2000a; Zanetti et al., 1996) have been associated in etiologic studies with higher risk of CMM, BCC and SCC. In a meta-analysis of 60 studies of pigmentation factors and CMM conducted through 2002, Gandini et al. (2005a) found that those with blue eyes had nearly a 50% increased risk (RR=1.47; 95%CI=1.28-1.69) of melanoma compared to those with dark eyes. Those with fair skin had double the risk (RR=2.06; 95%CI=1.68-2.52) of melanoma compared with those with darker skin. Hair colour also affected melanoma risk, with blondes having a 2-fold elevated risk (RR=1.96; 95%CI=1.41-2.74) and redheads a more than 3-fold elevated risk (RR= 3.64; 95%CI=2.56-5.37) of melanoma compared with dark haired study subjects.

Risk of developing CMM is increased if one or more relatives have previously been diagnosed with melanoma (Osterlind et al., 1988a; Holly et al., 1995a; Westerdahl et al., 1995). In a meta-analysis of 14 informative studies, Gandini et al. (2005a) found that a family history conferred a relative risk of 1.74 (95%CI=1.41-2.14). Many of the studies included in the meta-analysis did not collect data on the nature of the relationship between the family member with the previous melanoma and the study subject.
However, an earlier meta-analysis conducted by Ford et al. (1995) analyzed data from eight case-control studies and found that having one or more first degree relatives increased the risk by more than 2-fold (RR=2.24; 95%CI=1.76-2.86). Degree of risk did not differ significantly whether the previously affected family member was a parent, sibling, or a child. An analysis of more detailed information in six of the studies revealed more than a five-fold elevated risk of melanoma if two or more first degree relatives were affected (RR=5.56; 95%CI=1.59-19.47), although the wide confidence intervals reflect the fact that in these case-control studies from unselected populations having two or more affected first degree relatives is rare.

Han et al. (2006) evaluated risk of melanoma, BCC, and SCC associated with a family history of skin cancer in a nested case-control study conducted within the Nurses Health Cohort. Those with a family history of any kind of skin cancer had more than a 2-fold increased risk of BCC (OR=2.05; 95%CI=1.49-2.81) after control for sun susceptibility, age, and demographic factors. Analysis of SCC showed an increased risk (OR=1.44; 95%CI=0.93-2.24) close to statistical significance after adjustment. Walther et al. (2004), in a study of 213 BCC patients and 411 controls, found an almost four-fold increased risk of BCC in patients with a first degree relative with the same cancer (RR=3.8; 95%CI=1.6-9.2). Adjustment for other significant risk factors produced a relative risk of 5.1 (95%CI=1.0-25.0).

In summary, the risk of each of the major types of skin cancer is increased in those with a family history of skin cancer, and the increased risk appears to be independent of susceptibility factors such as skin colour, and sun sensitivity. Of course, a family history of skin cancer in many cases is due to inherited genetic factors, and there is a significant literature on the effects of mutations in the CDKN2A gene, MC1R gene, and others on melanoma risk. However, all these studies rely on being able to genotype individuals and in population-based public health interventions this is not possible. Therefore this literature will not be reviewed in this report.

Sun Sensitivity
Measures of sun sensitivity are associated with increased risk of all three types of skin cancer in most studies. Sun sensitivity is usually self-assessed by study subjects as the propensity to burn rather than tan on initial exposure to the sun at the start of summer, or by the propensity to burn only and never tan if exposed to sun over longer periods of time. Some studies have used the Fitzpatrick scheme, which is of clinical origin, and ranks sun sensitivity in six categories, of which only the lightest four are used to classify whites into those who ‘burn and never tan in the sun’, (type I), through those who ‘tan easily and rarely burn’ (type IV) (Fitzpatrick, 1988).

No matter how the variable is defined, studies show consistently higher risk of developing melanoma in those who only burn and never tan after constant exposure to sunlight and in those who burn rather than tan on initial sun exposure (Holman and Armstrong, 1984; Elwood et al., 1985a; Titus-Ernstoff et al., 2005). The summary risk estimate from a recent meta-analysis of data from 36 studies showed a 67% increased risk for melanoma (RR=1.67; 95%CI=1.39-2.01) in those who burn easily in the sun compared to those who always tan (Caini et al., 2009).

Although BCC and SCC of the skin have been studied less than melanoma, most analytic studies examining sun sensitivity have found a relationship with SCC (Gallagher et al., 1995b; Zanetti et al., 1996; English et al., 1998a; Landi et al., 2002; Clouser et al., 2006) and with BCC (Zanetti et al., 1996; Rosso et al., 1999; Neale et al., 2007). The European ‘Helios’ study showed a 2.7-fold increased risk of BCC for those who ‘burn and never tan’ in the sun (OR= 2.71; 95%CI=2.11-3.47) and a 2-fold increased risk for SCC (OR=2.04; 95%CI=1.18-3.53) compared to those who ‘tan with no burn’.
**Freckling**

Freckling, whether reported as density in childhood or density as an adult, is strongly associated with risk of CMM (Elwood et al., 1984; Dubin et al., 1986; Osterlind et al., 1988a). Caini et al. (2009) combined data from 23 studies and found a summary relative risk of 1.79 (95%CI=1.60-2.00) for those with many freckles compared to those with none or few.

Evidence of the importance of freckling in risk of SCC and BCC is not as strong as that for melanoma. Two studies of SCC showed no significant association (Gallagher et al., 1995b; Zanetti et al., 2006) although the Australian study of English et al. (1998a) did demonstrate a modest positive relationship. Likewise studies of the association between freckling and BCC are mixed, with most studies showing an increased risk of BCC in those who freckle (Gallagher et al., 1995a; Zanetti et al., 1996; Zanetti et al., 2006; Vlajinac et al., 2000) but several showing no association (Walther et al., 2004; Gon and Minelli, 2011). As freckles are discrete melanin deposits secreted by melanocytes, the cells from which melanomas arise, it is not surprising that they are more strongly associated with melanoma than SCC and BCC.

**Nevi (Skin Moles)**

Acquired melanocytic nevi (common skin moles), particularly when present in large numbers, are strongly related to risk of melanoma. Nevi may actually be part of the causal pathway for a proportion of melanomas as detailed pathologic examination of melanomas often reveals the presence of pre-existing nevus remnants within the cancer (Skender-Kalnenas et al., 1995). Nevi start to develop early in life (Gallagher et al., 1990a) in an interaction between factors under genetic control such as skin pigmentation and phenotype (Gallagher et al., 1990b; Sigg and Pelloni, 1989; Green et al., 1986) and with exposure to solar UVR (Sorahan et al., 1990; Augustsson et al., 1992; Kelly et al., 1994; Harrison et al., 1994). White children develop the greatest nevus density between early childhood and teenage years, and ethnic groups with more highly pigmented skin such as East and South Asians, North American Aboriginals and others develop significantly fewer nevi (Gallagher et al., 1991; Hancock et al., 1996; English and Armstrong, 1994).

Nevus frequency or density is perhaps the strongest predictor of risk of CMM. Many studies have shown that risk of melanoma is strongly positively related to nevi (Halpern et al., 1991) whether counted on a single site such as the arms (Holman and Armstrong, 1984; Elwood et al., 1986; Osterlind et al., 1988a) or on all body sites (Holly et al., 1987; Marrett et al., 1992; Tucker et al., 1997; Naldi et al., 2000a). A large meta-analysis conducted by Gandini et al. (2005a) evaluated data from 46 studies and demonstrated a strong gradient of increasing melanoma risk with increasing nevus density, whether nevus counts were performed on the arms only or the whole body. Compared with those who had no nevi on the arms, those with 1-15 had nearly a 5-fold increased risk (RR=4.82; 95%CI=3.05-7.62). In studies where whole body counts were performed, subjects with counts of 101-120 had nearly a 7-fold elevated risk of melanoma (RR=6.89; 95%CI=4.63-10.25) compared to those with fewer than 15 nevi (Gandini et al., 2005a).

While nevus density has been shown to be a very good risk indicator for CMM, it appears to be less useful with non-melanocytic skin cancer. Evidence for an association between nevus density and BCC is scanty, with the study of Foote et al. (2001) showing no association. A more recent study carried out in Australia (Richmond-Sinclair et al., 2012) showed a 2.4-fold (95%CI=1.1-4.8) increased risk of BCC with the presence of 11 or more nevi on the forearms compared to study subjects with none. However nevi on the back did not appear to be related to risk of BCC. There is some evidence that nevus density is a not a predictor of risk of SCC (Foote et al., 2001; Bataille et al., 1998).
**Indicators of Sun Damage**

Solar elastosis is a type of skin damage due to chronic sun exposure and is characterized by degeneration of the skin with thinning, loss of secondary lines, and loss of skin tone. It is more common on sun exposed skin surfaces and in those with fair skin. It generally increases in prevalence with advanced age and serves as an indicator of elevated risk for subsequent melanoma (Purdue et al., 2005; Bataille et al., 1998). The meta-analysis of Gandini et al. (2005a), assessing studies conducted to September 2002, showed a 2-fold increased risk of melanoma with indicators of solar skin damage (RR=2.02; 95%CI=1.24-3.29). The presence of solar elastosis also appears to be an indicator of increased risk for subsequent SCC (Kricker et al., 1991; Green et al., 1988) and perhaps BCC as well (Kricker et al., 1991).

Solar keratoses are rough scaly lesions that occur primarily on sun exposed surfaces and are known to be potential precursor lesions for subsequent SCC of the skin (Thompson et al., 1993; Czarnecki et al., 2002). As well as indicating elevated risk for SCC, the presence of solar keratoses is a risk factor for CMM on the head and neck (Olsen et al., 2011) and upper limbs (Green and Siskind, 2012). They may also indicate an elevated risk for subsequent BCC (Richmond-Sinclair et al., 2012; Neale et al., 2007), although this is less well established.

**Ultraviolet Radiation**

Ultraviolet radiation (UVR) occupies part of the electromagnetic spectrum from roughly 100 nm through 400nm. Exposure to solar or artificial UV radiation is the principal environmental risk factor for CMM, BCC, and SCC (IARC 1992; IARC 2012). While skin cancer is the most common disease in Western populations due to exposure to UVR, it also increases the risk of melanoma of the eye, cortical cataract formation, and tumors of the conjunctiva of the eye (Lucas et al., 2006; Gallagher and Lee, 2006). UVR is also known to exacerbate several forms of auto-immune diseases and suppress cell-mediated immunity, activating latent viral infections such as Herpes simplex (cold sores) (Lucas et al., 2006).

Ultraviolet radiation is customarily divided into UV-C (100-280nm), UV-B (280-315 nm), and UV-A (315-400nm). UV-C carries the highest energy of the three but the earth’s ozone layer acts as a screen and filters out virtually all UV radiation below 290nm wavelength before it reaches the surface of the earth. UV-B, although carrying less energy than UV-C, still has enough energy to damage DNA directly through the formation of thymine and pyrimidine dimers (and causes mutations) which may ultimately lead to skin cancer. UV-B is known to cause skin cancers in experimental animals (deGruijl, 2002). UV-B is also critical in the production of vitamin D, most of which is synthesized in man by the action of UV-B on 7-deoxycholesterol in the skin. UV-A does not damage DNA directly, but does generate reactive oxygen species which can damage DNA indirectly (Svobodova et al., 2012). In mice, UV-A can cause skin cancers analogous to human SCC (Kelfkens et al., 1991) and UV-A is responsible for much of the immune suppression attributed to sunlight (Halliday et al., 2011). The question of whether UV-A can cause melanoma has not yet been fully answered as there is no universally recognized animal model for this cancer.
Sun Exposure

Melanoma

One quantitative assessment of the proportion of melanoma due to solar ultraviolet radiation (sunlight) suggests that a minimum of 65% of these cancers worldwide are attributable to this one environmental agent (Armstrong and Kricker, 1993). A more recent estimate suggests a range of between 50% and 90% for the proportion of melanoma due to solar UVR exposure (Lucas et al., 2008).

The exact relationship between UVR exposure and CMM is complex. Earlier examination of the descriptive epidemiologic features of melanoma such as the male/female ratio, the sex differences in sites of lesions, coupled with the absence of high incidence in low socioeconomic status males known to work predominantly outdoors led investigators to suggest that incidence of melanoma is determined more by the pattern of exposure than by the total accumulated dose of sunlight exposure (Elwood and Hislop, 1981; Holman et al., 1983). The theory, later summarized by Armstrong (1988), suggested that infrequent or intermittent exposure to high doses of sunlight on untanned skin is particularly effective in increasing risk of melanoma, while exposure to the same dose of sunlight daily or chronic exposure (resulting in tanning, and thickening of the epidermis, affording more protection to melanocytes) may be less effective in the genesis of melanoma. To test the theory, an initial group of large population-based case-control studies of melanoma were conducted in which continuous or chronic sunlight exposure was defined as that accrued on a daily basis from outdoor occupations, while intermittent exposure was defined as recreational and vacation outdoor exposure. The initial epidemiologic studies of CMM and sun exposure conducted in Australia (Holman and Armstrong 1986a,b; Green et al., 1986) and in Western Canada (Elwood et al., 1985b) demonstrated elevated risks of melanoma with increasing intermittent sun exposure (recreational, or vacation sun exposure or activities), but none with occupational exposure, and only one (Green et al., 1986) with cumulative (recreational plus occupational) sun exposure. Subsequent studies carried out in the USA (Holly et al., 1995b; White et al., 1994), Italy (Rosso et al., 1998), Denmark (Osterlind et al., 1988b), Germany (Kaskel et al., 2001), Sweden (Beitner et al., 1990), Holland (Nelemans et al., 1993), Spain (Rodenas et al., 1996), Germany, France and Belgium (Autier et al., 1994a), and Greece (Nikolaou et al., 2008), demonstrated similar patterns of increased risk with increasing intermittent solar UVR exposure.

A number of systematic reviews have been conducted evaluating human studies of sun exposure and subsequent CMM. A review by Elwood and Jopson, (1997) examined self-reported intermittent (recreational or vacation) sun exposure using data from 23 studies with 6934 melanoma cases and found an increased risk of melanoma (OR=1.71; 95%CI=1.54-1.90) with intermittent exposure. This review also looked at sunburn frequency, a measure combining sun sensitivity and sun exposure, in 19 studies and also found a positive relationship (OR=1.91; 95%CI=1.69-2.17). Sunburn history has been interpreted in several ways in studies of human melanoma. As sunburn is a result of both phenotypic sun sensitivity and sun exposure itself; it has been seen as both a direct causal factor in melanoma and as a more accurate - or more readily remembered - indicator of episodes of intense solar exposure than is seen with reported outdoor recreational activity.

A later meta-analysis (Gandini et al., 2005b) involving sun exposure data from 57 studies also demonstrated a positive relationship between sun exposure and melanoma. The analysis for intermittent exposure involved data from 34 studies and showed a significant association with CMM (RR=1.61; 95%CI=1.31-1.99). The analysis of the effect of chronic exposure, captured in individual studies as exposure accrued in outdoor occupations, showed no increased risk (RR=0.95; 95%CI=0.87-1.04). The study also looked at reported sunburn history and found an increased risk with a history of sunburns (RR=2.03; 95%CI=1.73-2.37). More recently an analysis by Chang et al. (2009) pooled comparable data on 5700 melanoma cases and 7216 controls and again demonstrated a relationship between intermittent
sun exposure and melanomas of the trunk (pooled OR=1.7; 95%CI=1.4-2.2) and limb (pooled OR=1.4; 95%CI=1.1-1.7), but not head and neck.

**Early Life Sun Exposure and Melanoma**

Data initially obtained through studies of cancer incidence among migrants indicates that early life UVR exposure may be important in determining adult risk of melanoma. The studies examined risk of melanoma among people from low-sunlight areas such as Europe who migrated to high sunlight areas such as New Zealand (Swerlow et al., 1995) or Australia (Khlat et al., 1992) at various ages by comparison with native born individuals of the same age. UK residents who moved to New Zealand demonstrated lower risks for melanoma than native born New Zealanders (Swedlow et al., 1995), and a similar finding was seen in the Australian data (Khlat et al., 1992). Further, New Zealanders who moved to the UK after childhood retained increased risks for melanoma by comparison with those born in England and Wales.

An analysis of data from a large Australian case-control study (Holman et al., 1986a) found that migrants to Australia before age 10 had melanoma risks similar to those in native born Australians, while those who arrived after age 19 had a melanoma risk only about one-quarter to one-third of that seen in native born Australians. An American study using data on 4611 cases of melanoma diagnosed in the Los Angeles area with known place of nativity showed that those who moved to Los Angeles from a more northerly state had a lower risk of melanoma even after decades of residence in Los Angeles than those born in the area, suggesting that early life sun exposure is important in adult melanoma (Mack and Floderus, 1991). These data are consistent with information showing that the density of melanocytic nevi increases with early life solar UVR exposure (Kelly et al., 1994; Harrison et al., 1994). Careful histologic examination of melanomas, as noted earlier, indicates that a significant proportion show signs of arising from a pre-existing nevus (Skender-Kalnenas et al., 1995). If some nevi are actually precursor lesions for later melanoma this would suggest at least one potential biologic mechanism to account for the importance of early life UVR exposure.

Taken together, the weight of evidence from the studies of the relationship between sunlight, melanoma, and nevus development, along with that from migration studies, indicates that melanoma is caused by intermittent sun exposure and that early life sun exposure may be critical in determining risk of melanoma among adults.

**Basal Cell Carcinoma**

BCC has been studied much less frequently than melanoma, likely because it is not a life-threatening disease. Studies in Canada (Gallagher et al., 1995a) and Europe (Rosso et al., 1996) have shown increased risk of BCC with high levels of sun exposure prior to age 20. The Canadian study, conducted in Alberta, showed a 2.6-fold elevated risk (95%CI=1.1-6.5) for those with the highest quartile of exposure. The European study examined beach vacations in childhood and found that individuals in the highest quartile of exposure had a 1.4-fold increased risk (95%CI=1.09-1.89) compared to those with no beach holidays in childhood. In addition the European study showed elevated risk with increasing lifetime holiday sun exposure (highest quartile OR=1.47; 95%CI=1.18-1.83). In the European study, the risk of BCC appears to plateau at around 8,000-10,000 hours of accumulated sun exposure. Similar findings of increased risk with early sun exposure were also seen in studies in Australia (Kricker et al., 1995) and Germany (Walthier et al., 2004). The Canadian study noted above showed no association with occupational or cumulative lifetime solar exposure, and the Australian study showed no association with sun exposure in the decades after age 20. This pattern, indicates the importance of intermittent and early life sun exposure in BCC, and is similar to that seen in melanoma.
Squamous Cell Carcinoma

Squamous cell carcinoma appears to have a more simple relationship with sun exposure than melanoma or BCC. An Australian study (English et al., 1998b) demonstrated a positive relationship between total accumulated hours of sun exposure and SCC, as did the Maryland watermen study of Strickland et al. (1989). In the Alberta study, Gallagher et al. (1995b) demonstrated increased risk of SCC with accumulated occupational sun exposure over the 10 years prior to diagnosis (highest quartile OR=4.0; 95%CI=1.2-13.1), but no association with intermittent exposure. In Europe, Rosso et al. (1996) also found a significant gradient of increasing risk of SCC with increasing chronic or occupational exposure (highest quartile OR= 1.60; p trend=0.029), but no association with vacation exposure. The dose-response curve for SCC in the European study showed relatively little increase in risk until 70,000 hours accrued sunlight exposure, at which point risk increased exponentially with further exposure (Rosso et al., 1996). This study was conducted in Southern European populations where a smaller proportion of the population have sun-sensitive skin. However, among the subset of study participants with sun-sensitive skin who were poor tanners, the dose-response curve for SCC risk began to rise at 10,000 hours of exposure. This latter figure may be more appropriate for light skin Canadians of European origin. Overall, the results of these studies suggest that cumulative sun exposure accrued over time is most important in determining risk of SCC.

Indoor Tanning

Background

High-pressure mercury vapour discharge lamps (275 Watt RS-M type) were readily available to consumers in table-top sunlamps from the early 1960s (IARC, 2005). The devices emitted about 20% UV-C, 30-50% UV-B, and roughly 30-50% UV-A (Diffey et al., 1990). While originally designed for medical treatment of skin conditions, they were soon discovered by those seeking a cosmetic tan. As such a high proportion of the lamp’s output was in the UV-C and UV-B range, the time of exposure required for perceptible reddening of the skin was very short - only about 6 minutes (Stepp and Schlitt, 2002). In the late 1960s and early 1970s a low-pressure fluorescent bulb was developed in 4 foot and 6 foot lengths, but this bulb still emitted very high levels of UV-B. Moreover, although this bulb was the right configuration for indoor overall body tanning, its initial purpose was treatment of skin disorders, where exposure times from a few seconds to one minute were employed. These lamps were not practical for indoor tanning due to the potential for erythema (sunburn) with very short duration of exposure (IARC 2005; Stepp and Schlitt, 2002).

In North America, large-scale commercial sunbed salon exposure did not really become popular until the 1980s with the introduction of low-pressure lamps emitting primarily UV-A (Bizzozero 2002). These lamps used a different phosphor lining for the inside glass of the bulbs to modify their emission spectrum compared to early UV-B lamps, and had a peak emission at 350 nm (UV-A range) with a UV-B emission of about 3% (Stepp and Schlitt, 2002).

Modern lamps were developed in the late 1990s. These very high output (VHO) devices still emit primarily UV-A (345-355 nm) but with enhanced UV-B (about 4%) to mimic the tropical sun. These lamps are designed for tanning sessions of 10-20 minutes (IARC, 2005). In addition to these devices, a new high-pressure lamp was also developed employing quartz glass with enhanced tanning ability. These lamps are sometimes used in salons for tanning of the face, often in conjunction with use of low-pressure bulbs for body tanning.
UVR Emission of Modern Sunbeds
Studies by Wester et al. (1999) and Gerber et al. (2002) indicate that sunbeds with 4-5% UV-B and 95-96% UV-A have a UVR emission equal to or exceeding that of the midday sun in the Mediterranean. Miller et al. (1998) have estimated that 20 tanning sessions using UV-A lamps produce 0.3-1.2 times the exposure received from the sun in typical tanners. For frequent tanners (100 times per year) this could lead to annual UV-A doses 1.2-4.7 times those received from the sun. For high-pressure sunlamps, Miller et al. suggest that such exposure could represent up to 12 times the annual exposure from the sun. In commercial use, the spectral characteristics of sunbeds vary considerably based on age of the appliance, age of the UVR lamps, and degree of maintenance and other variables. The output of fluorescent UVR lamps decreases with age, and the output of UV-B decreases more rapidly than UV-A (IARC, 2005).

Prevalence and Correlates of Indoor Tanning
Recent studies have shown some variation in the prevalence of indoor tanning in Europe and North America, although consistently greater use is found among young people, especially young women. In Denmark, a population based survey of 3437 Danes age 15-19 carried out in 2007 showed that in the previous 12 months 29% in that age group had used a sunbed (Koster et al., 2009). In females, the prevalence rate was even higher at 59%. In Germany, a population based cross-sectional study of 500 individuals age 18-45 living in Mannheim revealed an overall prevalence of use of 21.0% in the 12 months prior to the survey, although the figure was higher in females at 26.6% (Diehl et al., 2010). Unfortunately a more detailed age breakdown was not available in the paper. Thompson et al. (2010) surveyed sunbed use in children age 11-17 in six cities in the UK as part of the national Youth Omnibus Survey carried out in 2008-9. Sunbed use was relatively modest nationally with 6% responding that they had ever used a sunbed, although this proportion was higher in the North (11%) than in the Midlands or South (4.2%). However, in the six large cities, rates were greater with the highest being in Liverpool (20.0%) and Sunderland (18.0%). Among users in Liverpool, 62.6% had used a sunbed in the previous month.

The U.S. Centers for Disease Control, as part of the 2010 National Health Interview Survey which involved 25,233 individuals age 18 and up, found that 8.1% of white adults, 1.6% of Hispanics, 0.3% of blacks and 2.1% of other races had used an indoor tanning device at least once in the past 12 months (Centers for Disease Control and Prevention, 2012). A significantly greater proportion of white women (12.9%) reported use than white men (3.3%). Analysis of the data by age showed much higher rates of use in younger whites than those over age 30. Among white females age 18-21 and 22-25, 31.8% and 29.6% respectively reported use in the previous 12 months. Rates differed across regions in the US, with the highest rates for non-Hispanic white women ages 18-21 peaking at 44% in the mid-West. Of white women age 18-21 who tanned, 67.6% reported indoor tanning 10 or more times in the previous 12 months.

In Canada, the 2006 Second National Sun Survey interviewed 7121 adults age 16 or older about their sun exposure and indoor tanning habits as well as those of a sample of children age 1-12 (Marrett et al., 2010). Results showed that 9% of Canadians and 8% of Ontarians used indoor tanning equipment in a 12 month period prior to the survey (National Skin Cancer Prevention Committee, 2010). Use was higher among younger women; 27% of Canadian women age 16-24 used indoor tanning equipment in the previous 12 months, while only 8% of men of the same age group reported use. Of those reporting use, about one-third reported 13 or more sessions per year.

Further information on the prevalence of indoor tanning is available on populations in various health unit districts in Ontario from surveys of indoor tanning conducted by the Rapid Risk Factor Surveillance System (RRFSS) group at York University's Institute for Social Research. The RRFSS was established in 1999 to provide data on health measures in Ontario similar to that collected in individual U.S. States
using the Behavioral Risk Factor Surveillance System. The RRFSS uses ongoing telephone surveys to monitor trends in risk factors in communities across Ontario. Respondents are chosen by randomly selecting household telephone numbers for contact. A second sampling stage occurs in homes reached with the selection of the adult aged 18 years or over with the most recent birthday. Questionnaires used by RRFSS for data collection and the methods for initial contact and interview are the same across each region of the province. The artificial tanning module of the RRFSS asks respondents about their use of tanning equipment in the 12 months prior to the survey. RRFSS data collected from 2005 through 2008 from selected Ontario public health units and available online indicate substantial use of indoor tanning equipment.

A survey of 1215 residents in Brant County in 2005-6 indicated that 14.0% of women 18+ and 4.7% of men 18+ had used artificial tanning equipment at least once in the previous 12 months. However, this figure rose to 25.2%, ±7.3 (95%CI) among those aged 18-24 years at the time of the survey (Brant County Health Unit, 2007).

In the Durham region in 2006, a survey of 1909 residents indicated that 9.6% of those aged 18+ had used tanning equipment in the last 12 months (Durham Region Health Department, 2009). In addition, more than 15% of unmarried respondents had used them in the past 12 months. The prevalence was also higher in those aged 18-44, with 13.1% reporting having used tanning equipment. Use was also higher among females than males (13.1% vs. 6.1%).

The Durham region report also included survey data from a number of other public health units, including Toronto Public Health. The report showed that among the 1193 respondents interviewed in Toronto in 2006, 4.5% reported having used tanning equipment in the last 12 months. The prevalence of indoor tanning was slightly higher among certain subgroups, including women (6%) and those 18-44 years of age (6.4%).

In the Haliburton, Kawartha, Pine Ridge District in 2007, 1126 respondents were questioned about their use of tanning equipment in the past 12 months. The results suggested that 4.6% of males 18+ and 9.7% of females 18+ reported artificial tanning. However, among those age 18-24 the rate was 25.0% (95%CI=13.8-36.2), although the report noted that the point estimate for this age group should be interpreted with caution due to small numbers of respondents (Haliburton, Kawartha Pine Ridge District Health Unit, 2007). Of those using tanning devices, 27.4% used them 2-5 times, over 18% used them 12-24 times, and 17.7% used them 25 or more times in the past 12 months.

The region of Waterloo survey of 1201 adults conducted in 2008 found that 12.1% of women 18+ and 4.7% of men 18+ had used tanning devices in the previous 12 months. Among those aged 18-24, 19.8% were estimated to have used such equipment (Region of Waterloo Public Health, 2008).

In the Halton Region in 2010, women were three times more likely than men to have used tanning equipment in the past 12 months (9% vs. 3%). Among those aged 18-24 an estimated 20% had used artificial tanning equipment in the past 12 months (Halton Region Health Department, 2010).

More worrisome evidence on use of indoor tanning equipment has recently emerged from an Ipsos-Reid survey of behavior among 1476 Ontario students in grades 7-12 (ages roughly 12-17) carried out in 2012 for the Canadian Cancer Society (2012a). Overall, 8.7% of Ontario students in Grades 7-12 reported having ever used a tanning device (i.e., sunbeds or sunlamps), and in Toronto (416 area code) this figure was 9.3%. Results by school grade indicate that use of indoor tanning devices begins early and that prevalence increases in each grade, with 11.8% of grade 11 students, and 21.3% of grade 12 students reporting ever use of sunbeds or sunlamps. Artificial tanning users averaged about 10 sessions per year. Figures for Toronto alone by gender, grade, or average usage are not presented in the report due to
relatively small numbers of responses available for analysis, with six regions and six school grades being surveyed. Of interest, 32.8% of tanners reported that they relied exclusively on use of tanning beds or sunlamps as a way to get a tan, suggesting that use of artificial devices could be quite important in accounting for annual UVR exposure.

Reasons for Indoor Tanning

Reasons for use of sunbeds in the Ontario youth polled by Ipsos Reid in the survey noted above and those noted in the pan-Canadian National Sun Survey in 2006 are similar. Some 61% of users in the Ipsos Reid poll felt they looked better with a tan, although this reason was more commonly noted for females (66%) than for males (53%). Females also noted building a ‘base tan’ and being tanned before going on vacation (57% and 51% respectively) more commonly as reasons than males (44% and 44% respectively). Being tanned for a special occasion was also more commonly noted by females (45% vs. 27%). Of interest, 41% of adults in the 2006 National Sun Survey reported using tanning equipment to enhance vitamin D levels, but only 17% of the youth in the Ipsos Reid poll noted this reason.

As might be expected in young people in high school, peer influence figured as a significant reason with 39% of females and 33% of males mentioning this reason. A surprise finding in the Ipsos Reid survey of Ontario youth was that 24% of indoor tanners reported being introduced to tanning by their parents.

A number of American studies (Geller et al., 2002; Hoerster et al., 2007; Yoo, 2009) have indicated that adolescents are strongly influenced by their perceptions of the desirability of use of tanning beds, even when they recognize tanning bed use as unhealthy (Yoo, 2009). In one American study (Hoerster et al., 2007) having a parent who had used indoor tanning equipment in the past was a predictor of adolescent use of indoor tanning equipment in the previous 12 months, although it was not stated if parental introduction was important.

Several studies have speculated that frequent tanners develop a physical or behavioral dependence on the activity, and a recent review (Nolan et al., 2009) outlined a number of models that could be investigated to account for possible addictive qualities of indoor tanning. These models include the possibility that cutaneous endorphins produced by UV radiation may reinforce tanning behavior (Kaur et al., 2006a), producing withdrawal like symptoms (Kaur et al., 2006b) if tanning ceases. Another study has produced some evidence that withdrawal from indoor tanning may produce symptoms of depression and anxiety and greater subsequent use of alcohol or marijuana (Mosher and Danoff-Burg, 2010). Difficulty in stopping indoor tanning appears to be greater in those who began tanning at an early age and those with a higher frequency of use of tanning beds (Zeller et al., 2006). This is a potentially important area of inquiry as findings may provide guidance for behavioral interventions to reduce indoor tanning in those who appear to be prone to dependency. However, more research is needed before significant progress can be made in understanding why some tanners find it difficult to stop.

Summary of Indoor Tanning Use

Population prevalence of indoor tanning varies in different countries with high rates seen in Denmark (Koster et al., 2009) and lower rates in high sunlight areas such as Australia (Gordon et al., 2012). In Canada, the 2006 National Sun Survey found that 9% of Canadians 16 years of age and older and 8% of Ontarians used indoor tanning equipment in a 12 month period prior to the survey (National Skin Cancer Prevention Committee, 2010). However, as noted above, the proportion of people age 18-24 using artificial tanning equipment in Ontario is much higher. In the Brant Health Unit survey conducted in 2007, 25% of respondents age 18-24 had used indoor tanning equipment in the 12 months prior to the survey. In addition although information is not available for many areas of Ontario, the frequency of use of these devices among indoor tanners in the Haliburton Health Unit area was high, with more than 35%
of tanners reporting more than 12 visits per year. This suggests that indoor tanners are getting substantial exposure to UVR through these machines. The Ipsos Reid survey released by the Canadian Cancer Society in April 2012 indicates that an alarming proportion of high school youth (21% of Grade 12 respondents) are using artificial tanning devices before the age of 18.

Prevalence of use of indoor tanning equipment is much higher in young females than in young males. For instance, in the Brant Health Unit survey conducted in 2007 females represented some 79% of those aged 18-24 who were tanners, and this female excess is seen in most surveys conducted of use among young people. Data is not available on female prevalence by ethnic group in Canada or Ontario, however in a recent US report (Center for Disease Control, 2012) rates in white women were much higher than those in women of colour. Toronto Public Health is currently analysing data on the prevalence of indoor tanning in Toronto using data from the 2011 Health Survey including analyses of prevalence by age, gender and ethnicity.

The known relationship between intermittent solar UVR, and both CMM and BCC, the findings from a number of studies that early life UVR exposure increases risk of these cancers; and the high prevalence of indoor tanning among young people, indicate that the potential for increased risk of skin cancers is becoming a significant public health problem.

**Indoor Tanning and Risk of Skin Cancer**

As part of an ongoing program to assess the carcinogenicity of chemical and physical agents in the workplace and the environment, the International Agency for Research on Cancer convened an expert group which met in 1992, examined all available animal and human scientific evidence, and determined that solar UVR was carcinogenic (IARC, 1992). The committee reviewing the evidence felt at the time that there was only limited evidence in humans for the carcinogenicity of exposure to UVR from sunlamps and sunbeds. The evaluation of sunbeds and sunlamps at the time was based on data from a relatively small number of studies. Most of these had been conducted primarily to determine the relationship between sunlight exposure and CMM, and information collected on artificial UVR exposure was somewhat limited.

Current evidence on the effect of artificial UV radiation for the purposes of indoor tanning will be reviewed for each of the three major skin cancers. It should be noted that artificial UV-A radiation and psoralens (PUVA therapy) are used together to treat skin conditions such as severe psoriasis, eczema, and vitiligo, and it is well known that side-effects of this medical treatment include an increased risk of skin cancer (Stern et al., 2001; Patel et al., 2009). PUVA patients are under intensive medical surveillance to ensure early diagnosis and treatment of skin cancers resulting from treatment. In this review we will omit studies of skin cancer in patients undergoing medically supervised UVR exposure for the purpose of treatment of existing disease.

**Melanoma**

**Studies prior to 2006:**

Information collected concerning sunlamp/sunbed use in early studies was rudimentary, and several studies collected no information on variables such as age that sunlamp or sunbed use began, and duration and frequency of sessions. In addition, some early analyses did not take into account other factors related to risk of melanoma such as host factors (hair and skin color, sun susceptibility, freckles, nevi, etc.) and concomitant sunlight exposure. Another significant limitation of some of the earlier research was the relatively small sample sizes and low prevalence of sunbed and sunlamp use by study subjects, leading to
low statistical power in individual studies to detect an association between use of tanning equipment and risk of skin cancer.

In an attempt to overcome this latter limitation, two meta-analyses were conducted that combined the results of a number of studies to estimate an overall association between use of tanning equipment and skin cancer risk. Gallagher et al. (2005), in a systematic analysis of 10 melanoma studies conducted in North America, Europe, UK and the Nordic countries and published between 1981 and the beginning of 2004, demonstrated that ever having used a sunlamp or sunbed resulted in a 25% increased risk of CMM (Summary OR=1.25; 95%CI=1.05-1.49). An analysis was also conducted summarizing the results of each study’s earliest users. In two of four informative case-control studies, early age at first use was defined as prior to age 30 while one was 35 and one was 25. The sole informative cohort study metric was use at ages 10-19. The summary estimate of risk over these studies for 'early age at first use' was 1.69 (95%CI=1.32-2.18). Similarly an analysis combining each study's either 'longest duration' or 'highest frequency' users also found an increased risk of CMM (Summary OR=1.61; 95%CI=1.21-2.12).

This paper was followed by that of the International Agency for Research on Cancer Working Group analysis originally completed and online in 2006, but published in hard (paper) form in 2007 (IARC, 2007) on artificial ultraviolet light and skin cancer. This analysis examined the evidence for melanoma risk as well as risk of basal and squamous cell carcinoma in peer reviewed papers published through 2005. The IARC analysis, which included data from 19 studies published between 1981 and 2005, showed an increased risk of melanoma for ever versus never use of indoor tanning devices (Summary RR=1.15; 95%CI=1.00-1.31). In addition, those who had their first exposure to indoor tanning before age 35 showed an elevated risk of about 75% for melanoma (Summary RR=1.75; 95%CI=1.35-2.26). The IARC meta-analysis (2007) abstract noted that there was no consistent evidence overall of a dose-response gradient between sunbed/sunlamp use and risk of melanoma, but the authors further noted that the metrics used for assessing duration were all different among the studies and did not permit meta-analytic synthesis. The authors noted several potential weaknesses in the studies, including poor recall of exposure by individuals and possible confounding due to sun exposure.

A further analysis was published as a non-peer reviewed report by Gordon and Hirst (2007). Based on data from 23 studies, the authors found that use of indoor tanning equipment increased risk of melanoma (Summary RR=1.22; 95%CI=1.07-1.39).

Since the publication of these papers, a number of additional studies have appeared evaluating risk of CMM due to indoor tanning. These investigations are characterized in general by collection of more extensive information on the nature of subjects' indoor tanning exposure, relatively greater numbers of exposed subjects, and greater efforts to control confounding due to host factors and sun exposure.

Summary findings from studies on melanoma that were evaluated in the meta-analyses of Gallagher et al. (2005) and the IARC working group (IARC, 2007), as well as findings from the newer studies to date are presented as Tables 3-8.

- Tables 3-4 assess the risk of melanoma for 'ever use' vs. 'never use' of indoor tanning devices. A number of papers which noted sunlamp or sunbed use in subjects could not be included in the table due to lack of critical information, as noted in the footnote beneath Table 3.
- Tables 5-6 summarize the evidence (where available) as to whether commencing use of indoor tanning devices _early in life_ heightens melanoma risk by comparison with never users or those initiating use later in life.
- Tables 7-8 summarize the evidence from studies of melanoma on the risk level of those with the _longest duration or highest frequency of use_ of indoor tanning devices.
Following Tables 3-8, an in-depth review of studies published since the 2007 IARC meta-analysis is provided.

Studies of cancer invariably adjust risk estimates for factors such as age and gender to ensure that these known variables do not affect the analyses, and the studies of sunbed use are no exception. However, as noted in the sections above, skin cancer risk is affected by both a person’s phenotype (skin, hair colour, sun sensitivity etc.) and solar UVR exposure. Therefore in Tables 3-8 on CMM as well as in Tables 9-10 on BCC and Tables 11-12 on SCC, a simple 'yes' or 'no' is used to denote whether the authors of each study attempted to adjust the skin cancer risk estimate seen in those using indoor tanning devices for susceptibility factors and for sun exposure. However, it should be noted that there is no 'gold standard' for measures of individual susceptibility or solar UVR exposure, and there is substantial variation in how the authors of each study adjusted for host factors and solar UVR exposure. Therefore, in the tables, a 'yes' for host factors means that one or more measures (skin colour, hair colour, sun sensitivity, freckling, nevus count, etc.) have been chosen by the authors to control for susceptibility factors. A 'yes' for sun exposure denotes the fact that one or more measures (such as annual recreational sun exposure, lifetime sun exposure, time spent in sunny vacations) have been used to control for solar UVR exposure. A 'yes' in both these columns indicates the authors tried to ensure that the reported relationship between indoor tanning exposure and skin cancer is independent of potential confounding factors. It is worth noting that the use of different metrics to control for susceptibility factors and solar UVR may be a factor contributing to the range of risk estimates for indoor tanning seen in the various studies.
Table 3: Indoor Tanning and Cutaneous Malignant Melanoma: Ever vs. Never Exposed (Case-Control Studies)\(^1\)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Place and Period</th>
<th>Total Cases</th>
<th>Total Controls</th>
<th>% Cases Exposed</th>
<th>% Controls Exposed</th>
<th>Metric</th>
<th>Adjusted for Host Factors?</th>
<th>Adjusted for Sun Exposure?</th>
<th>OR/RR/HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adam et al. (1981)</td>
<td>UK 1971-1976</td>
<td>169 females only</td>
<td>507</td>
<td>8%</td>
<td>3%</td>
<td>Ever used sunlamps</td>
<td>No</td>
<td>No</td>
<td>2.93 (1.16-7.40)(^2)</td>
</tr>
<tr>
<td>Holman et al. (1986b)</td>
<td>West Australia 1980-1981</td>
<td>511</td>
<td>511</td>
<td>9% of all participants (cases and controls)</td>
<td>9% of all participants (cases and controls)</td>
<td>Ever used sunlamps</td>
<td>No</td>
<td>No</td>
<td>1.1 (0.6-1.8)</td>
</tr>
<tr>
<td>Osterlind et al. (1988b)</td>
<td>East Denmark 1982-1985</td>
<td>474</td>
<td>926</td>
<td>14%</td>
<td>18%</td>
<td>Ever used sunbeds</td>
<td>Yes</td>
<td>No</td>
<td>0.7 (0.5-1.0)</td>
</tr>
<tr>
<td>Zanetti et al. (1988)</td>
<td>Italy 1984-1986</td>
<td>208</td>
<td>416</td>
<td>7.2%</td>
<td>5%</td>
<td>Ever used UVA lamps</td>
<td>Yes</td>
<td>No</td>
<td>0.9 (0.4-2.0)</td>
</tr>
<tr>
<td>Swerdlow et al. (1988)</td>
<td>UK (Scotland) 1979-1984</td>
<td>180</td>
<td>197</td>
<td>21%</td>
<td>8%</td>
<td>Ever used ultraviolet lamps or sunbeds</td>
<td>Yes</td>
<td>Yes</td>
<td>2.9 (1.3-6.4)</td>
</tr>
<tr>
<td>MacKie et al. (1989)</td>
<td>UK (Scotland) 1987</td>
<td>99 males</td>
<td>99 males</td>
<td>13% males</td>
<td>1% males</td>
<td>Ever used sunlamps or sunbeds</td>
<td>Yes</td>
<td>No</td>
<td>Males: 1.3 (0.2-7.9) Females: 1.2 (0.5-3.0)</td>
</tr>
<tr>
<td>Dunn-Lane et al. (1993)</td>
<td>Ireland 1985-1986</td>
<td>100</td>
<td>100</td>
<td>17%</td>
<td>15%</td>
<td>Ever used sunlamps or sunbeds</td>
<td>No</td>
<td>No</td>
<td>1.16 (0.54-2.47)</td>
</tr>
<tr>
<td>Garbe et al. (1993)</td>
<td>Germany 1984-1987</td>
<td>856</td>
<td>705</td>
<td>7.7%</td>
<td>7.1%</td>
<td>Ever used sunbeds</td>
<td>Yes</td>
<td>No</td>
<td>1.5 (0.9 – 2.4)</td>
</tr>
<tr>
<td>Autier et al. (1994b)</td>
<td>Germany, Belgium, France 1991-1993</td>
<td>420</td>
<td>447</td>
<td>Sunbeds 14.5%</td>
<td>Sunbeds 15%</td>
<td>Ever used sunbeds for tanning</td>
<td>No</td>
<td>No</td>
<td>Sunbeds: 0.95 (0.64-1.41)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sunlamps 9%</td>
<td>Sunlamps 5%</td>
<td>Ever used sunlamps for tanning</td>
<td></td>
<td></td>
<td>Sunlamps: 1.77 (1.00-3.23)</td>
</tr>
<tr>
<td>Reference</td>
<td>Place and Period</td>
<td>Total Cases</td>
<td>Total Controls</td>
<td>% Cases Exposed</td>
<td>% Controls Exposed</td>
<td>Metric</td>
<td>Adjusted for Host Factors?</td>
<td>Adjusted for Sun Exposure?</td>
<td>OR/RR/HR (95%CI)</td>
</tr>
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</tr>
<tr>
<td>Westerdahl et al.</td>
<td>South Sweden 1988-1990</td>
<td>400</td>
<td>640</td>
<td>29%</td>
<td>24%</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>1.3 (0.9-1.8)</td>
</tr>
<tr>
<td>Holly et al.</td>
<td>California USA 1981-1986</td>
<td>452</td>
<td>930</td>
<td>37%</td>
<td>38%</td>
<td></td>
<td>No</td>
<td>No</td>
<td>0.94 (0.74-1.2)</td>
</tr>
<tr>
<td>Chen et al.</td>
<td>Connecticut USA 1987-1989</td>
<td>624</td>
<td>512</td>
<td>22.6%</td>
<td>18.5%</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>1.13 (0.82-1.54)</td>
</tr>
<tr>
<td>Walter et al.</td>
<td>Ontario Canada 1984-1986</td>
<td>277 males</td>
<td>283 males</td>
<td>24% males</td>
<td>14% males</td>
<td></td>
<td>Yes</td>
<td>No</td>
<td>Males: 1.88 (1.20-2.98)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>306 females</td>
<td>325 females</td>
<td>28% females</td>
<td>21% females</td>
<td></td>
<td></td>
<td></td>
<td>Females: 1.45 (0.99-2.13)</td>
</tr>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M+F: 1.62 (1.21-2.16)</td>
</tr>
<tr>
<td>Naldi et al.</td>
<td>Italy 1992-1995</td>
<td>542</td>
<td>538</td>
<td>5.5%</td>
<td>6.7%</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>0.78 (0.45-1.37)</td>
</tr>
<tr>
<td>Westerdahl et al.</td>
<td>South Sweden 1995-1997</td>
<td>571</td>
<td>913</td>
<td>44%</td>
<td>41%</td>
<td></td>
<td>Yes</td>
<td>No</td>
<td>1.2 (0.9-1.6)</td>
</tr>
<tr>
<td>Landi et al.</td>
<td>Italy 1994-1999</td>
<td>183</td>
<td>179</td>
<td>17.6%</td>
<td>21.2%</td>
<td></td>
<td>Yes</td>
<td>No</td>
<td>1.3 (0.7-2.4)</td>
</tr>
<tr>
<td>Bataille et al.</td>
<td>UK 1989-1993</td>
<td>413</td>
<td>416</td>
<td>28% females</td>
<td>34% females</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>Overall: 1.19 (0.84-1.68)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>17% males</td>
<td>15% males</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bataille et al.</td>
<td>Belgium, France, Holland, Sweden, UK</td>
<td>597</td>
<td>622</td>
<td>53%</td>
<td>57%</td>
<td></td>
<td>Yes</td>
<td>No</td>
<td>0.90 (0.71-1.14)</td>
</tr>
<tr>
<td></td>
<td>1998-2001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>Place and Period</td>
<td>Total Cases</td>
<td>Total Controls</td>
<td>% Cases Exposed</td>
<td>% Controls Exposed</td>
<td>Metric</td>
<td>Adjusted for Host Factors?</td>
<td>Adjusted for Sun Exposure?</td>
<td>OR/RR/HR (95%CI)</td>
</tr>
<tr>
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</tr>
<tr>
<td>Han et al. (2006)</td>
<td>USA Nested case-control study from Nurses cohort study; age 30-55 at inception in 1976</td>
<td>200</td>
<td>804</td>
<td>23%</td>
<td>12%</td>
<td>Ever used sunlamps or tanning salon</td>
<td>Yes</td>
<td>Yes</td>
<td>2.06 (1.30-3.26)</td>
</tr>
<tr>
<td>Clough-Gorr et al. (2008)</td>
<td>New Hampshire USA 1995-1998</td>
<td>423</td>
<td>678</td>
<td>Sunlamps 20% Sunbeds 23% Both 6.4%</td>
<td>Sunlamps 15% Sunbeds 21% Both 3.8%</td>
<td>Ever used sunlamps Ever used sunbeds Ever used both</td>
<td>Sunlamp use: 1.39 (1.00-1.96)</td>
<td>Yes</td>
<td>Sunbed use: 1.14 (0.80-1.61) Use of both: 1.96 (1.06-3.61) Use of either: 1.22 (0.83-1.08)</td>
</tr>
<tr>
<td>Fortes et al. (2008)</td>
<td>Italy 2001-2003</td>
<td>304</td>
<td>305</td>
<td>21%</td>
<td>20%</td>
<td>Ever used sunlamps or sunbeds in adulthood</td>
<td>No</td>
<td>No</td>
<td>1.30 (0.83-2.04)</td>
</tr>
<tr>
<td>Lazovich et al. (2010)</td>
<td>Minnesota, USA 2004-2007</td>
<td>1167</td>
<td>1101</td>
<td>63%</td>
<td>51%</td>
<td>Ever used indoor tanning</td>
<td>Yes</td>
<td>Yes</td>
<td>1.74 (1.42-2.14)</td>
</tr>
<tr>
<td>Cust et al. (2011)</td>
<td>Australia 2000-2002</td>
<td>604</td>
<td>479</td>
<td>23%</td>
<td>18%</td>
<td>Ever used sunbeds or sunlamps</td>
<td>Yes</td>
<td>Yes</td>
<td>1.41 (1.01-1.96)</td>
</tr>
<tr>
<td>Elliott et al. (2011)</td>
<td>UK 2000-2005</td>
<td>959</td>
<td>513 population controls</td>
<td>51.6%</td>
<td>46.6%</td>
<td>Ever used sunbeds or sunlamps</td>
<td>Yes</td>
<td>Yes</td>
<td>1.06 (0.83-1.36)</td>
</tr>
<tr>
<td>Reference</td>
<td>Place and Period</td>
<td>Total Cases</td>
<td>Total Controls</td>
<td>% Cases Exposed</td>
<td>% Controls Exposed</td>
<td>Metric</td>
<td>Adjusted for Host Factors?</td>
<td>Adjusted for Sun Exposure?</td>
<td>OR/RR/HR (95%CI)</td>
</tr>
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</tr>
<tr>
<td>Fears et al.</td>
<td>USA 1991-1992</td>
<td>718</td>
<td>944</td>
<td>26%</td>
<td>30%</td>
<td>Ever used sunlamps or tanning booths</td>
<td>No&lt;sup&gt;3&lt;/sup&gt;</td>
<td>No&lt;sup&gt;3&lt;/sup&gt;</td>
<td>0.83(0.67-1.04)&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>1</sup> Studies of Klepp and Magnus (1979); Gallagher et al. (1986); Elwood et al. (1986); Holly et al. (1987); Beitner et al. (1990); Loria and Matos (2001) are omitted as estimates of risk were not provided in the original papers. Walter et al. (1990) was also omitted as the data from this study was included in the re-analysis of Walter et al. (1999).

<sup>2</sup> OR based on 111 case and 342 control questionnaires.

<sup>3</sup> Crude odds ratios and confidence intervals calculated from values given in Table 1 p. 576 of Fears et al. (2011), using Fisher's Exact Test, without control for host factors and sun exposure.
Table 4: Indoor Tanning and Cutaneous Malignant Melanoma: Ever vs. Never Exposed (Cohort Studies)\(^1\)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Place and Period</th>
<th>No. of Events</th>
<th>Cohort Size</th>
<th>% of Cohort Exposed</th>
<th>Metric</th>
<th>Adjusted for Host Factors?</th>
<th>Adjusted for Sun Exposure?</th>
<th>RR/HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veierod et al. (2003)</td>
<td>Sweden and Norway; female cohort age 30-50 at inception of study in 1991-92; follow-up through 1999</td>
<td>187 incident melanomas in 183 women</td>
<td>Total cohort 106,379 women</td>
<td>18% of cohort exposed ≥1 per month in any decade age 10-19, 20-29 or 30-39</td>
<td>Exposed to solarium (sunbeds/sunlamps) ≥1/month in any decade from age 10-39 vs. rarely or never exposed</td>
<td>Yes</td>
<td>Yes</td>
<td>1.55 (1.04-2.32)</td>
</tr>
<tr>
<td>Veierod et al. (2010a)</td>
<td>Sweden and Norway; female cohort age 30-50 at inception of study in 1991-92; follow-up through 2005</td>
<td>412 incident melanomas in 294 women</td>
<td>Total cohort 106,366 women</td>
<td>51% of cohort exposed between ages 10-39</td>
<td>Ever vs. never exposed to solarium (sunbeds/sunlamps) at age 10-39</td>
<td>Yes</td>
<td>Yes</td>
<td>1.31 (1.03-1.66)</td>
</tr>
<tr>
<td>Nielsen et al. (2011)</td>
<td>Sweden female cohort; age 25-64 at inception of study in 1990-1992; follow-up through 2007</td>
<td>215 incident melanomas in 206 women</td>
<td>Total cohort 29,520 women age 25-64 at inception of study</td>
<td>3% of cohort exposed to sunlamps 47% of cohort exposed to sunbeds</td>
<td>Ever exposed to sunlamps Ever exposed to sunbeds</td>
<td>No(^2)</td>
<td>No(^2)</td>
<td>1.78 (0.87-3.38)(^2)</td>
</tr>
</tbody>
</table>

1 Study of Zhang et al. (2012) does not provide an ‘ever vs. never’ exposed risk estimate.
2 Crude odd ratios for ever vs. never exposed were calculated from Supplementary data on Int J Cancer site for Nielsen et al. (2011) using the Fisher exact test.
Table 5: Indoor Tanning and Cutaneous Malignant Melanoma: First Exposure Early in Life (Case-Control Studies)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Place and Period</th>
<th>Total Cases</th>
<th>Total Controls</th>
<th>% Cases Exposed</th>
<th>% Controls Exposed</th>
<th>Metric</th>
<th>Adjusted for Host Factors?</th>
<th>Adjusted for Sun Exposure?</th>
<th>OR/RR/HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swerdlow et al.</td>
<td>UK (Scotland) 1979-1984</td>
<td>180</td>
<td>197</td>
<td>10%</td>
<td>3%</td>
<td>First use &lt;age 30 years</td>
<td>Yes</td>
<td>Yes</td>
<td>3.8 (0.9-16.5)</td>
</tr>
<tr>
<td>Walter et al.</td>
<td>Ontario Canada 1984-1986</td>
<td>277 males</td>
<td>283 males</td>
<td>12% males</td>
<td>7% males</td>
<td>First use &lt;age 30 years</td>
<td>Yes</td>
<td>No</td>
<td>Males: 2.13 (1.13-4.13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>306 females</td>
<td>325 females</td>
<td>17% females</td>
<td>12% females</td>
<td></td>
<td></td>
<td></td>
<td>Females: 1.55 (0.94-2.59)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M+F: 1.75 (1.18-2.59)</td>
</tr>
<tr>
<td>Westerdahl et al.</td>
<td>Southern Sweden 1988-1990</td>
<td>400</td>
<td>640</td>
<td>4%</td>
<td>7.2%</td>
<td>Used prior to melanoma diagnosis &lt;age 30 years</td>
<td>Yes</td>
<td>Yes</td>
<td>2.7 (0.7-9.8)</td>
</tr>
<tr>
<td>Chen et al.</td>
<td>Connecticut USA 1987-1989</td>
<td>624</td>
<td>512</td>
<td>12%</td>
<td>8%</td>
<td>First use of sunlamps &lt;age 25 years</td>
<td>Yes</td>
<td>Yes</td>
<td>1.35 (0.88-2.08)</td>
</tr>
<tr>
<td>Westerdahl et al.</td>
<td>Southern Sweden 1995-1997</td>
<td>571</td>
<td>913</td>
<td>12%</td>
<td>9%</td>
<td>First use ≤ age 35 years</td>
<td>Yes</td>
<td>Yes</td>
<td>2.3 (1.2-4.2)</td>
</tr>
<tr>
<td>Battaile et al.</td>
<td>Belgium, France, Holland, Sweden, UK 1998-2001</td>
<td>597</td>
<td>622</td>
<td>4%</td>
<td>2%</td>
<td>First use &lt;age 15 years</td>
<td>Yes</td>
<td>No</td>
<td>1.82 (0.92-3.62)</td>
</tr>
<tr>
<td>Clough-Gorr et al.</td>
<td>New Hampshire USA 1995-1998</td>
<td>423</td>
<td>678</td>
<td>Sunlamps 12.3%</td>
<td>Sunlamps 9.9%</td>
<td>First use of sunlamps &lt;age 20 years</td>
<td>Yes</td>
<td>Yes</td>
<td>1.23 (0.81-1.88)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sunbeds 4.3%</td>
<td>Sunbeds 2.5%</td>
<td>First use of sunbeds &lt;age 20 years</td>
<td>Yes</td>
<td>Yes</td>
<td>1.78 (0.76-4.15)</td>
</tr>
<tr>
<td>Reference</td>
<td>Place and Period</td>
<td>Total Cases</td>
<td>Total Controls</td>
<td>% Cases Exposed</td>
<td>% Controls Exposed</td>
<td>Metric</td>
<td>Adjusted for Host Factors?</td>
<td>Adjusted for Sun Exposure?</td>
<td>OR/RR/HR (95%CI)</td>
</tr>
<tr>
<td>------------------------</td>
<td>--------------------------</td>
<td>-------------</td>
<td>----------------</td>
<td>-----------------</td>
<td>-------------------</td>
<td>--------------------------------------------</td>
<td>---------------------------</td>
<td>---------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Lazovich et al. (2010)</td>
<td>Minnesota, USA 2004-2007</td>
<td>1167</td>
<td>1101</td>
<td>17.9%</td>
<td>14.6%</td>
<td>First use &lt;age 18 years</td>
<td>Yes</td>
<td>Yes</td>
<td>1.85 (1.33-2.57)</td>
</tr>
<tr>
<td>Elliott et al. (2011)</td>
<td>UK 2000-2005</td>
<td>959</td>
<td>513 population controls</td>
<td>23.5%</td>
<td>18.3%</td>
<td>First use of sunbeds or sunlamps &lt;age 25 years</td>
<td>Yes</td>
<td>Yes</td>
<td>1.16 (0.84-1.62)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>144 cases subset with sibling controls</td>
<td>20.8%</td>
<td>20.8%</td>
<td>First use of sunbeds or sunlamps &lt;age 25 years</td>
<td>Yes</td>
<td>Yes</td>
<td>0.96 (0.46-2.02)</td>
</tr>
<tr>
<td>Cust et al. (2011)</td>
<td>Australia 2000-2002</td>
<td>604</td>
<td>479</td>
<td>14%</td>
<td>8.6%</td>
<td>First use of sunbeds or sunlamps age &lt;25 years</td>
<td>Yes</td>
<td>Yes</td>
<td>1.64 (1.07-2.51)</td>
</tr>
<tr>
<td>Fears et al. (2011)</td>
<td>USA 1991-1992</td>
<td>718</td>
<td>944</td>
<td>11.4%</td>
<td>13.3%</td>
<td>First use of sunlamps or tanning booths age &lt;20 years</td>
<td>No¹</td>
<td>No¹</td>
<td>0.84 (0.61-1.14)¹</td>
</tr>
</tbody>
</table>

¹ Crude odds ratios and confidence intervals calculated from values given in Table 1 p. 576 of Fears et al. (2011) using Fisher’s Exact Test, without control for host factors and sun exposure.
Table 6: Indoor Tanning and Cutaneous Malignant Melanoma: First Exposure Early in Life (Cohort Studies)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Place and Period</th>
<th>No. of Events</th>
<th>Cohort Size</th>
<th>% of Cohort Exposed at This Age</th>
<th>Metric</th>
<th>Adjusted for Host Factors?</th>
<th>Adjusted for Sun Exposure?</th>
<th>RR/HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veierod et al. (2003)</td>
<td>Sweden and Norway; female cohort age 30-50 at inception in 1991-1992; follow-up through 1999</td>
<td>4 incident melanomas among those exposed</td>
<td>Total cohort 106,379 women</td>
<td>2% of cohort</td>
<td>Use ≥ 1 time per month at age 10-19</td>
<td>Yes</td>
<td>Yes</td>
<td>1.52 (0.56-4.12)</td>
</tr>
<tr>
<td>Veierod et al. (2010a)</td>
<td>Norway; female cohort, age 30-50 at inception in 1991-1992; follow-up through 2005</td>
<td>7 incident melanomas among those exposed</td>
<td>Total cohort 106,366 women</td>
<td>2% of cohort</td>
<td>Use ≥ 1 time per month at age 10-19</td>
<td>Yes</td>
<td>Yes</td>
<td>1.19 (0.56-2.53)</td>
</tr>
<tr>
<td>Nielsen et al. (2011)</td>
<td>Sweden; female cohort age 25-64 at inception in 1990-1992; follow-up through 2007</td>
<td>No. of melanomas among those exposed not given</td>
<td>Total cohort 29,520; age 25-64 at inception</td>
<td>Not given</td>
<td>Sunbed use &gt;10 times/year and diagnosis at age 25-39</td>
<td>Yes</td>
<td>Yes</td>
<td>2.5 (1.0-6.2)</td>
</tr>
</tbody>
</table>
Table 7: Indoor Tanning and Cutaneous Malignant Melanoma: Longest Duration or Highest Frequency of Use (Case-Control Studies)\(^1\)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Place and Period</th>
<th>Total Cases</th>
<th>Total Controls</th>
<th>% Cases Exposed</th>
<th>% Controls Exposed</th>
<th>Metric Description</th>
<th>Adjusted for Host Factors?</th>
<th>Adjusted for Sun Exposure?</th>
<th>OR/RR/HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swerdlow et al. (1988)</td>
<td>UK (Scotland) 1979-1984</td>
<td>180</td>
<td>197</td>
<td>4%</td>
<td>2%</td>
<td>Duration of use &gt;1 year</td>
<td>Yes</td>
<td>Yes</td>
<td>3.4 (0.6-20.3)</td>
</tr>
<tr>
<td>Walter et al. (1990)</td>
<td>Ontario, Canada 1984-1986</td>
<td>277 Males</td>
<td>283 Males</td>
<td>Males 7%</td>
<td>Males 4%</td>
<td>Sunbed/sunlamp use ≥1/month for ≥12 months</td>
<td>Yes</td>
<td>No</td>
<td>Males: 2.12 (0.90-5.28)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>306 Females</td>
<td>325 Females</td>
<td>Females 5%</td>
<td>Females 2%</td>
<td></td>
<td></td>
<td></td>
<td>Females: 2.99 (1.08-9.57)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M+F: 2.44 (1.27-4.71)</td>
</tr>
<tr>
<td>Westerdahl et al. (1994)</td>
<td>South Sweden 1988-1990</td>
<td>400</td>
<td>640</td>
<td>10%</td>
<td>5%</td>
<td>&gt;10 exposures/year to sunbeds/sunlamps</td>
<td>Yes</td>
<td>Yes</td>
<td>1.8 (1.0-3.2)</td>
</tr>
<tr>
<td>Chen et al. (1998)</td>
<td>Connecticut USA 1987-1989</td>
<td>624</td>
<td>512</td>
<td>10%</td>
<td>8%</td>
<td>≥10 uses of sunlamp</td>
<td>Yes</td>
<td>Yes</td>
<td>1.15 (0.60-2.20)</td>
</tr>
<tr>
<td>Naldi et al. (2000b)</td>
<td>Italy 1992-1995</td>
<td>542</td>
<td>538</td>
<td>2.2%</td>
<td>3.7%</td>
<td>&gt;15 sunlamp or sunbed exposures</td>
<td>Yes</td>
<td>Yes</td>
<td>0.54 (0.24-1.20)</td>
</tr>
<tr>
<td>Westerdahl et al. (2000)</td>
<td>South Sweden 1995-1997</td>
<td>571</td>
<td>913</td>
<td>7%</td>
<td>6%</td>
<td>&gt;250 sunbed uses</td>
<td>Yes</td>
<td>No</td>
<td>1.5 (0.7-3.2)</td>
</tr>
<tr>
<td>Bataille et al. (2004)</td>
<td>UK 1989-1993</td>
<td>413</td>
<td>416</td>
<td>4.6%</td>
<td>3.3%</td>
<td>≥100 hours cumulative use</td>
<td>Yes</td>
<td>Yes</td>
<td>0.89 (0.42-1.88)</td>
</tr>
<tr>
<td>Bataille et al. (2005)</td>
<td>Belgium, France, Holland, Sweden, UK 1998-2001</td>
<td>597</td>
<td>622</td>
<td>7%</td>
<td>6%</td>
<td>&gt;100 hours cumulative use</td>
<td>Yes</td>
<td>No</td>
<td>1.19 (0.73-1.93)</td>
</tr>
<tr>
<td>Reference</td>
<td>Place and Period</td>
<td>Total Cases</td>
<td>Total Controls</td>
<td>% Cases Exposed</td>
<td>% Controls Exposed</td>
<td>Metric</td>
<td>Adjusted for Host Factors?</td>
<td>Adjusted for Sun Exposure?</td>
<td>OR/RR/HR (95%CI)</td>
</tr>
<tr>
<td>-------------------</td>
<td>-----------------------------------------</td>
<td>-------------</td>
<td>----------------</td>
<td>-----------------</td>
<td>--------------------</td>
<td>----------------------------------</td>
<td>---------------------------</td>
<td>--------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Han et al. (2006)</td>
<td>USA Nested case-control study from Nurses cohort study; age 30-55 at inception in 1976</td>
<td>200</td>
<td>804</td>
<td>Not given</td>
<td>Not given</td>
<td>Use of sunlamps or sunbeds ≥10 times</td>
<td>Yes</td>
<td>Yes</td>
<td>2.05 (1.08-3.90)</td>
</tr>
<tr>
<td>Clough-Gorr et al. (2008)</td>
<td>New Hampshire, USA 1995-1998</td>
<td>423</td>
<td>678</td>
<td>Sunlamps 8.5%</td>
<td>Sunlamps 5.5%</td>
<td>Use of sunlamps ≥6 times</td>
<td>Yes</td>
<td>Yes</td>
<td>Sunlamps: 1.54 (0.93-2.57) Sunbeds: 1.25 (0.79-1.98)</td>
</tr>
<tr>
<td>Lazovich et al. (2010)</td>
<td>Minnesota, USA 2004-2007</td>
<td>1167</td>
<td>1101</td>
<td>23.6%</td>
<td>14%</td>
<td>&gt;100 indoor tanning sessions</td>
<td>Yes</td>
<td>Yes</td>
<td>2.72 (2.04-3.63)</td>
</tr>
<tr>
<td>Cust et al. (2011)</td>
<td>Australia 2000-2002</td>
<td>604</td>
<td>479</td>
<td>10.3%</td>
<td>5.6%</td>
<td>&gt;10 sunbed or sunlamp uses</td>
<td>Yes</td>
<td>Yes</td>
<td>2.01 (1.22-3.31) 3.18 (2.28-4.43) 2.45 (1.83-3.28)</td>
</tr>
<tr>
<td>Elliott et al. (2011)</td>
<td>UK 2000-2005</td>
<td>959</td>
<td>513 population controls</td>
<td>22.7%</td>
<td>20.7%</td>
<td>&gt;20 sunbed or sunlamp uses</td>
<td>Yes</td>
<td>Yes</td>
<td>0.99 (0.72-1.37) 1.49 (0.70-3.17)</td>
</tr>
<tr>
<td>Fears et al. (2011)</td>
<td>USA 1991-1992</td>
<td>718</td>
<td>944</td>
<td>12.5%</td>
<td>13.1%</td>
<td>&gt;10 sunlamp or tanning booth uses</td>
<td>No²</td>
<td>No²</td>
<td>0.95 (0.70-1.28)²</td>
</tr>
</tbody>
</table>

¹ Study of Landi et al. (2001) omitted from the table. The study showed OR=1.4 (95%CI =0.5-3.6) for more than 10 sunlamp uses, but exposure prevalence information for cases and controls was missing.
² Crude odds ratios and confidence intervals calculated from values given in Table 1 p. 576 of Fears et al. (2011), using Fisher’s Exact Test without control for host factors and sun exposure.
Table 8: Indoor Tanning and Cutaneous Malignant Melanoma: Longest Duration or Highest Frequency of Use (Cohort Studies)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Place and Period</th>
<th>No. of Events</th>
<th>Cohort Size</th>
<th>% of Cohort Exposed at this Level</th>
<th>Metric</th>
<th>Adjusted for Host Factors?</th>
<th>Adjusted for Sun Exposure?</th>
<th>RR/HR (99%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veierod et al.</td>
<td>Sweden and Norway; female cohort age 30-50 at inception in 1991-1992; follow-up through 2005</td>
<td>16 incident melanomas among those exposed at this exposure level</td>
<td>Total cohort 106,366 women</td>
<td>4%</td>
<td>Exposed to solarium (sunbeds/sunlamps) ≥1 time/month in 2 or 3 decades, at age 10-39</td>
<td>Yes</td>
<td>Yes</td>
<td>2.37 (1.37-4.08)</td>
</tr>
<tr>
<td>Nielsen et al.</td>
<td>Sweden; female cohort age 25-64 at inception in 1990-1992; follow-up through 2007</td>
<td>2 incident melanomas among those exposed at this sunlamp exposure level 32 incident melanomas among those exposed at this sunbed exposure level</td>
<td>Total cohort 29,520 women</td>
<td>16%</td>
<td>Sunlamp &gt;10 times per year Sunbed &gt;10 times per year</td>
<td>Yes</td>
<td>Yes</td>
<td>1.6 (0.2-11.9)</td>
</tr>
<tr>
<td>Zhang et al.</td>
<td>USA Female Nurses cohort II; age 25-42 at inception in 1989; follow-up through 2009</td>
<td>No. of melanomas among those exposed not given for this exposure level</td>
<td>Total cohort 116,678; 73,494 in sunbed study</td>
<td>9.3% exposed at high school/college age 19.8% exposed at age 25-35</td>
<td>Exposed &gt;6 times/year high school/college Exposed &gt;6 times/year age 25-35</td>
<td>Yes</td>
<td>Yes</td>
<td>1.23 (0.69-2.20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total 412 melanomas in 206 women</td>
<td>Total 215 melanomas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Studies from 2006 to January 2012:

Han et al. (2006) studied the risk of melanoma associated with sunbed exposure in a case-control study nested within the first Nurses' Health Study, which at inception in 1976 enrolled 121,700 female nurses age 30-55. Follow-up for diagnosis of melanoma continued through May 2000. Melanoma risk was found to be elevated in women who had ever used sunlamps or tanning salons compared with those who had never used them (OR=2.06; 95%CI=1.30-3.26) after control for host factors and sun exposure. Risk of melanoma appeared to be the same for subjects using sunlamps or sunbeds 10 or more times (OR=2.05; 95%CI=1.08-3.90) and those using them less than 10 times (OR=2.06; 95%CI=1.15-3.68).

A small cohort study of 1518 patients from a single Midwest US hospital-based dermatology clinic (Ting et al., 2007) demonstrated an increased risk of CMM in those ever using sunbeds. Of those who reported using a sunbed at least once, 7% reported a history of melanoma, and of the 1031 with no history of using sunbeds, only 4.4% reported a history of melanoma (OR=1.65; 95%CI=1.01-2.67). Among women age 45 or less (presumably at diagnosis of melanoma), the risk of CMM was higher (OR=3.22; 95%CI=1.01-11.46). Finally, the highest risk of melanoma was among women age 45 or less who reported their tanning bed session to last 20 minutes or more (OR=4.12; 95%CI=1.41-12.02). There are a number of difficulties with this study. First of all, the authors note that only 551 of the 1518 patients approached provided full data, a response rate of only 36.3%. Demographic information is provided only on the 551 responders, so it is not clear that responders and non-responders are comparable demographically. Notwithstanding this, the indoor tanning analysis utilizes data from all 1518. Further, diagnosis of melanoma was self-reported and of the total of 79 patients who gave a history of CMM, only 29 diagnoses were able to be confirmed by study staff. Further, it is not possible to determine what proportion of the melanomas included in the tanning bed analyses were confirmed histologically and what proportion were not. Data on sun exposure was reported to have been collected, but it is not clear how complete this was, and in any event, the risk ratios for sunbed use do not appear to be adjusted for this variable. Because of concerns with a number of methodological issues surrounding the conduct and write-up of this study, it has not been included in the melanoma tables, and will not be further considered.

The New Hampshire population-based case-control study (Table 3) of Clough-Gorr et al. (2008) examined sunlamp and tanning bed use among 423 melanoma cases age 20-60 at diagnosis and 678 controls. The results showed a significantly elevated risk of melanoma for ever-use of sunlamps (OR=1.39; 95%CI=1.00-1.96) but not tanning beds (OR=1.14; 95%CI=0.80-1.61). Among those who used both sunlamps and tanning beds, an elevated risk is seen for CMM (RR=1.96; 1.06-3.61). Categorical analysis of age at first use of sunlamps showed an increasing trend in melanoma risk from non-users through those beginning prior to age 20, to those beginning at or after age 20 (p trend=0.05). No similar trend was seen in age at first tanning bed use. Categorical analysis of data on frequency of use of sunlamps also appeared to indicate a trend of increased risk with usage from no use; through < 6 times; to ≥ 6 times (p trend=0.02) (RR ≥ 6 times 1.54; 95%CI=0.93-2.57) (Table 7). No similar trend was seen with use of tanning beds. All analyses controlled for host susceptibility (pigmentation and sun sensitivity) as well as sun exposure. The authors conclude that there was an increasing risk of melanoma with increased frequency and duration of sunlamp use, but not tanning bed use. They also note that insufficient time may have elapsed since tanning bed use began to assess melanoma risk in study participants.

The Norwegian-Swedish cohort study of Veierod et al. (2010a) extends findings on solarium use (sunbeds/sunlamps) which first appeared in the 2003 analysis (Veierod et al., 2003). At the time of the 2003 paper, follow-up of the cohort was relatively short (median=8.3 years) and only 187 melanomas were available for analysis, whereas 412 melanomas were available in the 2010 paper. The relative risk
for those ever exposed to solaria versus those not exposed was 1.31 (95%CI= 1.03-1.66), roughly similar to that seen in the 2003 analysis. Among those reporting use of solaria at age 30-39 and 40-49, a significant increasing trend in risk of melanoma was seen over three groups - those who used devices never, rarely, and once or more per month. Similar results were seen in those using solaria at age 20-29, but the trend was not statistically significant. The paper does not appear to present a formal analysis of risk of melanoma by age at first use of solaria. However, those who reported use at age 10-19 had a modest and non-significant elevated risk of melanoma (RR=1.19; 95%CI=0.56-2.53), although use was rare prior to age 20. Analysis of those with exposures more than once per month in more than one decade showed that those with highest exposure (exposure in any 2 or 3 of the decades 10-19, 20-29, 30-39) had significantly increased risk of melanoma (RR=2.37; 95%CI=1.37-4.08) compared with those with no exposure in all 3 decades (Table 8). Analyses included adjustment for hair and skin colour and solar exposure.

The population-based case-control study of Lazovich et al. (2010) was initiated to study the effects of indoor tanning on risk of melanoma by collecting high quality data on use of tanning devices. Many of the earlier studies on which the 2007 IARC meta-analysis was conducted were limited by incomplete information on type of indoor tanning devices used, time since use began, age at commencement of use and other variables. The Lazovich et al. (2010) study compared indoor tanning among 1167 cases of CMM diagnosed in Minnesota at ages 25-59 between 2004 and 2007, to 1101 Minnesota controls frequency matched by age group and gender to the cases. The relatively young age cut off for melanoma cases was instituted because use of sunbeds for indoor tanning declines substantially with age. The Minnesota investigation used illustrations of typical sunlamps and sunbeds to assist respondents in remembering the types of indoor tanning devices used and the time period during which they were used. The study also adjusted the analyses of sunbed use for a range of host factors (eye colour, natural hair colour, skin colour, freckles, moles) and sun exposure variables (routine sun exposure, outdoor activity sun exposure, outdoor job exposure, and number of lifetime painful sunburns).

Results indicate an increased risk of melanoma for ever versus never use of devices for indoor tanning (OR=1.74; 95%CI=1.42-2.14). Measures of relative risks for ever use of each of the different kinds of devices (sunlamps, high speed/high intensity sunbeds, high pressure sunbeds) showed similar (and statistically significant) point estimates of risk, suggesting that newer sunbeds emitting higher levels of UV-A and lower levels of UV-B confer similar increased risks of melanoma to those seen in older high UV-B devices. Age at first exposure to indoor tanning did not appear to be related to ultimate risk of melanoma; a similar elevated risk of melanoma was seen regardless of whether they commenced use at ages <18, 18-24, 25-34 or 35+. A significant dose-response gradient (p trend=0.0002) in melanoma risk over quartiles of exposure was seen with number of sunbed sessions (OR highest quartile, >100 sessions=2.72; 95%CI=2.04-3.63) (Table 7). Similar significant dose-response relationships were seen with frequency of hours of use (p trend<0.0001) (OR 50+ hours=3.18; 95%CI=2.28-4.43), and with duration of use in years (p trend=0.006) (OR 10+ years use=2.45;95%CI=1.83-3.28). Finally a gradient of risk (p trend <0.001) was seen between number of burns from indoor tanning and risk of melanoma (OR highest quartile ≥4 burns = 6.90; 95%CI=2.92-16.31).

The finding of increased risk with increasing measures of exposure coupled with a lack of increased risk for those beginning tanning at earliest ages, led the authors to suggest that early age of exposure, may simply be a marker for high levels of cumulative exposure, or an indicator of longer duration of time since first exposure, and not an indication of enhanced sensitivity in young people.

An Australian population-based case-control study (Cust et al., 2011) was carried out in Brisbane, Sydney, and Melbourne to evaluate the risk factors for early-onset CMM. The study recruited 604
melanoma cases diagnosed between ages 18 and 39, and 479 controls frequency matched to cases by age, gender, and city of residence. Analyses of risk due to sunbed use were adjusted for demographic variables, skin colour, sun sensitivity, and lifetime sun exposure. Ever use of sunbeds/sunlamps increased the risk of melanoma about 40% (OR=1.41; 95%CI=1.01-1.96) compared to never use. Use of sunbeds/sunlamps early in life; in this case, prior to age 25 (Table 5), resulted in an enhanced relative risk of 1.64 (95%CI=1.07-2.51) compared with those who never used sunbeds/sunlamps. However, those beginning sunbed use at age 25 or later did not appear to be at greater risk for melanoma compared to those who had never used indoor tanning equipment (OR=1.06; 95%CI=0.66-1.72).

The authors of this study evaluated lifetime number of sunbed sessions and risk of melanoma, and found a significant dose-response relationship (p trend=0.01) with a relative risk of 2.01 (95%CI=1.22-3.31) in the highest tertile of use (>10 times) after control for skin colour, sun sensitivity and cumulative sun exposure (Table 7). Further, among those diagnosed with melanoma at age 19-29 years, an even stronger gradient of risk was seen (p trend=0.005), with the highest tertile of exposure (>10 sessions) conferring a relative risk of 6.57 (95%CI=1.41-30.49). This highest tertile however, was based on only 20 cases. Notwithstanding the small numbers, this appears to indicate that indoor tanning may be an important factor in accounting for early-onset melanomas. In fact the authors estimated that 76% of melanomas in users age 18-29 were attributable to sunbed/sunlamp use. The study results also suggested that sunbed/sunlamp use may be more important in accounting for melanomas on the trunk than those on the head and neck as the exposure-response gradient in sunbed use for trunk melanomas was much stronger than that for the head and neck. Head and neck melanomas are known to be more related to continuous sun exposure, and those on the trunk are more associated with intermittent exposure (Westerdahl et al., 2000; Whiteman et al., 2003; Whiteman et al., 2006). This may add to the credibility of the association as indoor tanning is, by definition, intermittent exposure to UVR.

Another study published the same year (Elliott et al., 2011) was conducted in the UK and compared 959 CMM cases age 17 to 76 who were diagnosed between 2000-2005 in Northern England with 513 population controls and a group of 174 sibling controls. The authors noted that they conducted, as near as possible, the same analysis as Cust et al. (2011). However, the study showed markedly different results from the Australian study. No increased risk of melanoma (Table 3) was seen with ever use of sunbeds in a comparison of cases with population controls (RR=1.06; 95%CI=0.83-1.36), or cases with sibling controls (RR=1.10; 95%CI=0.63-1.94) after adjustment for age, sex and education as well as sun sensitivity and lifetime sun exposure. Further, no elevated risk of melanoma was seen with commencement of sunbed use prior to age 25, or among study participants with the highest frequency of sunbed use. One major difference between studies is that while Australian melanoma cases (and controls) were all under age 40, only 22% of the UK study subjects were under age 40. Although the analyses in the UK paper were adjusted for age, separate analysis was not conducted to examine use in the subset of cases and population controls of the same age range as the Australian study participants. It should be noted however, that an analysis comparing young UK cases to controls might have been impractical due to the small number of age-eligible population and sibling controls. Of interest, the data on sunlight exposure and CMM risk in the UK study (as presented by Newton-Bishop et al., 2011) also showed unusual findings in that intermittent sunlight exposure on weekends showed an inverse or protective effect against melanoma, as opposed to a positive association seen with most other melanoma studies (Gandini et al., 2005b). In addition holiday sun exposure, again a variable which shows a positive association with risk in other melanoma studies, was not related to risk. In fact an inverse relationship was seen with holiday sun exposure and risk of head and neck melanomas (RR for highest exposure level=0.39; 95%CI=0.23-0.68). Examination of basic characteristics of the case and control samples for this study however, reveals a number of critical differences between the case and control groups which may help account for the unusual findings. Controls were significantly more affluent than cases perhaps
providing them with more vacation time. In addition, the control sample had a significantly lower body mass index (BMI) distribution compared to cases, suggesting higher activity levels and perhaps more outdoor leisure exposure, which control of lifetime sun exposure may have only partially adjusted for.

A Swedish cohort of 29,520 women recruited in 1990-1992 and followed through 2007 explored the relationship between indoor tanning and risk of melanoma (Nielsen et al., 2011). The women were recruited at age 25-64, and by the end of 2007, a total of 155 invasive and 60 in situ melanomas had been diagnosed. Some 3% of the cohort members had ever used a sunlamp and 47% reported ever using sunbeds. Unadjusted risk of CMM (Table 4) in ever-users of sunbeds (OR=1.05; 95%CI= 0.79-1.40), or ever users of sunlamps (OR=1.78; 95%CI=0.87-3.38) as calculated from the supplementary tables online using the Fisher Exact Test, was not statistically significantly elevated compared with never-users. However, the authors report an increased risk of CMM among younger women (25-39 at enrolment) who used sunbeds more than 10 times before diagnosis (HR=2.5; 95%CI=1.0-6.2) after simultaneous adjustment for host factors, sunburns and sun exposure (Table 6). The authors interpreted this finding to indicate that use of sunbeds might increase risk disproportionally in early CMM. Finally, in those who used sunbeds more than 10 times independent of age at first use, there was an elevated (HR=1.5; 95%CI=0.8-2.8) but not statistically significant elevated risk (Table 8). The authors note that sunlamp use was relatively rare in the cohort resulting in limited power to detect increased risk of CMM due to use. The study is somewhat unusual in that analyses appear to have combined invasive and in situ lesions for the purpose of increasing study power.

One further case-control melanoma study (Fears et al., 2011) deserves mention. This study was conducted to contrast use of sunbeds in females versus males using data collected in 1991-1992 as part of a large multi-centre investigation. The results indicate that, at the time the data were collected, females used sunbeds more than males, particularly before age 20. The study results also indicated that, among female users, those who believed that they could get a deep tan were most likely to become long-term users. Overall, calculation of risk of CMM using the Fischer exact test from data available in the paper showed no elevated risk of CMM for ever versus never use of sunbeds or sunlamps; nor did the data indicate that use at an early age increased CMM risk.

Zhang et al. (2012) have recently completed a study of the effect of sunbed use on risk of the three major types of skin cancer within the Nurses’ Health Study II. This large prospective health cohort enrolled 116,678 nurses age 25-42 residing in the US in 1989 and followed them for over 20 years. In 2005, the study collected information on use of sunbeds in high school and college as well as use at ages 25-35. A total of 73,494 nurses provided information on these exposures and constituted the study group in which 349 melanomas, 5506 BCCs and 403 SCCs were diagnosed. Separate analyses were conducted for sunbed use in high school/college and for use at ages 25-35 to evaluate whether use at earlier ages conferred different risks than exposure at ages 25-35. Compared to nurses with no exposure at age 25-35 women using sunbeds 4 times per year during that period had no increased risk of developing melanoma (HR=1.16; 95%CI=0.92-1.47). Comparing use 4 times per year in early life while at high school/college with no use during that period of life conferred a slightly increased but non-significant risk (HR=1.17; 95%CI=0.83-1.63) - essentially the same as that seen in use at later ages. None of the data suggested that exposure to sunbeds at high school/university age conferred a greater risk of melanoma than exposure later in life (age 25-35). The highest risks for melanoma was seen in women using sunbeds more than 6 times per year (Table 8) in high school/college (HR=1.23; 95%CI=0.69-2.20) and at age 25-35 (HR=1.31; 95%CI=0.90-1.91). Evaluation of the data for a dose-response relationship between number of sunbed sessions and melanoma risk suggested an incremental increase in melanoma risk of 11% (HR=1.11; 95%CI=0.97-1.27) with each additional 4 sessions per year at in either age period.
A final investigation which should be mentioned is an ecologic correlation study (Hery et al., 2010). This analysis noted an increase in sunbed salons in Reykjavik, the capital of Iceland, from 3 in 1979 to 56 salons with 207 sunbeds in 1988; followed by a large increase in incidence of melanoma in younger women (<age 50) from 1992-2001. The increase in reported melanomas was seen in both genders, but was larger in young women. The authors noted that women use sunbeds in Iceland much more than men, and that the increase in incidence in women was driven to a large extent by melanomas of the trunk, exposure of which is likely to take place in solaria. The authors investigated the prevalence of foreign travel, a potential source of UVR exposure, and noted that such travel was more likely to be undertaken by those over age 50, while sunbed use was much more prevalent in those under 50. The authors’ examination of incidence trends showed a sharp decline in rates of melanoma in young women beginning in 2001 and continuing through 2007. They also noted a program instituted by public health officials in 2004 to reduce the usage of sunbeds had resulted in a reduction in the numbers of sunbeds available for use in Reykjavik from 144 in 2005 and to 97 in 2008. The authors suggested that the rapid increase in trunk melanomas in women between 1992 and 2001 might be due to the very rapid increase in young women using solaria, as a 2002 survey indicated that 70% of (presumably younger) women and 35% of men had used a solarium at some time, versus a rate of only 2% in women and 1% in men over age 50. While this study is of interest, and perhaps indicative of a role for sunbed use in the sudden increase and subsequent decrease in melanomas in young women, it cannot be considered an addition to the body of analytic data addressing the issue of a possible causal relationship between sunbed use and melanoma.

**Risk of Melanoma by Type of Tanning Device**

The introduction of sunbeds with lamps emitting mostly UV-A was primarily for the purpose of avoiding burns due to sunbed use (Lazovich et al., 2010). It is not yet clear whether UV-A has a significant role in development of melanoma (Sage et al., 2012) and because it does not directly damage DNA (Svobodova et al., 2012) it has been claimed by the solarium industry that use of UV-A lamps for tanning might not cause skin cancer (Gordon and Hirst, 2007). Several epidemiologic studies have attempted to determine whether the switch to primarily UV-A sunbeds resulted in lower relative risks for melanoma by comparison with older high pressure mercury vapour sunlamps. These studies (Chen et al., 1998; Autier et al., 1994b; Veierod et al., 2003) used date of reported exposure to try to determine which type of sunbed had been used by respondents. However, melanoma risk of those reporting use beginning in the 1980s was not significantly different from that of respondents reporting use earlier.

The only investigation that addressed the issue directly is the study of Lazovich et al. (2010), which used photographs of different tanning devices to collect detailed information on type of sunbed used. The analysis revealed that after control for sun exposure and host factors, CMM risk for all types of tanning devices were elevated (conventional sunbed OR=1.76; 95%CI=1.43-2.17, high speed/high intensity type OR=2.86; 95%CI=2.03-4.03, high pressure type OR=4.44; 95%CI=2.45-8.02, sunlamp OR=1.85; 95%CI=1.27-2.70). Although point estimates of risk for the types differed, confidence intervals showed a great deal of overlap. Analyses of use by time periods (before 1990; after 1990; both periods) showed significantly elevated odds ratios for use in each period, similar to the results seen in other studies. These analyses were interpreted to indicate that all sunbed use, regardless of emission spectrum, increases the risk of CMM.

**Summary – Risk of Melanoma and Ever Use of Indoor Tanning Devices**

In summary, the initial indications that indoor tanning increased risk of melanoma came from three independent meta-analyses of early studies. The first analysis (Gallagher et al., 2005) showed an increased risk (Summary RR=1.25; 95%CI=1.05-1.49) of melanoma for ever vs. never use based on 10
studies. The IARC meta-analysis (2007) showed a similar finding for ever vs. never use (Summary RR=1.15; 95%CI=1.00-1.31) based on 19 informative studies. Although not in the peer-reviewed literature, the analysis of Gordon and Hirst (2007) using the same criteria as the 2007 IARC meta-analysis and based on 23 studies also found an increased risk of melanoma for ever vs. never use (RR=1.22; 95%CI=1.07-1.39).

Nine further analytic studies have been published since the 2007 IARC meta-analysis (complete tabular data available in Tables 3 and 4). Five of these studies show increased risk of melanoma with ever use of sunbeds (Han et al., 2006; Clough-Gorr et al., 2008; Lazovich et al., 2010; Veierod et al., 2010a; Cust et al., 2011) while four studies did not (Fears et al., 2011; Nielsen et al., 2011; Elliott et al., 2011; Zhang et al., 2012). The negative analysis of Elliott et al. (2011) was conducted to mimic that of Cust et al.; however, CMM cases were older than would be required to replicate the Australian analysis. The study of Fears et al. (2011) was also negative, but it relied on limited data on indoor tanning collected in 1991-1992, well before sunbed use became very common. Further, examination of the demographics of the dataset the analysis was conducted on, originally described in a paper by Tucker et al. (1997), revealed that only 25% of subjects were under the age of 40 at diagnosis. The Nurses' Health Study of Zhang et al. (2012), a well conducted cohort investigation, also showed no significantly elevated risk of melanoma, although several estimates of risk came close to statistical significance.

Finally a recently published systematic review of indoor tanning and melanoma has appeared (Boniol et al., 2012), which includes data from case-control and cohort studies completed after the 2007 IARC meta-analysis. Based on 27 cohort studies and population-based case-control studies, ever use of sunbeds conferred an increased risk of melanoma (RR=1.20; 95%CI=1.08-1.34) compared with never use of such devices.

Summary – Risk of Melanoma and Age at Inception of Use of Indoor Tanning Devices

Data from the initial two meta-analyses indicated that early age at first exposure might further increase risk for melanoma. Gallagher et al. (2005) showed an enhanced risk of melanoma with those ‘first exposed as a young adult’ (Summary RR=1.69; 95%CI=1.32-2.18), based on four case-control studies with age at inception of use between 25 and 35 and one cohort analysis with first use at age 10-19. The IARC meta-analysis reached the same conclusion, showing that those who first used indoor tanning equipment before age 35 were at enhanced risk (Summary RR=1.75; 95%CI=1.35-2.26). The Gordon and Hirst, (2007) meta-analysis found a higher relative risk in those who began use of indoor tanning equipment before age 35 (RR=1.98, 95%CI=1.60-2.45).

Since 2006, three studies (Clough-Gorr et al., 2008; Veierod et al., 2010a; Cust et al., 2011) of the nine conducted, have produced data which appears to show further increased risk with exposure early in life, but the other studies have not, including that of Lazovich et al. (2010), perhaps the most detailed to date. The recent meta-analysis by Boniol et al. (2012) which includes older as well as recent studies has shown an enhanced risk in those whose first exposure occurred before age 35 (RR=1.59; 95%CI=1.36-1.85). However, it should be noted that early age at first use might also be a marker for high cumulative use, or for a longer elapsed duration of time since sunbed/sunlamp exposure began. As most cancers do not appear until some years after exposure to a carcinogen, it is biologically plausible that time since initiation of use is the variable of significance in accounting for the increased risk seen in many of the positive studies. It is of note that several studies which have shown strong associations between CMM and use of sunbeds have focused on relatively young melanoma patients. The study of Cust et al. (2011) recruited patients who were diagnosed between the ages of 18 and 39, and Lazovich et al. (2010) studied those diagnosed between 25 and 59. The increased risk with early use may point to a greater potential for
accrual of UVR exposure and in those at higher genetic risk of melanoma, which might prompt earlier appearance of melanoma. More research is urgently needed to determine the true significance of findings concerning early age at first use of indoor tanning equipment given the high prevalence of use by Ontario and Canadian youth.

Summary – Risk of Melanoma and Duration and Frequency of Use of Indoor Tanning Devices

Based on six studies, the meta-analysis of Gallagher et al. (2005) found subjects with the longest duration or highest frequency of use had an enhanced point estimate of CMM risk over those who had ‘ever used’ sunbeds and sunlamps (Summary RR=1.61; 95%CI=1.21-2.12). Ever users would presumably include a significant number of infrequent users. The IARC meta-analysis (2007) abstract noted that there was no consistent evidence overall of a dose-response gradient but the authors further noted that the metrics used for assessing duration were all different among the studies and did not permit meta-analytic synthesis.

Tables 7-8 show summary data, where available, from each study on risk of CMM in those with the highest frequency or longest duration of exposure. This is not necessarily the sub-group in a study with the highest risk - it is simply the group with longest duration or highest frequency of use. A number of studies show risk estimates in the highest use groups which are greater than risk estimates from the same study on ever versus never use (Swerdlow et al., 1988; Walter et al., 1999; Autier et al., 1994b; Westerdahl et al., 1994; Westerdahl et al., 2000; Clough-Gorr et al., 2008; Lazovich et al., 2010; Veierod et al., 2010a; Cust et al., 2011). The risk estimates of Zhang et al. (2012) were also higher even though the 95% confidence intervals around these estimates overlapped 1.0.

The studies of Lazovich et al. (2010) and Cust et al. (2011) show true dose-response gradients with use of sunbeds, and Clough-Gorr et al. (2008) shows a modest gradient with use of sunlamps but not sunbeds. The studies of Lazovich et al. (2010) and Cust et al. (2011) were designed to examine melanoma and sunbed use specifically in younger melanoma patients. These studies collected much more detailed information than earlier investigations and were able to more thoroughly look for a dose-response relationship while maintaining control for host susceptibility factors and sun exposure. These studies provide the strongest evidence for a causal relationship between indoor tanning and melanoma.

As noted above, a new meta-analysis (Boniol et al., 2012) has become available which includes data from the most recent studies and the authors found a summary 20% increased risk (RR=1.20; 95%CI=1.08-1.34) over 27 studies for those who ever used sunbeds compared to those never using such devices. Restricting the analysis only to population-based case-control studies and cohorts produced a similar summary relative risk (RR=1.25; 95%CI=1.09-1.43). Perhaps more importantly, the study noted a dose-response relationship between use and melanoma, with an increase of 1.8% in risk of CMM (95%CI=0%-3.8%) for each additional session of sunbed use.

Overall Summary – Risk of Melanoma and Indoor Tanning

There is a strong and consistent body of evidence indicating that use of indoor tanning equipment increases the risk of melanoma. Recent studies have been better conducted than earlier ones, with better control for host characteristics and sun exposure. The study of Beane et al. (2005) indicates that reliability of recall of use of indoor tanning equipment is good, indicating that reported exposure data is of good quality. As sunbeds and sunlamps have come much more into the public eye, several studies have been conducted specifically to study this relationship (Lazovich et al., 2010; Cust et al., 2011). Both of these studies have relatively high risk estimates with use, and both have shown dose-response relationships between CMM risk and indoor tanning, at least in early onset melanoma patients. In addition, as noted
above, the meta-analysis of Boniol et al. (2012) has shown an exposure-response gradient in summary analysis of the melanoma data to date. The high relative risks and dose-response gradients seen in studies of younger CMM patients, along with the significant gradient of risk with exposure seen in the Boniol et al. meta-analysis are important hallmarks of a causal relationship (Hill, 1965).

In 2009, the International Agency for Research on Cancer convened a new expert panel of scientists to re-examine the question of carcinogenicity of artificial UV radiation, and determined that exposure to artificial ultraviolet radiation from sunbeds and sunlamp is carcinogenic (El Ghissassi et al., 2009; IARC, 2012). The evidence at this point in time strongly indicates that indoor tanning causes CMM, and this weight of evidence is sufficient for public health action.

**Basal Cell Carcinoma**

**Studies prior to 2006:**

Relatively little evidence was available concerning BCC at the time of the IARC (2007) meta-analysis. This was partly due to the fact that several studies which had collected data on both BCC and SCC reported on the two tumors grouped together as non-melanocytic skin cancer (O’Loughlin et al., 1985; Herity et al., 1989; Hogan et al., 1991). Based on four informative studies, the IARC working group (2007) found no association between use of indoor tanning equipment and risk of BCC (RR=1.03; 95%CI=0.56-1.90). The meta-analysis by Gordon and Hirst (2007), based on five studies, also showed no significant association between use of indoor tanning devices and risk of BCC (RR=1.18; 95%CI=0.92-1.52). Since the IARC report of 2007 a further four studies have been published.

Tables 9-10 present summary findings of studies that examined the association between use of indoor tanning devices and risk of BCC. Following Tables 9-10, an in-depth review of studies published since 2006 is provided.
### Table 9: Indoor Tanning and Basal Cell Carcinoma: Ever vs. Never Exposed (Case Control Studies)\(^1\)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Place and Period</th>
<th>Total Cases</th>
<th>Total Controls</th>
<th>% Cases Exposed</th>
<th>% Controls Exposed</th>
<th>Metric</th>
<th>Adjusted for Host Factors?</th>
<th>Adjusted for Sun Exposure?</th>
<th>OR/RR/HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bajdik et al.</td>
<td>Canada 1983-1984</td>
<td>226</td>
<td>406</td>
<td>10%</td>
<td>8%</td>
<td>Ever used sunlamps</td>
<td>Yes</td>
<td>Yes</td>
<td>1.2 (0.7-2.2)</td>
</tr>
<tr>
<td>Corona et al.</td>
<td>Italy 1995-1997</td>
<td>166</td>
<td>158</td>
<td>11%</td>
<td>20%</td>
<td>Ever used sunbed or sunlamp</td>
<td>Yes</td>
<td>Yes</td>
<td>0.6 (0.3-1.2)</td>
</tr>
<tr>
<td>Karagas et al.</td>
<td>USA 1993-1995</td>
<td>603</td>
<td>540</td>
<td>21%</td>
<td>14%</td>
<td>Ever used tanning device</td>
<td>Yes</td>
<td>Yes</td>
<td>1.5 (1.1-2.1)</td>
</tr>
<tr>
<td>Walther et al.</td>
<td>Germany 1997-1999</td>
<td>213</td>
<td>411</td>
<td>0.4%</td>
<td>0.6%</td>
<td>Used UV beds &gt;5 times/year</td>
<td>No</td>
<td>No</td>
<td>0.7 (0.3-1.5)</td>
</tr>
<tr>
<td>Han et al.</td>
<td>USA Nested case-control study from Nurses cohort study; age 30-55 at inception in 1976</td>
<td>283</td>
<td>804</td>
<td>17%</td>
<td>12%</td>
<td>Ever used sunlamp or suntan salon</td>
<td>Yes</td>
<td>Yes</td>
<td>1.32 (0.87-2.03)</td>
</tr>
<tr>
<td>Ferrucci et al.</td>
<td>USA 2007-2010</td>
<td>376</td>
<td>390</td>
<td>66%</td>
<td>64%</td>
<td>Ever indoor tanned</td>
<td>Yes</td>
<td>Yes</td>
<td>1.69 (1.15-2.48)</td>
</tr>
</tbody>
</table>

\(^1\) Studies of O’Loughlin et al. (1985); Herity et al. (1989), Hogan et al. (1991) are omitted as they did not give separate estimates of risk for SCC and BCC.
### Table 10: Indoor Tanning and Basal Cell Carcinoma: Ever vs. Never Exposed (Cohort Studies)

<table>
<thead>
<tr>
<th>Study</th>
<th>Place and Period</th>
<th>No. of Events</th>
<th>Cohort Size</th>
<th>% of Cohort Exposed</th>
<th>Metric</th>
<th>Adjusted for Host Factors?</th>
<th>Adjusted for Sun Exposure?</th>
<th>OR/HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhang et al. (2012)¹</td>
<td>USA Female Nurses Cohort II; age 25-42 at inception in 1989; follow-up through 2009</td>
<td>5506 incident BCCs</td>
<td>Total cohort 116,678; 73,494 in sunbed study</td>
<td>9.3% of women exposed at high school/college age; 19.8% of women exposed at age 25-35</td>
<td>High school/college; &gt;6 sunbed sessions/year vs. none; Age 25-35; &gt;6 sunbed sessions/year vs. none</td>
<td>Yes</td>
<td>Yes</td>
<td>1.73 (1.52-1.98)</td>
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</table>

¹ Study of Zhang et al. (2012) does not provide an ‘ever vs. never’ exposed risk estimate.
Studies from 2006 to January 2012:

Han et al. (2006) evaluated risk of BCC among 283 cases and 804 controls in a case-control study nested within the U.S. Nurses' cohort study. Women who reported ever having used sunlamps or tanning salons did not have a significantly elevated risk of BCC compared with those who never used sunlamps or tanning salons (OR=1.32; 95%CI=0.87-2.03).

A very small study conducted by Bakos et al. (2011) in Germany demonstrated an increased risk of BCC with sunbed use among patients diagnosed with this tumour at an early age (25-40). However the study was based on only 25 cases age 19-40 at diagnosis who were selected out of a total of 2058 patients seen for BCC at a German institution. Their use of indoor tanning equipment was compared with that of controls with other skin problems selected from the same clinic. Analysis of the data indicated an elevated risk of BCC with ever use of indoor tanning equipment (RR=6.73; 95%CI=1.94-23.36). Adjustment for a number of factors including sunscreen use, parents' sunscreen use and smoking increased the estimate of risk (OR=25.0; 95%CI=2.26-277.36). It appears from the description of study methods that data were not collected on host factors, and although a measure of sun exposure was collected, this was not significantly related to BCC risk and was not included in the multivariate model. The small number of patients and relative lack of information on the characteristics of the controls and how they were chosen, combined with the paucity of detail on study methods, make the findings of this study of limited value. This study is not included in Table 9.

Two larger studies have been published in the last two years. The first (Ferrucci et al., 2012) examined risk factors among a group of 376 early-onset (biopsy before age 40) BCC patients seen at the Yale dermatology centre from 2007-2010. About 68% of the cases were female. Control patients (n=390) under 40 years of age attending the same institution from 2006-2010 for 'minor skin conditions', the most common being seborrheic keratosis (16%), cyst (16%) or wart (11%), were frequency matched to cases by 5-year age group, gender, and site of biopsy (head and neck, trunk, extremities). After control for confounding factors including host characteristics and sun exposure, those ever using indoor tanning facilities had an elevated risk of BCC (OR=1.69; 95%CI=1.15-2.48) (Table 9) compared to those never having used indoor tanning facilities. Those who began indoor tanning at the youngest age (≤ 16 years) had a slightly enhanced risk of BCC (OR=1.83; 95%CI=1.12-2.97) compared to those beginning at age 17-18 years (OR=1.67; 95%CI=1.01-2.76) or those beginning after 18 years (OR=1.64; 95%CI=1.04-2.58), although the differences were slight. A significant gradient of risk (p trend=0.028) was seen with number of indoor tanning sessions (OR highest quartile ≥ 136 sessions=1.71; 95%CI=1.04-2.81). A similar gradient (p trend=0.003) was seen with years of regular tanning bed use (OR highest quartile 6-26 years=2.16; 95%CI=1.34-3.48).

Risks appeared also to be higher on the trunk and extremities, sites which might be less likely to be exposed to incident sunlight, than the head and neck, which only showed non-significant increases in risk. This would be consistent with the increased risk being due to indoor tanning. Finally, the study noted a strong exposure-response gradient (p trend <0.001) when the anatomic site of origin of the BCC had been previously burned during indoor tanning sessions (OR highest quartile ≥4 prior burns to site=6.90; 95%CI=2.92-16.31). This study has a number of strengths including a large and age-relevant sample size, control for known risk factors for BCC including skin color, sun sensitivity, sunbathing, and occupational sun exposure, although it is not clear if recreation and vacation exposure data were included.

Perhaps the most important study on risk of BCC and indoor tanning, in terms of numbers of cases and study methodology is that of Zhang et al. (2012). As noted in the section on CMM above, the study evaluated indoor tanning in 73,494 non-Hispanic white women recruited into the Nurses’ Health Study II.
cohort in 1989 at age 25-42, with 5506 reporting a diagnosis of BCC through follow-up in 2009. BCCs were self reported by the nurses, but previous studies had shown high validity of self reports of this tumour by the nurses (Colditz et al., 1986; Hunter et al., 1992). For women who had six or more sunbed sessions in high school or college, a significant increased risk was seen for BCC (HR=1.73; 95% CI=1.52-1.98). In women with six or more sunbed sessions per year later in life (age 25-35), an increased risk was also seen (HR=1.28; 95% CI=1.16-1.41). Both hazard ratios were adjusted for host factors and solar UV exposure. The data on tanning bed use was collected from cohort members in 2005, introducing the possibility that recall bias may have been involved for women whose cancer had been detected prior to 2005. In order to investigate this potential source of bias, a sub-analysis was carried out restricted to BCCs diagnosed after collection of the tanning bed data. The results for women who used sunbeds four times per year either during high school/college or age 25-35 (OR=1.16; 95% CI=1.11-1.22) in the sub-set analysis was also significantly elevated, indicating that the effect of potential bias on results due to collection of sunbed use after diagnosis was minimal. Perhaps more importantly, after adjustment for age, host factors and solar UV exposure, the study found a significant dose-response relationship, with a 15% incremental increase in risk of BCC for four sunbed sessions per year (HR=1.15; 95% CI=1.11-1.19), regardless of whether the sunbed sessions were accrued during high school/college or at age 25-35.

Strengths of this study include large numbers of subjects with BCC, good information on host factors and sun exposure, long cohort follow-up, and assessment of possible recall bias which might have affected reported sunbed use.

**Overall Summary – Risk of Basal Cell Carcinoma and Indoor Tanning**

The original two meta-analyses conducted by the IARC working group (2007) and Gordon and Hirst (2007) showed summary risk estimates which did not indicate a significantly elevated risk of BCC from indoor tanning, although the Gordon and Hirst (2007) estimate was close to statistical significance (Summary RR=1.18; 95% CI=0.92-1.52). Boniol et al. (2012), in a new meta-analysis, re-examined the relationship between indoor tanning and BCC and based on data from six studies found a significantly elevated risk of this cancer in sunbed users (RR=1.09; 95% CI=1.01-1.18).

The studies of Ferrucci et al. (2012) and Zhang et al. (2012) involve large numbers of cases with significant exposure to indoor tanning devices. In addition, both collected data enabling control for potential confounders such as host susceptibility factors and concomitant sun exposure. Both studies found strong exposure-response relationships between use of indoor tanning equipment and risk of BCC, after adjustment for host factors and measures of sun exposure. The Ferrucci et al. (2012) study also demonstrates a further exposure-response gradient with burns due to indoor tanning at the site of the subsequent BCC, analogous to that seen for CMM (Lazovich et al., 2010; Cust et al., 2011).

Results from the Zhang et al. (2012) study suggest that BCC risk might be further elevated by commencement of tanning at an early age (high school/college), although as noted in the discussion in CMM, early age may be simply be a marker for adequate duration of time between first exposure and diagnosis. Such an interpretation would, again, be biologically consonant with the delay between exposure and appearance of cancer observed with many tumours.

There is now strong evidence for a causal relationship between indoor tanning and BCC, and the weight of evidence is sufficient for public health action.
Squamous Cell Carcinoma

Studies prior to 2006:

The IARC meta-analysis for SCC (2007), based on three studies, suggested a statistically elevated risk of SCC for those who ever used indoor tanning equipment compared with those who never used indoor tanning equipment (Summary RR=2.25; 95%CI=1.08-4.70). The IARC working group noted that while the evidence was limited, the positive association among studies and the dose-response relationship seen in the Karagas et al. (2002) study were consistent with the known dependence of SCC on cumulative dose of UVR to the skin. The non-peer reviewed analysis by Gordon and Hirst (2007) based on four informative studies also found a significantly elevated risk of SCC with exposure to indoor tanning devices (RR=1.78; 95%CI=1.19-2.67).

Since the IARC (2007) meta-analysis was completed, only two new studies have appeared assessing the relationship between SCC and indoor tanning. Tables 11-12 present summary findings for use of indoor tanning devices and risk of SCC. Following Tables 11-12, an in-depth review of studies published since 2006 is provided.
### Table 11: Indoor Tanning and Squamous Cell Carcinoma: Ever vs. Never Exposed (Case-Control Studies)\(^1\)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Place and Period</th>
<th>Total Cases</th>
<th>Total Controls</th>
<th>% Cases Exposed</th>
<th>% Controls Exposed</th>
<th>Metric</th>
<th>Adjusted for Host Factors?</th>
<th>Adjusted for Sun Exposure?</th>
<th>OR/RR/HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aubry and MacGibbon (1985)</td>
<td>Canada 1977-1978</td>
<td>92</td>
<td>174</td>
<td>4.3% (4 cases)</td>
<td>0.6% (1 control)</td>
<td>Ever used long-tube sunlamp</td>
<td>Yes</td>
<td>Yes</td>
<td>13.4 (1.38-130.5)</td>
</tr>
<tr>
<td>Bajdik et al. (1996)</td>
<td>Canada 1983-1984</td>
<td>180</td>
<td>404</td>
<td>10%</td>
<td>8%</td>
<td>Ever used sunlamps</td>
<td>Yes</td>
<td>Yes</td>
<td>1.4 (0.7-2.7)</td>
</tr>
<tr>
<td>Karagas et al. (2002)</td>
<td>USA 1993-1995</td>
<td>293</td>
<td>540</td>
<td>21%</td>
<td>14%</td>
<td>Ever used tanning devices</td>
<td>Yes</td>
<td>Yes</td>
<td>2.5 (1.7-3.8)</td>
</tr>
<tr>
<td>Han et al. (2006)</td>
<td>USA Nested case-control study from Nurses cohort study; age 30-55 at inception in 1976</td>
<td>275</td>
<td>804</td>
<td>16%</td>
<td>12%</td>
<td>Ever used sunlamp or tanning salon</td>
<td>Yes</td>
<td>Yes</td>
<td>1.44 (0.93-2.24)</td>
</tr>
</tbody>
</table>

\(^1\) Studies of O'Loughlin et al. (1985); Herity et al. (1989), Hogan et al. (1991) omitted as they did not give separate estimate of risk for SCC or BCC.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Place and Period</th>
<th>No. of Events</th>
<th>Cohort Size</th>
<th>% of Cohort Exposed</th>
<th>Metric</th>
<th>Adjusted for Host Factors?</th>
<th>Adjusted for Sun Exposure?</th>
<th>RR/HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhang et al. (2012)</td>
<td>USA Female Nurses cohort II; age 25-42 at inception in 1989; follow-up through 2009</td>
<td>403 incident SCCs</td>
<td>Total cohort 116,678; 73,494 participants in sunbed study</td>
<td>9.3% of women exposed at high school/college age 19.8% of women exposed at age 25-35</td>
<td>High school/College; &gt;6 sunbed session/year vs. none Age 25-35; &gt;6 sunbed session/year vs. none</td>
<td>Yes</td>
<td>Yes</td>
<td>1.12 (0.60-2.11)</td>
</tr>
</tbody>
</table>

1 Study of Zhang et al. (2012) does not provide an ‘ever vs. never’ exposed risk estimate
Studies from 2006 to January 2012:

The investigation by Han et al. (2006) is a case-control study nested in the U.S. Nurses' cohort. The Nurses' Health Study was initiated in 1976, when women age 30-55 were recruited into a prospective health cohort by investigators at Harvard University. A total of 275 patients with SCC were compared with 804 nurses without this cancer for use of sunlamps and tanning salons. Cases showed an elevated, but not statistically significant increased risk of SCC (OR=1.44; 95%CI=0.93-2.24) with ever use of indoor tanning devices after control for a constitutional susceptibility score incorporating skin colour, hair colour, childhood tendency to burn, number of palpable moles on arms, and a measure of solar exposure (sun exposure while wearing a bathing suit).

Zhang et al. (2012) recently completed a study of indoor tanning and SCC in the Nurses' Health Study II cohort. A total of 73,494 non-Hispanic white nurses, initially enrolled in the cohort in 1989, completed a questionnaire in 2005 on their indoor tanning habits, and were followed up through 2009 for SCC. At analysis, women who used indoor tanning devices six times per year or more during high school or college did not show a statistically significant increased risk of SCC (OR=1.12; 95%CI=0.60-2.11) compared to women not using tanning beds during this period of life. Women using sunbeds six times per year or more at age 25-35 experienced a significantly increased risk of SCC, which persisted after adjustment for host factors and sun exposure (OR=1.61; 95%CI=1.13-2.31). The fact that a dose-response relationship is seen in women with sunbed exposure at age 25-35 and not with those exposed in high school/college may be commensurate with evidence from studies of solar exposure that SCC is related more to cumulative exposure (Rosso et al., 1996; Gallagher et al., 1995b) rather than early age exposure, as appears to be the case with melanoma. Most importantly, the study demonstrated a significant dose-response relationship between sunbed use and SCC. After control for hair colour, number of moles on legs, childhood tendency to sunburn, and outdoor sun exposure, as well as several other measures, an incremental increase of four sunbed sessions per year conferred a 15% increased risk of SCC (HR=1.15; 95%CI=1.01-1.31) regardless of whether sunbed use took place during high school/college or at age 25-35.

The recent meta-analysis of Boniol et al. (2012) re-examined the available data on indoor tanning and risk of SCC and found a summary elevated risk (RR=2.23; 95%CI=1.39-3.57) of this tumour in sunbed users based on five informative studies.

Overall Summary – Risk of Squamous Cell Carcinoma and Indoor Tanning

Only two large new studies appeared since the IARC meta-analysis (2007) and the analysis of Gordon and Hirst (2007). That of Han et al. (2006) showed a point estimate of risk among users to be higher than that among non-users, but the increase was not statistically significant. The study of Zhang et al. (2012) demonstrated a significantly elevated risk of SCC in women using indoor tanning devices six or more times per year at age 25-35, by comparison with non-users. As noted above, the study of Zhang et al. (2012) also showed a significant exposure-response gradient between use of sunbeds and risk of SCC after control for host factors and solar exposure, regardless of whether use took place during high school/college or at age 25-35.

In summary, the Zhang et al. (2012) dose-response relationships, coupled with the Boniol et al. (2012) meta-analysis results, support the conclusion that indoor tanning is causally related to SCC of the skin. The weight of evidence is sufficient for public health action.
Indoor Tanning and Risk of Other Cancers

Ecologic correlation studies indicating lower risks of non-skin cancers in the presence of high vitamin D levels due to sun exposure (Grant et al., 2010; Grant, 2011) have led some investigators to examine whether indoor tanning reduces risk of other cancers. Although investigations on this topic have been relatively rare to date, a review of the literature up to the end of 2011 found several case-control or cohort studies of tanning bed use and non-Hodgkin Lymphoma, breast cancer and other tumors. These studies are summarized below.

Non Hodgkin Lymphoma (NHL)

Smedby et al. (2005) conducted a study of NHL among 3740 cases and 3187 population-based controls in Denmark and Sweden and found a reduced risk of NHL among those using solaria or sunlamps 50 or more times (OR=0.8; 95%CI=0.7-1.0) compared to those who had never used such devices. The inverse association was attributable largely to diffuse large B-Cell lymphomas (OR=0.7; 95%CI=0.5-1.0) with a significant dose-response gradient (p=0.007) after control for sex and sun sensitivity.

A U.S. study (Hartge et al., 2006) also assessed the risk of NHL with use of sunlamps or tanning booths and showed no association, with an odds ratio for use 10 or more times of 0.90 (95%CI=0.61-1.30) compared to those with no use, and no indication of a dose-response gradient. Grandin et al. (2008) evaluated ‘esthetic use’ of sunlamps and sunbeds among 395 NHL cases and 698 hospital controls in France and found no association between risk of NHL and ever use of such devices (OR=0.8; 95%CI=0.4-1.5). Among regular users a lower point estimate of risk was found but this was based on only 2 cases and 11 controls (OR=0.3; 95%CI=0.1-1.5) and was not significant. Zhang et al. (2007) evaluated use of tanning devices in Connecticut among 601 women with NHL and 717 controls. No association was seen with ever use and NHL risk (OR=1.1; 95%CI=0.8-1.5). No dose-response gradient was seen with years of use or lifetime sessions.

The European study of Boffetta et al. (2008) found a significantly reduced risk of NHL among those who had used tanning devices 25 or more times (OR=0.69; 95%CI=0.51-0.93). The analysis was adjusted for sex, education level, and sun sensitivity, although it is not clear from the text of the paper whether sun exposure was controlled for. The inverse association was principally seen for diffuse B-cell lymphomas (OR=0.63; 95%CI=0.38-1.03) with a significant dose-response trend (p<0.01) over the three exposure tertiles. Other subtypes of NHL showed non-significant results. A potential concern with this study is that the inverse association between sunlamp use and NHL risk may be due to sun exposure as the analysis did not adjust for concomitant sun exposure.

Veierod et al. (2010b) investigated risk of NHL in a Swedish and Norwegian cohort of 104,953 women recruited in 1991 and 1992 and followed to 2006. Ever use of artificial tanning devices at ages 10 through 39 was not associated with NHL (OR=0.93; 95%CI=0.52-1.68), although use rarely or ≥ once per month early in life (age 20-29) appeared to be protective for users (OR=0.47; 95%CI=0.24-0.91) compared to those not using the devices at that age.

In summary, several studies show an inverse association between sunbed use and NHL, but several other equally well conducted studies do not. Among the studies that do show an inverse association, questions remain about the possibility that the inverse relationship may be due to sun exposure. More research is needed on this question.

Breast Cancer

Several studies have examined the relationship between sunbed and sunlamp use and subsequent breast cancer risk. A Canadian study carried out in Ontario to examine the relationship between vitamin D and
breast cancer also asked about use of sunlamps (Knight et al., 2007). No relationship with use of sunlamps was seen for ever vs. never use at age 20-29 (OR=0.88; 95%CI=0.66-1.18). A dose-response gradient showing a protective effect on breast cancer risk with outdoor activities at ages 10-19 and 20-29 was seen, so a similar analysis was carried out for indoor tanning during the same age period. Use of sunlamps at age 10-19 did not significantly reduce the risk of breast cancer (OR=0.81; 95%CI=0.57-1.14). Detailed information was not collected on frequency and duration of use; thus, a dose-response gradient among users could not be explored.

A study of solarium use among 41,889 Swedish women recruited at ages 30-50 into a prospective cohort in 1991 and 1992 and followed through 2004 was carried out by Kuper et al. (2009). A total of 840 cases of breast cancer were included in the study. No reduced risk was seen with use of solaria once or more per month at age 10-19 (OR=0.9; 95%CI=0.3-2.9), age 20-29 (OR=1.0; 95%CI=0.7-1.4), age 30-39 (OR=0.8; 95%CI=0.7-1.0), or age 40-49 (OR=0.9; 95%CI=0.8-1.2) compared to women not using solaria at these ages. In addition, no association with sunbathing vacations or annual number of sunburns at the ages noted above were seen.

Yang et al. (2011) re-analyzed the breast cancer data from the same cohort with follow-up extending through 2006, resulting in 1053 cases of breast cancer. A significantly reduced risk of breast cancer was seen in women using solaria at ages 10-39 rarely but not more than one or more times per month in any decade, 10-39 years' (HR=0.81; 95%CI=0.68-0.96). A further reduction was noted in women using solaria one or more times per month in two or three decades between the ages of 10-39, suggestive of a dose-response relationship, although it does not appear that the analyses controlled for sun exposure.

A prospective Norwegian health cohort consisting of women recruited in 1991-1997 at ages 40-70 and followed through 2006 (Edvardsen et al., 2011) was analysed to determine whether there was an inverse association between UVR exposure and breast cancer. A total of 41,811 women were included in the study, and of these 948 had received a diagnosis of breast cancer. Analysis of use of solaria demonstrated no gradient of decrease in risk over the 4 quartiles of use (Highest quartile RR=1.10; 95%CI=0.89-1.36).

In summary, the evidence for a reduction in risk of breast cancer attributable to use of indoor tanning devices is limited. Only one study (Yang et al., 2011) found that use of indoor tanning devices was associated with a reduced risk of breast cancer and one case-control study showed a non-significant reduction in risk of breast cancer with sunlamp use at ages 10-19 (Knight et al., 2007).

Other Cancers
To date, only one analytic study has investigated the association between colon cancer and use of sunbeds. Yang et al. (2011) investigated colon cancer and solaria use in a Swedish cohort of women initially recruited in 1992 and followed through 2006. A total of 133 cases of colorectal cancer were available for study. The results presented by the authors showed no evidence of risk reduction in colon cancer in those using solaria one or more times/month in two or three of the decades age 10-39 (HR=1.77; 95%CI=0.68-4.59) compared with those never using solaria at ages 10-39.

The study of Yang et al. (2011) also examined the association between solarium use and a number of other cancers in women. For all cancers combined, no association was seen with solarium use (Highest quartile HR=1.11; 95%CI=0.87-1.40). Neither ovarian cancer (Highest quartile HR=0.54; 95%CI=0.13-2.28), lung cancer (Highest quartile HR=0.49; 95%CI=0.07-3.63), nor brain cancer (Highest quartile HR=0.21; 95%CI=0.03-1.56) showed statistically significant associations. However, all point estimates of risk were lower than 1.0 and more research is needed on these cancers. It should be noted that the confidence intervals around all the point estimates for all these cancers are wide due to the fact that few
cases were available for analysis. As more women develop cancers, re-analysis of the Swedish cohort would be useful.

**Summary – Indoor Tanning and Risk of Other Cancers**
In summary, the evidence for a reduction in risk of NHL with indoor tanning is mixed with several studies showing an inverse association and others not. In the studies showing a protective effect however, it does not appear that sunbed and sunlamp analyses were adjusted for sun exposure. More research is clearly needed particularly on diffuse large B-cell and follicular lymphomas with better control for concomitant sun exposure. There is at present little analytic evidence of a protective effect against any other cancer, although, as noted, the literature is relatively sparse at the present time.
Vitamin D

There is a voluminous literature on vitamin D, and the findings on all aspects of vitamin D and health clearly cannot be covered in this brief review. For a more complete assessment of this field, along with recommendations concerning vitamin D intake, readers are encouraged to access the US Institute of Medicine’s recent comprehensive report which critically reviewed more than 1000 studies on vitamin D status and health (IOM, 2011). For the purposes of this report, a PubMed and EBSCO search was conducted specifically on the analytic studies of serum vitamin D levels and subsequent cancer, the effect of indoor tanning on serum vitamin D levels and the effect of oral supplementation on serum vitamin D levels. The search was conducted by cross linking the following key words: vitamin D, serum vitamin D, vitamin D insufficiency, cancer, breast cancer, non Hodgkin lymphoma, colon cancer, prostate cancer, breast cancer, ovarian cancer, oral supplementation, sunbed, sunlamp, indoor tanning, and artificial ultraviolet radiation for the years 1990 through January 2012. This resulted in thousands of citations, and the authors of this report have selected a small number of studies which they consider representative of current findings concerning indoor tanning, vitamin D levels, oral supplementation, and cancer.

Vitamin D was first identified as a vitamin early in the 20th century and is now recognized as being important to health. It can be obtained through the consumption of foods of animal origin such as meat, eggs, and fish in Canada. It is added to milk, margarine and a number of other foods, and is also synthesized in the body by the action of UV-B. It is crucial, along with calcium, in maintaining bone health. In most Canadians, vitamin D levels can only be partially maintained through dietary sources, and sun exposure plays a major part in accounting for serum vitamin D levels (Greene-Finestone et al., 2011). However during winter in Canada when sunlight exposure is minimal, many Canadians are thought to be vitamin D insufficient or even vitamin D deficient (Schwalfenberg and Whiting, 2011). Greene-Finestone et al. (2011) found 18% of Canadians had serum levels of 27.5-50nmol/L, which was defined in that study as insufficient, and 2.3% had levels of <27.5nmol/L regarded as deficient. Whiting et al. (2011) using data from the Canadian Health Measures Survey, found 24.5% of white Canadians had levels less than 50nmol/L in winter. In non-supplement users this figure rose to 37.2% overall, and 60.7% in non-whites.

UV radiation plays a key role in synthesizing vitamin D in humans. Vitamin D production is initiated by the action of UV-B (280-315 nm) radiation on 7-dehydrocholesterol in the skin (Moan et al., 2009). The product, pre-vitamin D, is converted in the liver to 25-hydroxyvitamin D, and finally to its active form, 1,25dihydroxyvitamin D in the kidneys (Binkley et al., 2012).

Health Effects of Vitamin D

The recent vitamin D report from the Institute of Medicine (IOM, 2011) was commissioned by the US and Canadian governments to examine the scientific evidence on vitamin D levels and chronic diseases such as cancer, as well as non-chronic diseases and to assess the strength and quality of the evidence available as a basis for determining adequate vitamin D intake. This resulted from the recent appearance of studies suggesting that high serum levels might reduce mortality from cancer, cardiovascular disease, diabetes, multiple sclerosis, certain forms of dementia and a host of infectious diseases (Grant et al., 2010; Grant, 2011; Hollis, 2011). Such descriptive studies have correlated state or country-wide mortality rates for diseases with degree of sunlight in these areas, and indicate lower rates of certain diseases in high sunlight areas. These ecologic correlation studies are based on the assumption that individuals residing in high sun areas have higher serum levels of vitamin D than those in lower sun areas. However, it should be noted that vitamin D levels in individuals with and without a given disease in high and low sunlight areas are not actually available. In addition, such studies cannot control for other lifestyle or environmental
variables among individuals which might affect both risk of mortality from a disease and/or serum vitamin D levels. Thus while the studies serve to generate hypotheses about relationships between vitamin D levels and chronic diseases, these theories need to be tested in studies with much more detailed individual-level data.

While these initial ecologic studies are being followed up at a rapid pace by higher quality studies designed to determine whether the initial results seen in descriptive studies for cancer can be confirmed, the IOM report concluded that none of the evidence to date, with the exception of that on bone health is of high enough quality to provide evidence for making recommendations concerning vitamin D intake. The IOM report concluded that based on the high-quality scientific data currently available, recommended daily allowances (RDA) for vitamin D ranged from 800IU per day in children aged 1-3 to 800IU for older males and females. The RDA is the level determined to meet or exceed the requirements of 97.5% of the population.

To date relatively few prospective cohort studies in which vitamin D levels are determined some time prior to diagnosis of a disease have been conducted. However, in 2008, the International Agency for Research on Cancer (IARC) convened a working group to evaluate the evidence surrounding the hypothesis that low vitamin D levels might be associated with an increased risk of colon, breast and prostate cancer. The working group conducted meta-analyses of the observational studies available for each of the cancers and for colorectal adenomas, a precursor lesion for colorectal cancer (IARC, 2008).

The colorectal analysis, which included nine studies published between 1989 and 2008, showed a statistically significant reduction in risk per increase of 1ng/ml of vitamin D (RR=0.980; 95%CI=0.972-0.987). The meta-analysis of colorectal adenomas included seven studies and showed a similar reduction per 1 ng/ml increase in vitamin D (RR=0.993; 95%CI= 0.987-0.999). The meta-analysis of breast cancer included five studies and provided limited evidence for a possible reduction in risk with higher serum vitamin D. However, the upper 95% confidence interval surrounding the point estimate of reduction in risk per 1 ng/ml of vitamin D marginally included 1.0 (RR=0.984; 95%CI=0.964-1.004). The evaluation of prostate cancer included seven studies and showed no reduction of risk with increased vitamin D.

The working group noted that further case-control or cohort studies were unlikely to contribute significantly to resolving the controversy surrounding whether increased serum levels of vitamin D can reduce risk of cancer. The group noted that it is impossible to determine whether decreased vitamin D levels in case-control and cohort studies are due to low dietary intake, low sun exposure, or to underlying poor health. If due to poor health, the factors responsible for the poor health might be driving risk of subsequent chronic diseases such as cancer, rather than the vitamin D levels themselves. The working group recommended that large-scale randomized trials be carried out to evaluate the effect of vitamin D on all cause mortality as well as individual cancer incidence and mortality rates.

To date, few such trials have been reported. One randomized trial (Lappe et al., 2007) reported a reduction in ‘all cancers combined’, after four years of follow-up of 1179 women age 55+ in Nebraska. The women had been randomized to 1100 IU of vitamin D + calcium, calcium alone, or placebo. The reduced risk for all cancers combined was seen in the women randomized to vitamin D + calcium but not to calcium alone. Unfortunately the trial was too small to have the power to investigate individual cancer types. A further randomized trial was organized within the Women’s Health Initiative, which had enrolled 36,282 postmenopausal women to investigate diet and a number of other factors thought to be associated with breast and other cancers. Women were randomized to 1000mg elemental calcium and 400IU of vitamin D per day or placebo (Brunner et al., 2011). After seven years neither incidence of new cancers nor all cause mortality differed significantly between the intervention and placebo groups. The
trial has been criticized for providing women in the intervention arm with a vitamin D supplementation level that is too low.

In summary, it is clear that much more research, likely including well conducted clinical trials, will be necessary before the true value of vitamin D in reducing risk of incidence and mortality of cancer and other chronic diseases will become clear.

**Indoor Tanning, Oral Supplementation, and Vitamin D Levels**

Investigations have consistently indicated that use of sunbeds increases blood levels of vitamin D (Sahota et al., 2008; Carbone et al., 2008; Moan et al., 2009), with greater increases seen in those with low initial levels of vitamin D. After determination of individual susceptibility to sunburn, the trial of Moan et al. (2009) allocated 23 healthy volunteer subjects to one of two groups receiving either a total of 6.7 minimal erythemal doses (MED) or 13.5 MED over 15 sessions taken twice per week using a commercial sunbed. A minimal erythemal dose is that amount of exposure to UVR that stimulates minimal reddening of the skin. The resulting increase in vitamin D levels was found to average 25-30% for each of the exposed groups. Thieden et al. (2008), in a randomized trial, allocated 20, 15 and 21 women age 50 and over respectively to 8 sunbed sessions over 16 days with 0.5% UV-B, 1.4% UV-B, or to no intervention. At the end of the trial mean vitamin D levels in the group exposed to 0.5% UV-B had increased from 46.9nmol/L to 62.0nmol/L. Levels in those exposed to 1.4% UV-B had increased from 45.9nmol/L to 75.3nmol/L, and controls showed shown no change. Thus, there is good evidence that use of sunbeds will increase vitamin D levels in normal healthy individuals.

**Oral Supplementation and Vitamin D Levels**

Studies also indicate that oral supplementation raises blood levels of vitamin D. Gallagher et al. (2012) conducted a randomized trial among 163 women age 57-90 with vitamin D insufficiency (<50nmol/L), allocating women to oral supplementation of either 400, 800, 1600, 3200, 4000, 4800 IU of vitamin D or placebo once per day. Women were followed for one year. The study found that 800IU/day of vitamin D increased vitamin D levels to >50nmol/L in 97.5% of women.

Wicherts et al. (2011) found that oral supplementation was effective in increasing serum levels of vitamin D among non-Western immigrants from Turkey, Morocco, Dutch Antilles, Africa or Asia living in The Netherlands. The trial included three groups and compared levels of vitamin D in subjects randomized to 800IU/day, 100,000IU over three months in four 25,000IU capsules, or sunlight advice. Among those randomized to 800IU/day, serum vitamin D levels rose over the six month trial from a mean of 22.5nmol/L to 53nmol/L. For those receiving 100,000IU/three month period, levels rose to a mean of 50.5nmol/L. For those randomized to sunlight advice only, vitamin D levels increased to only to 29.1nmol/L. This is an important trial as it indicates that vitamin D supplementation is effective in increasing blood levels in those with darker skin, a group previously thought to be at greater risk than those with fair skin for vitamin D insufficiency or deficiency.

In a randomized trial of patients with Crohn’s disease (an inflammatory bowel disorder) who are at increased risk for inadequate vitamin D, supplements of 1200 IU/day for one year increased blood levels substantially compared with placebo, and reduced the risk of relapse in patients over the period of the trial to 13% vs. 29% among patients on placebo (Jorgensen et al., 2010). It appears that vitamin D oral supplementation increases blood levels of vitamin D, perhaps even in those with chronic conditions.
Supplementation vs. Artificial UV Radiation and Vitamin D Levels
Several studies have evaluated the effectiveness of UV radiation compared to oral supplementation in increasing blood levels of vitamin D. Toss et al. (1982), in an early study, investigated the effectiveness of UV radiation from a Westinghouse FS 40 fluorescent source once per week compared with oral supplementation of 450 IU daily in raising vitamin D levels in 42 elderly institutionalized subjects. After 12 weeks the authors concluded that the methods were comparable in the degree to which they raised vitamin D levels. Chel et al. (1998) conducted a further study on older patients and found that 12 weeks of vitamin D supplementation or exposure to artificial UVR were of equivalent effectiveness in raising serum levels of vitamin D. Genuis et al. (2009), in a cross sectional study carried out in Edmonton to estimate the prevalence of vitamin D insufficiency and deficiency, noted that tanning bed use and oral supplementation were both associated with adequate vitamin D levels, but oral supplementation was only effective at daily levels >400IU.

Summary – Vitamin D and Skin Cancer
It is clear that sunbed use raises blood levels of vitamin D, although there is good evidence that sunbed use also raises risk of melanoma, basal cell carcinoma, and squamous cell carcinoma of the skin. Studies which have directly compared oral supplementation to artificial UVR exposure indicate that they are of comparable effectiveness in raising vitamin D levels, at least at supplementation levels greater than 400IU per day. Due to the potential for increasing risk of skin cancer with use of sunbeds the Canadian Dermatology Association has recommended oral supplementation as a means of increasing levels of vitamin D (Canadian Dermatology Association, 2009). A similar recommendation has been made by the Ontario Division of the Canadian Cancer Society (Canadian Cancer Society, 2012b).
Overall Summary and Conclusions

Skin cancer is the most common cancer in Canada, with an estimated total of over 79,000 new neoplasms diagnosed in 2011 (Canadian Cancer Society’s Steering Committee on Cancer Statistics, 2011), including 5500 cutaneous malignant melanomas. Although the overall mortality rate for skin cancer is more favourable than many other tumours, there were 950 deaths from melanoma and 270 from non-melanocytic skin cancer in Canada in 2011. Skin cancer is also a major financial drain across Canada and in Ontario in 2011 is estimated to have consumed over $296 million for direct treatment and other indirect costs.

Although skin cancer is a major public health problem, it is also preventable. The major susceptibility factors, including light skin and hair colour, sun sensitive skin, and in the case of melanoma, freckling and high nevus counts are well known, and are easily recognized by the lay public. The major environmental risk factor, exposure to solar and artificial UV radiation, is also well recognized. Prevention programs should be initiated therefore, tailored to those at high risk, taking into account the population mix of a multi-ethnic area such as Toronto. The focus of such programs should be on curbing over-exposure to sunlight, and on avoidance of exposure to artificial ultraviolet radiation, the major source of which is indoor tanning.

Sunlight has long been known to cause skin cancer but substantial recent scientific evidence indicates that use of sunlamps, sunbeds, and tanning booths for the purposes of indoor tanning also increases the risk of melanoma, basal cell carcinoma, and squamous cell carcinoma of the skin. There is presently very little data from analytic studies that use of sunbeds and other indoor tanning devices can reduce risk of other kinds of cancers. The International Agency for Research on Cancer, after a wide ranging review, reaffirmed their 1992 position that solar radiation is carcinogenic, and also classified the use of UV-emitting tanning devices as carcinogenic to humans (El Ghissassi et al., 2009; IARC, 2012).

Use of indoor tanning devices in the province of Ontario among young people age 18-24 is very common, with more than 20% reporting use in the preceding 12 months in several regions of the province. Furthermore, there is evidence from a 2012 Ipsos Reid survey carried out for the Canadian Cancer Society that Ontario youth in high school are also using indoor tanning devices in alarming numbers, with up to 21% of grade 12 students reporting ever having used these devices. Prevalence figures for young females are much higher than in males. One of the reasons noted by survey respondents for engaging in indoor tanning is that these devices raise levels of vitamin D. While it is true that indoor tanning does raise vitamin D levels, the same benefit may be obtained through use of oral supplements without increasing risk of skin cancer.

Recent epidemiologic evidence indicating that indoor tanning contributes substantially to risk of melanoma at an early age, and that indoor tanning is very common in youth, particularly among young women have led a number of jurisdictions in Canada and around the world to take steps to regulate access to indoor tanning devices in commercial salons. These regulations customarily take the form of a prohibition of use prior to age 18. Toronto, and perhaps Ontario, may wish to consider such a regulation in addition to current ongoing measures aimed at preventing skin cancer.
References


Autier P, Dore JF, Lejeune F et al. (1994b). Cutaneous malignant melanoma and exposure to sunlamps or sunbeds: for the EORTC multicentre case-control study in Belgium, France and Germany. Int J Cancer 58:809-813.


### Appendix 1: Skin Cancer Statistical Tables Used for Figures, and Supplementary Figure

**Appendix 1 Table 1.1: Melanoma Age-Standardized Incidence and Mortality Rates and Counts, Toronto and the Rest of Ontario, by Sex, 1986–2008**

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Source: Cancer Care Ontario (Ontario Cancer Registry, 2011)
Prepared by: Cancer Care Ontario, Prevention and Cancer Control (Surveillance)

Notes: Rest of Ontario combined excludes cases with unknown residence
Melanoma (Incidence = ICD-O-3 C44; Mortality = ICD-10 C43)
Rates are per 100,000 and standardized to the age distribution of the 1991 Canadian population
### Appendix 1 Table 1.2: Incidence and Mortality Rates, Confidence Intervals, and Rate Ratios for Toronto Compared to the Rest of Ontario, for Specific Periods, by Sex, 1989-2008

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Source: Cancer Care Ontario (Ontario Cancer Registry, 2011)
Prepared by: Cancer Care Ontario, Prevention and Cancer Control (Surveillance)
Notes: Rates are per 100,000 and age-standardized to the 1991 Canadian population
* Indicates that the rate for Toronto is significantly different than the rate for the rest of Ontario (p<0.05).
-The Rest of Ontario combined excludes cases with unknown residence
### Appendix 1 Table 1.3: Estimation of Race-Specific and Race-Adjusted Incidence Rates for Melanoma of the Skin, Rest of Ontario and Toronto, by Sex and Year, 1991-2006

<table>
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<tr>
<th>Year</th>
<th>ASIR&lt;sup&gt;1&lt;/sup&gt; (A)</th>
<th>(B)</th>
<th>Prevalence&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Race- &amp; Sex-Specific ASIRs&lt;sup&gt;3&lt;/sup&gt;</th>
<th>Race-Adjusted ASIR&lt;sup&gt;4&lt;/sup&gt;</th>
<th>Percentage Change</th>
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<td>Males</td>
<td>White</td>
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<td>95%</td>
<td>5%</td>
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<td>Rest of Ontario 2001</td>
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<td>93%</td>
<td>7%</td>
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<td>3.1</td>
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<tr>
<td>Rest of Ontario 2006</td>
<td>18.7</td>
<td>14.6</td>
<td>91%</td>
<td>9%</td>
<td>20.2</td>
<td>3.4</td>
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<tr>
<td>Toronto 1991</td>
<td>12.6</td>
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<td>73%</td>
<td>27%</td>
<td>16.3</td>
<td>2.7</td>
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<td>Toronto 1996</td>
<td>11.6</td>
<td>8.6</td>
<td>68%</td>
<td>32%</td>
<td>15.9</td>
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<td>37%</td>
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<td>58%</td>
<td>42%</td>
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</table>

Source: Ontario Cancer Registry

1 ASIR - Age standardized incidence rate, per 100,000, 3-year moving average (standardized to 1991 Canadian population)

2 Prevalence for males and females combined - Source: Census 2011, Statistics Canada

3 Race-specific ASIRs were estimated on the basis of the reported ASIRs (columns A and B), the prevalence of whites and visible minorities in the population (columns C and D), assuming a melanoma Rate Ratio for (Whites: Visible Minorities) of 6.0

4 Race Adjusted ASIR is adjusted to the 1991 racial distribution for the rest of Ontario and Toronto (per 100,000)

Notes: Vis.Min = Visible Minority
Appendix 1 Figure 1.1: Age Standardized Incidence Rates for Cutaneous Malignant Melanoma, for Canada and Ontario, by Year, both Sexes Combined, 1992-2009 (with 95% confidence limits, per 100,000, standardized to 1991 Canadian population)

Source: Statistics Canada, online CanSim system accessing the 2011 Canadian Cancer Registry (Table 103-0553)
### Appendix 1 Table 1.4: Data Points for Appendix Figure 1.1 (ASIRs per 100,000)*

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Source: Statistics Canada, online CanSim system accessing the 2011 Canadian Cancer Registry (Table 103-0553)
Appendix 2: The Economic Burden of Skin Cancer

Evaluating the economic impact of any disease in a consistent manner over many different studies in different countries is difficult for a number of reasons. Some assessments will include direct medical and treatment costs such as physician visits, in-hospital costs, out-patient costs and follow up, while omitting indirect costs associated with morbidity from the disease and its treatment, such as informal caregiver costs, lost work time for those recovering from treatment, and potential losses to society for those dying prematurely due to the disease. Other studies will include some or all of the indirect costs noted above. Furthermore the national and health system context is important as differences in the organization and funding of health care have significant implications for overall disease-specific treatment costs.

We have chosen to concentrate largely on a single source for information on the specific financial impact of skin cancer – namely the monograph researched and written for the Canadian Partnership Against Cancer by Krueger and Associates and published in 2010 (Krueger et al., 2010). This publication has a number of advantages compared to the other economic impact studies on skin cancer (Chen et al., 2006; Cashin et al., 2008; Periera deSouza et al., 2011; Mudigonda et al., 2010). First of all, it is carried out in the Canadian context, which is particularly important for costing of procedures and ensuring relative consistency in treatment guidelines across provinces. It takes into account the fact that some provinces may under-ascertain skin cancers. In addition, it is a recent assessment — although the costs are based on 2004 estimates adjusted for inflation. Finally it evaluates costs for both melanoma and non-melanocytic skin cancer in the same manner, contributing to uniformity in assumptions about estimates for the three different skin cancers in time and place.

Direct costs included in the financial estimate included primary care, outpatient clinic/day care treatment, and hospitalization costs. Hospital costs were calculated from information from the Canadian Institute for Health Information for skin malignancies and based on a 7 day stay for melanoma and a 2.5 day stay for hospitalized SCC. Cost estimates are adjusted for the fact that a similar proportion of melanoma patients experience recurrent disease as experience a second primary lesion. Costs were determined on a province-by-province basis based on wages and actual dollar figures for operation of clinics. For instance, in Ontario, median costs for day care treatment of a CMM from 2004 through 2007/8 were estimated to be $2085.

Indirect costs for loss of work time during recuperation from treatment, and an estimate of costs related to years of life lost for those dying of disease were included. For skin cancer in retired persons, Krueger et al. valued indirect cost contributions at the minimum wage level of the province of residence of the incident cases.

Summing figures from the Krueger et al. report for all three types of skin cancer for: a) primary care costs; b) day surgery costs; c) inpatient costs; d) indirect costs associated with death; and e) indirect costs associated with morbidity results in a final estimate of $296.48 million in costs in 2011 for skin cancer in the province of Ontario.