The association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: A systematic review

The International Agency for Research on Cancer Working Group on artificial ultraviolet (UV) light and skin cancer

Exposure to solar ultraviolet (UV) radiation is a known cause of skin cancer. Sunbed use represents an increasingly frequent source of artificial UV exposure in light-skinned populations. To assess the available evidence of the association between sunbed use and cutaneous malignant melanoma (melanoma) and other skin cancers, a systematic review of the literature till March 2006 on epidemiological and biological studies on sunbed use was performed in Pubmed, ISI Web of Science, Embase, Pascal, Cochrance library, Lilacs and Medcarib. Search for keywords in the title and in the abstract was done systematically and supplemented by manual searches. Only case-control, cohort or cross-sectional studies were selected. Data were abstracted by means of a standardized data-collection protocol. Based on 19 informative studies, ever-use of sunbeds was positively associated with melanoma (summary relative risk, 1.15; 95% CI, 1.00–1.31), although there was no consistent evidence of a dose–response relation. First exposure to sunbeds before 35 years of age significantly increased the risk of melanoma, based on 7 informative studies (summary relative risk, 1.75; 95% CI, 1.35–2.26). The summary relative risk of 3 studies of squamous cell carcinoma showed an increased risk. For basal cell carcinoma, the studies did not support an association. The evidence does not support a protective effect of the use of sunbeds against damage to the skin from subsequent sun exposure. Young adults should be discouraged from using indoor tanning equipment and restricted access to sunbeds by minors should be strongly considered.

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Key words: artificial UV; sunbeds; melanoma; skin cancer; meta-analysis

Sun exposure is the main environmental cause of skin cancer, and ultraviolet (UV) radiation is the solar wavelength involved in skin cancer, including the malignant cutaneous melanoma. People may also be exposed to UV radiation through many artificial sources at home and in the workplace, with some individuals receiving high doses. Sources of artificial UV radiation include various lamps used in medicine, industry, business and research, as well as for domestic and cosmetic purposes. Sunbeds and sunlamps used for tanning purposes are the main source of deliberate exposure to artificial UV radiation. Although the contexts of sun exposure and indoor tanning differ, both deliver UV radiation, and their health effects would therefore be expected to be similar.

UV radiation wavelengths range between 100 and 400 nm and are broadly categorized into UVA (>315–400 nm), UVB (>280–315 nm) and UVC (100–280 nm). Modern indoor tanning equipment mainly emits in the UVA range, but a fraction (i.e., <5%) of this spectrum is in the UVB range.

Before 1990, UVB was usually considered the only carcinogenic part of the solar spectrum, but since then UVA as well has been suspected of having carcinogenic potential. In 1992, the International Agency for Research on Cancer (IARC) classified UVB and UVA radiation, as well as “use of sunbeds and sunlamps,” as “probably carcinogenic to humans” (Group 2A of the IARC classification of carcinogenic agents). More recently, the 10th Report on Carcinogens published by the National Toxicology Program in the USA classified UVA radiation as a “known to be a human carcinogen.” Biological mechanisms by which chronic sun exposure causes squamous cell cancer (SCC) of the skin have become better known and chronic exposure to high UVB doses is now considered as the main environmental cause of that skin cancer. Biological mechanisms implicated in basal cell carcinoma (BCC) start to be better known. In contrast, we still have poor knowledge of the UV wavelength and the dose delivery patterns at skin level implicated in the genesis of melanoma and of BCC.

Indoor tanning is widely practiced in most developed countries, particularly in Northern Europe and the USA, and is gaining popularity even in sunny countries such as Australia. The likely impact of this fashion on skin cancer incidence is of substantial concern, mainly for cutaneous malignant melanoma (hereafter melanoma), a cancer of poor prognosis when diagnosed at an advanced stage.

This paper summarizes a systematic review of epidemiological and experimental studies on use of indoor tanning equipment and skin cancer developed by a Working Group convened by IARC.

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*The device used for tanning may be referred to as sunbed, sunlamp, artificial UV, artificial light or tanning bed, among other terms. Also, a number of terms are used to define a place where indoor tanning may occur: salon, tanning room, tanning parlor, tanning booth, indoor tanning salon, indoor tanning facility. In addition, indoor tanning may also occur in non-commercial premises. For the purpose of this report, the term indoor tanning equipment has been used throughout.

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In the 1990s, regulations in some countries (e.g., France, Sweden) limited to 1.5% the maximum percentage of UVB in the UV output of tanning appliances. However, in practice, the UV output and spectral characteristics (i.e., amounts of UVA, UVB, visible light and infrared radiation) of tanning appliances vary considerably. The proportion of UVB in UV energy output could vary from 0.5 to 4%, and may attain an emission spectrum similar to the sun spectrum in the UVB range. These differences are due to sunbed design (e.g., the numbers and type of fluorescent tubes, the presence of high pressure UV lamps, the materials composing filters, the distance from canopy to the skin), sunbed power and tube ageing.

Biological effects of exposure to artificial UV radiation relevant to carcinogenesis

A large body of experimental and epidemiological data strongly indicates that the spectrum of UV radiation reaching the Earth’s surface causes skin cancer. UVB is a complete carcinogen that is absorbed by DNA and can damage DNA directly. Evidence of the mutagenic properties of UVA in humans has been found in several studies. UVA radiation does cause UVB-like cyclobutane pyrimidine dimers and 6-4 photoproducts, albeit with a much lower efficacy than does UVB radiation. Most of the DNA damage induced by UVA is indirect, through the absorption of UVA photons by other cellular structures (chromophores), with formation of reactive oxygen species that can transfer UV energy to DNA via mutagenic oxidative intermediates.

Skin of human volunteers exposed to UVA lamps used in tanning appliances show DNA damage, p53 mutations induced by oxidative damage and alterations of the p53 protein similar to those observed after sun exposure or after exposure of experimental animals.

UVA penetrates deeper into human skin than does UVB. Because UVA represents the largest proportion of the UV spectrum of tanning appliances and of solar radiation reaching the Earth’s surface, far more UVA than UVB reaches the basal layers of the epidermis where melanocytes and early keratinocytic cells are located.

Both UVA and UVB radiation can affect the immune response that may be involved in the promotion of melanoma, but the 2 types of radiation seem to act differently. UVB induces immunosuppression at both the local and systemic levels, while UVA does not induce systemic immune suppression.

To date, evidence obtained from experimental studies on the involvement of high UVB doses in the causation of SCC is consistent with observations in humans. In contrast, experimental studies give conflicting results regarding the roles of UVB and UVA in the induction of melanoma in humans. The same uncertainties hold true for BCC, a type of tumor that shares some epidemiological characteristics of melanoma.

Experiments carried out in animals cannot reproduce the complex interplay in individuals between highly variable natural susceptibilities to UV radiation, sun exposure behaviors and exposure to various sources of UV radiation. During indoor tanning, such interrelationships may be critical, as users are more inclined than the average population to engage in outdoor tanning activities, and indoor tanning sessions often precede or follow active sun exposure or outdoor tanning.

Effects of artificial UV on human skin

Skin redness or burning are reported by 18–55% of users of indoor tanning equipment in Europe and North America. Although UVB is far more potent than UVA in causing sunburn, high fluxes of UVA are capable of inducing skin redness in individuals sensitive to sunlight or with only moderate tanning ability.

In individuals who tan easily, exposure to tanning appliances will lead first to the oxidation of melanin already present in superficial keratinocytic layers of the skin, known as immediate pigmentation. A more permanent tan is acquired with accumulation of exposure, depending on tanning ability and the amount of UVB present in the UV spectrum of the lamps.

Immediate pigmentation darkening has no photoprotective effect against UV-induced skin redness or sunburn. Moreover, a UV-induced permanent tan provides little photoprotection, and the skin thickening caused by UVA affords only very little photoprotection.

Studies in humans show that a prevacation tan induced artificially offers virtually no protection against sun-induced DNA damage.

Exposure to artificial UV for tanning purposes

Few people had used indoor tanning equipment before 1980 but by the end of the 1990s more than 60% of women and 50% of men aged 18–50 years in Northern Europe reported having ever used indoor tanning equipment. Indeed, prevalence of indoor tanning is increasing so rapidly in many countries that current estimates may be outdated rapidly. The most frequent motivations for indoor tanning are the acquisition of a so-called safe tan and preparation of the skin before sun exposure.

Use of indoor tanning equipment is more prevalent among women and among both men and women younger than 35 years. Earliest studies in Sweden and in the USA tended to find indoor tanning to be more prevalent among adolescents with fair skin types who are more prone to sunburn. More recent studies in the USA found either the opposite or no association.

Few studies have assessed the compliance of indoor tanning facility operators or consumers with recommendations and regulations. Overall, information provided by tanning salon operators on health risks and on duration and frequency of exposure is often incomplete, and there is a lack of identification of highly sun-sensitive subjects or of subjects taking photosensitizing medications.

About 17–35% sunbed users reported that they did not wear eye protection. In some surveys, 16% of sunbed users may have had more than 100 sessions per year, and most users tend to exceed the recommended exposure times.

Since 1989, a total of 16 studies (18 reports) have examined prevalence of indoor tanning among children and adolescents aged 8–19 years in Australia, Europe and the USA. All studies showed a frequent use by adolescents and children, sometimes at a very young age. According to the most recent studies, 30% of adolescents in Sweden and 24% of adolescents in the USA aged 13–19 years reported ever-use of indoor tanning equipment and 8 and 12% respectively were frequent users (10 times per year or more). In a recent survey in the United Kingdom, while 7% of children aged 8–11 years reported exposure to a sunbed in the past 6 months, many as 48% expressed a desire to use a sunbed.

Epidemiological studies on indoor tanning and skin cancer

As existing animal models of human melanoma are inconsistent, evidence of an association between indoor tanning and skin cancer must be sought predominantly from epidemiological studies. Few studies have addressed this topic specifically, but some studies included 1 or more secondary questions about indoor tanning. We systematically analyzed the results from the relevant studies and compiled them in a metaanalysis.

Methods

The methodology used for the literature search is summarized in Table I. The minimal common information about exposure to indoor tanning appliances for all studies was “ever exposed.” For those studies wherein “ever exposed to indoor tanning appliances versus never” was not strictly assessed, we used the information closest to this category.

Most estimates included all subjects and combined sexes in the analysis. Some studies presented results separately for women and men, with no combined data, in which case both estimates were
included. Since the studies used different age categories for classifying age at first exposure, we considered as "young exposure" those exposures that started before 35 years of age.

Every measure of association adjusted for the maximum number of confounding variables, and corresponding confidence inter-

TABLE I – METHOD USED FOR THE LITERATURE SEARCH

The literature to March 2006 was searched using the following databases: Pubmed, ISI Web of Science (Science Citation Index Expanded), Embase, Pascal, Cochrane library, Lilacs and Medcarib. The following keywords and their corresponding French translation were used for search in the PASCAL database: skin cancer, squamous cell carcinoma, SCC, basal cell carcinoma, BCC and melanoma for diseases. To define exposure, the following keywords were used: sunbed, sunlamp, artificial UV, artificial light, solaria, solarium, indoor tanning, tanning bed, tanning parlour, tanning salon and tanning booth.

Search for keywords in the title and in the abstract was done systematically. Manual search was done of references cited in the selected articles, and in selected reviews or books on melanoma and skin cancer. All participants of the working group were asked to report any additional published or submitted study. No language restriction was applied.

Primary inclusion criteria were developed for the selection of relevant articles, which were case–control, cohort or cross-sectional studies published as an original article. Ecological studies, case reports, reviews and editorials were not considered eligible.

The selected articles were reviewed, and data were abstracted by means of a standardized data-collection protocol. When another article on the same study was published simultaneously, additional relevant or missing information was retrieved from the companion paper.

TABLE II – CHARACTERISTICS OF THE STUDIES CONSIDERED FOR THE METAANALYSIS ON MELANOMA

| Reference | Country | Number | Relative risk
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<tbody>
<tr>
<td></td>
<td></td>
<td>Cases</td>
<td>Controls</td>
</tr>
<tr>
<td>Cohort study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population-based case–control studies</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Adam et al. (1981)</td>
<td>UK</td>
<td>169 207</td>
<td>2.93 (1.16–7.40)</td>
</tr>
<tr>
<td>Gallagher et al. (1986)</td>
<td>Canada</td>
<td>595 595</td>
<td>1.1 (0.6–1.8)</td>
</tr>
<tr>
<td>Holman et al. (1986)</td>
<td>Australia</td>
<td>511 511</td>
<td>0.73 (0.53–1.01)</td>
</tr>
<tr>
<td>Osterlind et al. (1988)</td>
<td>Denmark</td>
<td>474 926</td>
<td>0.9 (0.4–2.0)</td>
</tr>
<tr>
<td>Zanetti et al. (1988)</td>
<td>Italy</td>
<td>208 416</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Beinert et al. (1990)</td>
<td>Sweden</td>
<td>523 505</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Walter et al. (1990)</td>
<td>Canada</td>
<td>583 608</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Westerdahl et al. (1994)</td>
<td>Sweden</td>
<td>400 640</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Holly et al. (1995)</td>
<td>USA</td>
<td>452 930</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Chen et al. (1998)</td>
<td>USA</td>
<td>624 512</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Wallow et al. (1999)</td>
<td>Canada</td>
<td>583 608</td>
<td>1.3 (0.9–1.8)</td>
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<tr>
<td>Westerdahl et al. (2000)</td>
<td>Sweden</td>
<td>571 913</td>
<td>1.2 (0.9–1.6)</td>
</tr>
<tr>
<td>Other case-control studies</td>
<td></td>
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<td></td>
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<tr>
<td>Klepp and Magnus (1979)</td>
<td>Norway</td>
<td>78 131</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Holly et al. (1987)</td>
<td>USA</td>
<td>121 139</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Swerdloff et al. (1988)</td>
<td>UK</td>
<td>180 120</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>MacKie et al. (1989)</td>
<td>UK</td>
<td>280 180</td>
<td>1.3 (0.9–1.8)</td>
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<tr>
<td>Dunn-Lane et al. (1993)</td>
<td>UK</td>
<td>100 100</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Garbe et al. (1993)</td>
<td>Germany</td>
<td>280 280</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Autier et al. (1994)</td>
<td>Belgium, France, and Germany</td>
<td>420 447</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Naldi et al. (2000)</td>
<td>Italy</td>
<td>542 538</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Kaskel et al. (2001)</td>
<td>Germany</td>
<td>271 271</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Bataille et al. (2004)</td>
<td>UK</td>
<td>413 416</td>
<td>1.3 (0.9–1.8)</td>
</tr>
<tr>
<td>Bataille et al. (2005)</td>
<td>Belgium, France, the Netherlands</td>
<td>597 622</td>
<td>1.3 (0.9–1.8)</td>
</tr>
</tbody>
</table>

ALM, acral lentiginous melanoma; HC, histologically confirmed; LMM, lentigo maligna melanoma; M, melanoma; MM, malignant melanoma; NM, nodular melanoma; SSM, superficial spreading melanoma.

cCohort size.–Values in parentheses are 95% CI. –Because no estimate of risk was reported in these studies, we did not include them in the metaanalysis.–The study by Walter et al. (1990) was reanalyzed in the 1999 publication. We used the relative risk adjusted for potential confounders presented in the 1999 publication.
these 2 major types of skin cancer were also excluded from review, leaving 5 studies for consideration.

Relative risk for melanoma

Thirteen of 19 studies presented positive estimates for “ever” versus “never” exposed to indoor tanning equipment, but only 4 were statistically significant (Fig. 1). Seven of these studies reported only crude relative risks, and 1 adjusted for age and sex only. Results of the metaanalysis are shown in Table III. The summary estimate indicated a significant positive association between “ever” versus “never” indoor tanning and melanoma (RR, 1.15; CI, 1.00–1.31) and the \( \chi^2 \)-test for heterogeneity was statistically significant.

To decrease the influence of possible biases, estimates were calculated including only the cohort and the 9 population-based case–control studies. The summary relative risk was very similar apart from having wider CIs (RR, 1.17; CI, 0.96–1.42). In an analysis restricted to the 8 studies that adjusted for confounders related to sun exposure and sun sensitivity, the summary relative risk remained similar to that obtained from all 19 studies, but the CI widened (RR, 1.19; CI, 0.33–4.30).

Seven studies presented estimates relevant for the evaluation of “first exposure in youth” versus “never” (Fig. 2). All relative risks were adjusted for confounders related to sun exposure or sun sensitivity, except in the study by Walter et al. A significant 75% increase in risk was detected (Table III) and the \( \chi^2 \)-test for heterogeneity was nonsignificant.

Five studies investigated time since exposure and reported estimates that allowed comparisons between recent and more distant exposure. Metaanalytic estimates were greater for exposures more distant in time when compared to those for more recent exposures (Table III).

There was some indication for a dose-effect relationship in 2 studies, but not in the other two. But metrics used for assessing duration were all different and therefore did not permit metaanalytic synthesis. Only 4 studies explored the role of natural sensitivity to sunlight on risk associated with indoor tanning, and overall, they found no consistent result.

Type of indoor tanning equipment

No epidemiological study has been able to explore in a rigorous way amounts of UVA and UVB received by indoor tanning users. The study by Chen et al. obtained information concerning the type of sunbed or sunlamp used (e.g., desktop models, floor models, beds or walk-in booths). This information was obtained by showing to subjects pictures of various types of sunlamps and sun-
The study found a nonsignificant elevated risk of malignant melanoma associated with the use of desktop sunlamps and heavy-weight floor-model sunbeds and a statistically significant tripled risk associated with use of more than 2 types of sunlamps, compared with no use of sunbeds. The study by Bataille et al.\textsuperscript{34} reported no impact of the type of device used on melanoma risk.

The relative risks of melanoma associated with ever-use of sunbed/sunlamp reported in the studies did not vary with year of publication or first year of study period, and funnel plot regression gave no indication of publication bias (ever-use of sunbed/sunlamps, $p = 0.80$; first exposure in youth, $p = 0.10$). This observation suggests that the apparent increased risk for ever use and for age at first use were unlikely to be explained by the earlier types of indoor tanning appliance used.

Before 1980, exposure to artificial UV radiation was more likely to take place at home with devices that emitted greater amounts of UVB radiation, whereas exposure in the 1980s increasingly occurred in commercial salons using equipment that emitted mainly UVA. The Norway–Swedish prospective study provided evidence that the increased melanoma risk associated with exposure to tanning appliances was not due to the type of UV lamps used before 1983.\textsuperscript{83}

### Discussion

Investigation of the association between indoor tanning and skin cancers poses challenging problems, as indoor tanning has been in widespread use only recently. Based on our knowledge about the relationship between sun exposure and risk for melanoma, it could be stated that associations after long latency periods, such as would be expected for melanoma and BCC, may not be detectable yet. Also, since the fashion of indoor tanning has been increasing steadily, the failure to distinguish between distant and recent exposures in most epidemiological studies may mask an actual increase in risk with exposure early in life.

Our systematic review of published studies mainly from Europe and North America of the association of use of indoor tanning equipment with skin cancers revealed an association of age at first use of less than 35 years with melanoma risk. These studies consistently indicated a moderate strength of association, with a summary relative risk of 1.75 (1.35–2.26). This result suggests a greater vulnerability of younger people to the carcinogenic impact of indoor tanning. Also, it is in agreement with the knowledge that age at exposure may influence the relative risk for skin cancer associated with UV exposure, and that exposure to sunlight in childhood is an important contributing factor for melanoma risk in adults.\textsuperscript{84,85}

The association with ever-use of such equipment, or use more than 15–20 years prior to diagnosis of melanoma, was weak, and evidence regarding a dose–response relationship was scant. The evidence is limited by concerns over characterization of exposure and recall of exposure by individuals, potential confounding by sun exposure or other variables and the low power to detect associations that become evident only following a prolonged lag period after exposure. Our results are similar to a previous metaanalysis,\textsuperscript{86} but our systematic review is more exhaustive and included more studies.

In Scandinavian countries use of indoor tanning equipment has been popular since the late 1970s and the prevalence of use in those countries is the highest in the world. In the Norwegian–Swedish prospective study the highest risk for melanoma was found in women who used indoor tanning equipment at least once per month when they were 20–29 years old. These results support the hypothesis that a certain lag period is needed before the impact.
of exposure to tanning appliances on melanoma incidence becomes apparent. It also underlines the greater vulnerability of younger subjects to harmful effects of indoor tanning.

The positive association between use of indoor tanning equipment and melanoma risk reported here is consistent with the knowledge that melanoma is caused primarily by exposure to solar radiation. The limited evidence for a positive association between indoor tanning and SCC is consistent with its known dependence on dose of UV radiation to the skin. Thus the biological plausibility of a causal association between indoor tanning and risk for melanoma and SCC is strong.

On balance, the evidence pertaining to the strength, consistency, dose–response and temporal sequence of the association of the use of indoor tanning equipment with melanoma risk, and of the coherence and biologic plausibility of the association, leads us to conclude that there is convincing evidence to support a causal relationship, particularly with exposure before the age of 35 years. This evidence is strongly suggestive and further studies could clarify our understanding of this association and allow more definitive conclusions.

We are cognizant of the importance of this issue for the health of light-skinned populations. The strength of the existing evidence suggests that policy makers should strongly consider enacting measures such as restricting minors and discouraging young adults from using indoor tanning equipment, in order to protect the general population from additional risk for melanoma and squamous cell skin cancer.

References


