## **IN-DEPTH REVIEW**

# Solar ultraviolet radiation and skin cancer

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Background	Incidence rates of skin cancer, both non-melanoma skin cancer and (malignant/cutaneous) mela- noma, are rising in Great Britain. It is widely accepted that solar ultraviolet radiation (UVR) is the main causal factor for these neoplasms. Many people are occupationally exposed to solar UVR, including farmers, construction workers and some public service workers.
Aim	The aim of this article is to review the key epidemiologic papers on occupational solar exposure and skin cancer and discuss the relationships found.
Method	A literature search was conducted using online databases and article bibliographies. A full review of all available studies was not carried out, as only key studies on occupational exposure were required.
Results	There is a clear association between solar radiation and skin cancer. The mechanisms for induction vary between the types of skin cancer and these cannot be solely attributed to occupational exposures.
Conclusions	There is great difficulty in separating the effects of occupational and recreational solar UVR exposure; therefore, any results discussed in this review should be interpreted with caution. However, it is clear that solar UVR exposure does induce skin cancer and protective measures should be taken in an attempt to reduce the burden of occupational skin cancer in Great Britain.
Key words	Cancer burden; melanoma; NMSC; skin cancer; solar radiation.

## Introduction

Sunlight is visible light (UVC) from the sun. Solar radiation is the combination of ultraviolet radiation (UVR) and visible light that manages to reach the earth's surface (wavelengths >295 nm, classified as UVA and UVB). UVR that is <295 nm (the majority of UVC) does not reach the earth's surface because the atmosphere absorbs it. Solar UVR is ~95% UVA (315–400 nm) and 5% UVB (280–315 nm). UVB is much more effective at producing cancer in animals, sunburn in humans and DNA damage than UVA. In epidemiological studies, it is difficult to separate out the effects of UVB, UVA and visible light. Therefore, it is typically treated as a whole. Exposure to solar radiation is usually measured via exposure categorization (recreational or occupational) or job categorization (indoor or outdoor).

The exposed skin surface of individuals is irradiated differently depending on cultural/social behaviour, clothing preferences and the position of the sun in the sky relative to the body. The power of irradiation depends on many environmental factors:

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- Time of day: solar UVR is strongest at solar noon (the point halfway between sunrise and sunset), when the sun is at its highest in the sky.
- Latitude: UVR is strongest at the equator; at higher latitudes, the sun is lower in the sky resulting in lower UVR levels.
- Altitude: UVR intensity increases as altitude increases.
- Weather conditions: Thick cloud cover can reduce UVR levels, but some UVR will still reach the earth's surface.
- Reflection: UVR can be reflected off many surfaces, including snow, sand and water. The amount of UVR reflected can be as high as 90% or as low as 1% depending on the surface. Reflection puts parts of the body that are normally shaded at risk.

The International Agency for Research on Cancer (IARC) concluded in 1992 that there was 'sufficient evidence in humans for the carcinogenicity of solar radiation', classifying UVR as a Group 1 carcinogen. The agency went further stating, 'Solar radiation causes cutaneous malignant melanoma and nonmelanocytic skin cancer' [1].

In the UK, between February 1993 and January 1999, 22 710 new cases of skin disease were reported via the occupational skin disease surveillance schemes, EPI-DERM and OPRA (Occupational Physicians Reporting Activity). In total, 1608 cases of skin neoplasia

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[non-melanoma skin cancer (NMSC) and melanoma] were reported, of which all but 4% of cases could be attributed to sunlight or UVR [2]. Over three-quarters of such cases (78%) worked in agriculture, construction or the armed forces. Other causes, such as tar and tar pitches, mineral oils and ionizing radiation, accounted for <1% of cases each. Of the cases reported by dermatologists,  $\sim 6\%$  were melanoma and 55% were NMSC. For NMSC, just >43% were basal cell carcinomas (BCCs) and  $\sim 12\%$  were squamous cell carcinomas (SCCs).

The risk of NMSC and melanoma caused by exposure to solar radiation is difficult to estimate and interpret because everyone at some time in their life is exposed to sunlight at a greater or lesser degree depending on residential location and leisure-time activities. Epidemiological studies have used various methods to adjust risk estimates for non-occupational solar exposure. Typically, residential location is used as a surrogate for recreational sunlight exposure.

Solar radiation is an important occupational exposure to investigate since skin cancer incidence and mortality rates have been steadily increasing over the past decade. It is likely that these rates will increase further with the ongoing depletion of ozone, which protects and reduces UVR levels. Most UVR damage can be avoided by implementing a few protective measures; these measures could minimize the number of occupationally related skin cancers being diagnosed.

#### Methods

A literature search was conducted to identify epidemiologic papers on solar radiation and skin cancer using electronic databases (MEDLINE from 1950 onwards, PubMed from 1950 onwards, Web of Science from 1990 onwards and Google Scholar) and paper bibliographies. Key search terms were combined to obtain the most relevant papers (skin cancer, melanoma, occupational, solar radiation and outdoor workers).

#### Solar radiation and non-melanoma skin cancer

NMSC (ICD-10 C44; ICD-9 173) is the most common neoplasm in Caucasian populations. There are two main types of NMSC: BCC, the most common type accounting for  $\sim$ 75% of cases and SCC, accounting for  $\sim$ 20% of cases. NMSC is rarely fatal, with survival rates being close to 99% if diagnosed early. Unfortunately, the condition is largely under-reported in government statistics.

Increases in solar radiation exposure have been shown to lead to an increased risk of both BCC and SCC. More cases occur on the most sun-exposed parts of the body with fewer occurring on the least exposed. The disease is associated with total solar exposure (mainly SCC), occupational solar exposure (mainly SCC) and non-occupational or recreational sun exposure (mainly BCC) [3,4].

Epidemiological studies have consistently reported elevated risks associated with NMSC and exposure to sunlight [1]. Studies show that there is a strong inverse relationship between latitude and incidence (and mortality), as well as a positive association with estimated ambient UVR. Outdoor workers have higher mortality from skin cancer and some studies show evidence for increased incidence. Several studies have shown positive associations between measures of solar skin damage and the prevalence of both BCC and SCC. Actual measures of solar UVR exposure are not as strongly linked, possibly due to measurement error and inadequate control of confounders. However, a study of American fishermen found that annual and total UVB exposure was positively associated with SCC, but not BCC. Some key studies are described below. The results mentioned can be found in Table 1.

A review of epidemiologic evidence on solar radiation and skin cancer, both BCC and SCC, was published in 1994 [5]. There was strong indirect evidence that sun exposure causes skin cancer. This evidence was compiled from relationships observed with latitude, migration, ethnic group and the anatomic sites where cancers were located. Evidence for an association between NMSC and occupational solar exposure was weaker; however, outdoor workers were generally at a higher risk than indoor workers and risk appeared to increase with level of occupational exposure. Positive associations were also found for skin cancer and total sun exposure although most of these studies were unadjusted for other factors. Unfortunately, no pooled estimates were given.

Gallagher *et al.* [6,7] conducted two separate studies on newly diagnosed cases of BCC and SCC in the period 1983-1984. Cases were obtained from the Alberta Cancer Registry and were aged 25-79 years. A common control group, matched by gender and 5-year age group, was used from the Alberta Health Care Insurance Plan who had no previous diagnosis of NMSC. Occupational history was obtained for all jobs held for at least 6 months along with usual number of hours worked outside in summer and winter months. Since <5% of exposure occurred in winter, all results described assume that all exposure occurred in summer months. Estimates were adjusted for skin colour, hair colour and mother's ethnic origin. No association was seen for combined solar exposure and BCC or SCC. However, lifetime occupational and recreational childhood exposure was related to BCC. For SCC, lifetime occupational exposure showed a clear positive association, particularly with the most recent exposure to diagnosis.

A meta-analysis of 37 studies to assess whether farmers had an elevated cancer incidence rate was conducted in 1998 [8]. The studies used were identified from references of a previous meta-analysis conducted by Blair *et al.* in 1992 and MEDLINE. Studies that did not report findings for three or more diseases were excluded to reduce publication bias, along with additional studies that did

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### Table 1. Key studies on solar UVR and NMSC

Study	Country	Exposure	Numbers	Results	Adjusted
Kricker et al. [5]	Australia, USA, Canada, Ireland, Italy	Occupational: indoor, outdoor, farmer, work in agriculture >10 years	10 studies, varied by study from 26 to 883 cases	Varied depending on NMSC type: occupational: BCC: OR = 1.3–1.6; SCC: OR = 1.1–5.5	Some studies adjusted for age and gender
		Total: daily, cumulative		Total: BCC: OR = 0.7-9.3; SCC: OR = 2.1-11.1	
Gallagher et al. [6]	Canada	Recreational/ occupational history and usual number of hours spent outdoors per week for each	226 male BCC cases, 406 male controls	Childhood: 3.8–7.4 h/week, OR = 1.1; 7.5–12.4 h/week, OR = 1.4; 12.5+ h/week, OR = 2.6	Age, mother's ethnic origin, skin colour and hair colour
				Occupational (lifetime): 14–24.9 h/week, OR = 1.3; 25+ h/week, OR = 1.4 Cumulative (lifetime): 11.5–18.9 h/week, OR = 1.3; 19–27.9 h/week, OR = 1.2; 28+ h/week, OR = 1.3	
Gallagher <i>et al.</i> [7]	Canada	Recreational/ occupational history and usual number of hours spent outdoors per week for each	180 male SCC cases, 406 male controls	Childhood: 3.8–7.4 h/week, OR = 1.2; 7.5–12.4 h/week, OR = 1.1; 12.5+ h/week, OR = 1.6	Age, mother's ethnic origin, skin colour and hair colour
				Occupational (lifetime): 3.5–13.9 h/week, OR = 0.8; 14–24.9 h/week, OR = 1.5; 25+ h/week, OR = 1.4	
				Occupational (last 10 years); <7 h/week, OR = 1.9; 7-22.9 h/week, OR = 2.2; 23+ h/week, OR = 4.0	
				Cumulative (lifetime): 11.5-18.9 h/week, OR = 1.8; 19-27.9 h/week, $OR = 1.2; 28+$ h/week, $OR = 1.0$ Cumulative (last 10 years):	
				9.5–15.9 h/week, OR = 1.5; 16–23.9 h/week, OR = 1.7; 24+ h/week, OR = 1.1	
Acquavella <i>et al.</i> [8]	Europe, North America, New Zealand	White male farmers	19 studies, 9 original studies used by Blair, 6 follow-up studies, 10 PMR studies, 2 case-control studies	All RR = 1.15, original RR = 1.22, follow-up RR = 1.11, PMR studies RR = 1.20, case-control RR = 0.76	

Table 1. (continu	ed)
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Study	Country	Exposure	Numbers	Results	Adjusted
Freedman <i>et al.</i> [9]	USA	Residential: level of UVR: low, medium, high; occupation: indoor, mixed indoor/outdoor, outdoor non-farmers, outdoor farmers	6565 cases, 153 502 controls	Residential: medium OR = 1.14, high OR = 1.23 Occupational: mixed OR = 1.01, outdoor OR = 1.30, farmer OR = 1.15	Age, gender, race, occupational physical activity socio-economic status and residential/ occupational exposure

OR, odds ratio; PMR, proportional mortality ratio; RR, relative risk.

not provide adequate information to enable risk calculation. In total, there were 19 studies analysed for NMSC giving an elevated pooled random effects estimate of borderline significance. Pooled rates varied depending on study design: follow-up, proportional mortality rates or case-control. Unfortunately, there was no detail available to enable a specific exposure analysis.

A US-based case–control mortality study reported findings based on 6565 cases of NMSC between 1984 and 1995 [9]. All deaths were collected from a 24 state database and for each case, 25 controls were chosen, matched by 5-year age group. The usual occupation from the death certificate was used to classify occupation as indoor, mixed indoor/outdoor, outdoor non-farmer and outdoor farmer. Estimates were adjusted for age, sex, race, occupational physical activity, socio-economic status and residential or occupational sunlight exposure (for risk due to occupational or residential sunlight exposure, respectively). Positive associations were observed for both occupational and residential exposures to sunlight.

The key epidemiologic evidence described above shows that there is a clear association between NMSC (both BCC and SCC) and solar UVR. This increased risk can be attributed to both occupational and recreational solar exposure. For BCC, it appears that recreational childhood exposure is the most important, but an increase with lifetime occupational exposure has been demonstrated. Occupational solar UVR is mainly linked to SCC; particularly important are the 10 years prior to diagnosis. A relationship has also been shown for total solar radiation (occupational and recreational combined) and SCC.

#### Solar radiation and melanoma

Increased risk is most strongly linked to intermittent exposure to high-intensity sunlight (usually recreational and often resulting in sunburn), rather than chronic exposure, typical of outdoor occupations [4,10], although outdoor workers who have sustained repeated episodes of severe sunburn might be at increased risk [11].

For melanoma, the distributions by anatomic site, ethnic origin, place of residence and the effects of migration implicate solar radiation as a cause. Evidence that the condition is related to occupational exposure to the sun is limited; however, the risk appears to increase with increasing exposure at low levels. The patterns emerging may be due to differences in characteristics between indoor and outdoor workers, for example, more genetically susceptible individuals choose to work in an indoor occupation [4].

Epidemiological studies have consistently reported elevated risks associated with melanoma and UV radiation, solar and artificial [1]. Several descriptive studies report an association between incidence (and mortality) of melanoma and latitude, in particular a sunny environment at the place or places of residence throughout life. In contrast, there are inconsistent results for total solar exposure, either intermittent or chronic. This inconsistency may be due to differing effects that the exposures have. Three large studies show an apparent reduction in risk associated with occupational exposure, whereas several smaller studies showed either no effect or an increased risk. Most studies demonstrate a positive association with intermittent exposure. Some key studies are described below. The results mentioned can be found in Table 2.

Vågerö *et al.* [12] conducted an analysis based on melanoma cases diagnosed in Sweden between 1961 and 1979. Cases were obtained from the Swedish Cancer Environment Registry. Individuals were chosen who were economically active in 1960 and were classified into three exposure groups: office workers, other indoor workers and outdoor workers, based on their occupation code and description. The entire working population was used for reference. Overall, the morbidity ratios, standardized for age and county of residence (in 1960), showed a negative

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Table 2. Key studies	on solar	UVR and	melanoma
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Study	Country	Exposure	Numbers	Results	Adjusted
Vågerö et al. [12]	Sweden	Office, other indoor, outdoor	2 630 458 total; 567 393 office; 1 432 551 other; 630 514 outdoor; 4706 melanoma	Office SMR = 131; other indoor SMR = 94; outdoor SMR = 86; outdoor (uncovered) SMR = 107	Age, county of residence (in 1960)
Travier et al. [14]	Sweden	Male veterinarians	1178 total; 11 melanomas; 6 Vet in veterinary industry; 1 Vet in other industry; 3 other worker in veterinary industry	Total SIR = 2.86; Vet in Vet SIR = 2.77; Vet in other SIR = 1.84; other in Vet SIR = 3.12	Age, calendar period, geographic region, urban setting
Elwood and Jopson [13]	Norway, UK, USA, Canada, Italy, Denmark, Germany, Sweden, France, Belgium, Spain	Intermittent, occupational and total sun exposure	29 studies; 23 intermittent; 20 occupational; 11 total 16 991 melanomas;	Intermittent OR = 1.71; occupational OR = 0.86; total OR = 1.18	(If possible), age, sex, susceptibility
			6934 intermittent; 6517 occupational; 3540 total		
Acquavella <i>et al.</i> [8]	Europe, North America, New Zealand	White male farmers	21 studies; 10 original studies used by Blair; 6 follow-up studies; 8 PMR studies; 7 case- control studies	All RR = 0.95; 10 original RR = 1.12; follow-up RR = 0.87; PMR studies RR = 0.94; case-control RR = 1.14	
Gandini et al. [15]	USA, UK, Norway, Denmark, Germany, Ireland, France, Spain, others	Intermittent, chronic (occupational) and total sun exposure	57 studies; 33 intermittent; 41 chronic; 13 total	Intermittent RR = 1.61; chronic RR = 0.95; total RR = 1.34	

OR, odds ratio; PMR, proportional mortality ratio; RR, relative risk; SIR, standardized incidence ratio; SMR, standardized mortality ratio.

association between melanoma and outdoor workers and indoor non-office workers. A significantly elevated risk was discovered for office workers. This trend remained present when the analysis considered only melanomas on covered parts of the body (trunk, upper limb and lower limb), which suggests that recreational exposure is a cause. However, when melanomas on uncovered parts of the body (eyelids, ear/auricular canal, face and scalp/neck) were investigated, there was an elevated risk for all outdoor workers, implicating occupational exposure as a cause.

Elwood and Jopson [13] conducted a systematic review of all published case–control studies that had assessed melanoma and sun exposure. Studies were identified via many sources including the IARC review and MEDLINE. Results from the studies were classified as relating to intermittent, occupational or total sun exposure. Where possible, estimates that were adjusted for demographic factors and susceptibility characteristics were used. Overall, 29 studies contributed data on sun exposure yielding a significant positive risk for intermittent exposure and a significantly reduced risk for heavy occupational exposure. The authors state that a more detailed analysis of some of the large studies suggests that the relationship between melanoma and occupational sun exposure may be non-linear, with an increased risk related to small amounts of exposure, possibly due to intermittent outdoor work, and a decrease in risk for continued long heavy exposure, possibly due to constant solar radiation exposure resulting in adequate protection mechanisms.

The study conducted by Acquavella *et al.* [8] (described above) also investigated melanoma. Twenty-one studies were analysed resulting in a non-significant pooled random effects estimate of below one. Pooled rates again varied depending on study design. No clear conclusions could be drawn from the results, due to variations in the reported risks both above and below the null hypothesis.

Travier *et al.* [14] used the Swedish Cancer Environment Registry to compare cancer incidence, for the period 1971–1989, among male veterinarians to that of the remaining active population (excluding other occupational groups that have extensive contact with animals). Within the group, individuals were categorized into one of three subgroups: veterinarians in the veterinary industry, veterinarians in other industries and other workers in the veterinary industry. For males identified as employed in the veterinary industry, a significant increase in risk was observed. Estimates were adjusted for age, calendar period, geographic region and urban setting. The authors conclude that the excesses observed for melanoma could not be explained by the high socio-economic status of veterinarians, as the excess remained when comparisons were made with other high socio-economic groups.

A meta-analysis investigating sun exposure and melanoma found a positive association for intermittent exposure and an inverse association with high continuous exposure [15]. Relative risks for sun exposure were extracted from 41 studies published prior to September 2002 that investigated chronic (occupational) sun exposure. The majority of studies were carried out in European countries. There were several studies that presented risk estimates lower than one indicating an inverse association; however, the majority of these were non-significant. The pooled estimate showed a slight inverse association but was again non-significant. Further analyses showed that the variability between studies could be explained by 'inclusion of controls with dermatological diseases' and 'latitude'. It was shown that living at higher latitudes gave a greater association between chronic sun exposure and melanoma.

There is uncertainty regarding the mechanism by which melanoma develops in relation to different types of solar exposure (frequent or intermittent) and the relationship with potential cofactors such as age, gender and social class. The key epidemiologic evidence described above shows that there is a clear association between melanoma and solar UVR. The increased risk can mainly be attributed to recreational exposure. However, occupational solar exposure cannot be totally ruled out, as outdoor workers, farmers and veterinarians have been shown to be at increased risk. It appears that episodic exposure is more dangerous than continuous exposure, which can occur in an occupational setting but in studies tends to be combined with recreational exposure. Due to this difficulty in classifying solar exposure as occupational or recreational, and thus being treated as a single exposure, there have been negative associations found, which are misleading.

#### Protective and precautionary measures

It is accepted that overexposure to solar UVR is the main underlying cause of skin damage [16]. Many experts believe that 80% of skin cancer cases could be prevented by avoiding UVR damage. There are many measures that individuals and employers can put into practice to help minimize their risk of skin cancer of all kinds:

- Limit exposure particularly at solar noon. If possible schedule work to minimize exposure.
- UV index gives an indication of how strong the solar UVR rays are. The higher the index the higher the risk.
- Shade: take breaks in the shade, particularly lunch breaks and site water points and rest areas in the shade. Remember that UVR can be reflected from surrounding surfaces and some structures such as trees and umbrellas do not offer complete protection.
- Protective clothing: wear loose-fitting clothing that covers as much skin as possible, wide-brimmed hats with neck protection and sunglasses.
- Sunscreen: use a sunscreen with sun protection factor of 15 or higher that protects against UVA and UVB. Reapply frequently as it is easily washed off or rubbed off on clothes.
- Water: drink plenty of water to avoid dehydration.
- Self checks: check skin regularly for any unusual changes or moles.
- Training: alert all employees to the potential problems of overexposure and how to minimize the risk, including the factors that influence UVR levels.

#### Conclusions

This review shows that there is a clear positive association between solar UVR and all types of skin cancer. Cases of NMSC, particularly SCC, can be attributed to occupational exposure as well as recreational exposure. Intermittent exposure, which can occur occupationally, has been found to induce melanoma.

Information from key studies has been combined to highlight how solar UVR exposure is related to the three main forms of skin cancer. The studies provide evidence that all types of exposure are important. However, the difficulty in determining occupational exposure, which varies considerably between studies, complicates the interpretation of results from reviews and meta-analyses. Occupational exposure tends to be thought of as long continuous exposure, which can lead to biased estimates: from intermittent occupational exposure being grouped with recreational exposure. Some studies attempt to overcome this problem by calculating complete exposure from detailed questionnaires, but this can be troubled by recall bias.

Future studies need to investigate the relationships further and answer questions such as how similar/different are the induction mechanisms between the cancers, and is there a dose–response relationship such that after a certain amount of exposure the damage has already been done. For reliable results to be obtained, measurements of exposure need to be improved, along with eliminating the perception that occupational exposure has to be long and continuous.

It is apparent that there are different induction mechanisms for BCC, SCC and melanoma, although there may be similarities between BCC and melanoma. Protective measures should be taken against all types of solar radiation (recreational, occupational, intermittent and continuous) to minimize the risk of developing any form of skin cancer.

## **Conflicts of interest**

None declared.

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