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Global evidence on occupational sun exposure and keratinocyte cancers: a systematic review

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The authors declare they have no conflicts of interest.

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Summary

Individual studies have suggested that the association between occupational exposure to solar ultraviolet radiation (UVR) and the development of keratinocyte cancers (KCs) may only be valid in populations of European ancestry living in certain geographical regions. Comparative global data are scarce and so this review aimed to summarize current evidence on the association between occupational exposure to solar UVR and the development of KCs, with a specific focus on geographical location and skin colour. Ovid MEDLINE, PubMed, Embase and Web of Science were searched for potentially relevant records. Extracted data were summarized by study, country and region. We included one prospective cohort study and 18 case–control studies (n = 15 233) from 12 countries in regions where the majority of the population is white skinned (Americas, Europe and Oceania). Eighteen of the 19 studies reported effect estimates suggesting an increased risk of basal cell carcinoma (BCC) and/or squamous cell carcinoma (SCC) among outdoor workers. Only 11 studies found a significantly increased risk and many had imprecise estimates. There was a significantly increased risk of BCC and SCC in individual studies in North America, Latin America and the Caribbean, Western Europe and Southern Europe, but not across regions or countries. Overall, 95% of studies reported higher risks among outdoor workers, although the increases in risk were statistically significant in just over half of the studies. Well-designed and sufficiently powered occupational case–control and cohort studies with adequate adjustment for confounding factors and other risk factors are required to provide more accurate risk estimates for occupational KC.

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Keratinocyte cancers (KCs; basal cell carcinoma and squamous cell carcinoma; BCC and SCC, respectively) are the most common cancers in fair-skinned populations across the world.[1] The incidence of KC varies widely by geographical location and ethnic skin type.[2,3] Solar ultraviolet radiation (UVR) is the main cause of KC in fair-skinned populations, which are predominantly of European ancestry, accounting for approximately 50–90% of BCCs and 50–70% of SCCs.[4,5] Outdoor workers are a population susceptible to developing this type of cancer due to chronic or intermittent occupational solar UVR exposure depending on the nature of their job.

One challenge within the occupational KC literature is that different countries and organizations use various operational definitions for outdoor work. In Germany, a UVR-exposed outdoor worker, based on personal dosimetric measurements, is a person exposed to 1 h per day of work outside between

11·00 h and 16·00 h for > 50 days between April and October.[6] The European Agency for Safety and Health at Work defines an outdoor worker as someone who spends > 75% of their working time outdoors,[7,8] which is the same cutoff used by CAREX Canada to define workers with high occupational exposure.[9] This review considered a broader definition of an outdoor worker used in other studies,[10,11] namely someone working either indoors and outdoors (mixed) or only outdoors who is occupationally exposed to solar UVR.

Earlier systematic reviews, from around 10 years ago, showed that outdoor workers exposed to solar UVR are at an increased risk of BCC[12] and SCC.[13] In these meta-analyses, outdoor workers were 77% and 43% more likely to develop SCC and BCC, respectively, compared with indoor workers.[12,13] Evidence suggests that the risk of BCC and SCC among outdoor workers exposed to solar UVR increases with cumulative exposure.[14,15] Latitude is a major factor affecting ambient solar UVR, as shown by the strong inverse association with the UV index[16] at a specific geographical location. Therefore, the geographical locations where outdoor work activities are performed play an important role in influencing workers' total UV dose. This review aims to provide an update and summarize the current evidence on the association between occupational exposure to solar UVR and the development of KC by geographical region accounting for skin colour, where available.

Methods

We adapted a recently published protocol[17] as a framework to update the literature on the association between outdoor work and the development of occupational BCC and SCC by country or region, and if possible by skin type.

Eligibility criteria

We selected analytical observational studies including case–control, cohort and interventional studies to be included in the systematic review if they reported effect estimates on the association between BCC or SCC development and occupational exposure to solar UVR in outdoor workers. Studies reporting a combined effect estimate for more than one country, or only for KC (also known as nonmelanoma skin cancer) as a combined outcome were excluded from the review.

Information sources, search and study selection

The search proposed by Paulo *et al.*[17] to review the effect of occupational exposure to solar UVR and melanoma and nonmelanoma skin cancer was refined to search for BCC and SCC in four electronic databases (Ovid MEDLINE, PubMed, Embase and Web of Science) up to 31 December 2019. Duplicates were removed and a two-stage study selection was conducted using Covidence software.[18,19] Two review authors independently screened records against the eligibility criteria for titles and abstracts (step 1) and then for the full texts of potentially relevant records (step 2). A third independent review author resolved any conflicts.

Data collection process and items

One reviewer extracted the data and two reviewers independently double-checked the accuracy of the data extracted, which included study ID, population (including skin colour of study participants), study design, data collection period, setting of the study, country, latitude, UV index (average spring–summer), occupation ascertainment method, the occupational exposure definition used and the ascertainment method (including blinding status), nonoccupational exposure ascertainment, sample size (and its calculation), type of KC and outcome ascertainment method, and reported effect estimates [odds ratio (OR) and 95% confidence interval (CI)].

Summary measures and synthesis of results

A narrative synthesis is presented and summarized by study, country and region, as defined by the United Nations (UN) geoscheme, which divides countries into regional and subregional groups.[20]

Assessment of study quality

The Newcastle–Ottawa Scale[21] was used to assess the quality of the included studies. Each cohort or case–control study was evaluated on eight items grouped into three domains: selection, comparability of groups, and outcome/exposure ascertainment. Each item on the scale is scored one point (maximum score of eight), with lower scores indicating poorer-quality studies.

Results

Study selection and characteristics

In total 1732 records were identified from four electronic databases, and 19 study records satisfied the eligibility criteria (Figure 1). Twelve studies presented data on BCC, three studies on SCC, and four studies on both BCC and SCC (Tables 1–3).

The review included one prospective cohort study and 18 case–control studies ($n = 15\ 233$) from 12 countries in three UN regions where the majority of the population has white skin (Americas, Europe and Oceania) and six UN subregions (Northern America, Latin America and the Caribbean, Northern Europe, Western Europe, Southern Europe, and Australia and New Zealand) (Figure 2). The most commonly studied UN regions were Europe (10 studies) and the Americas (seven studies) (Figure 2). Detailed information on each included study is provided in Table S1 (see Supporting Information).

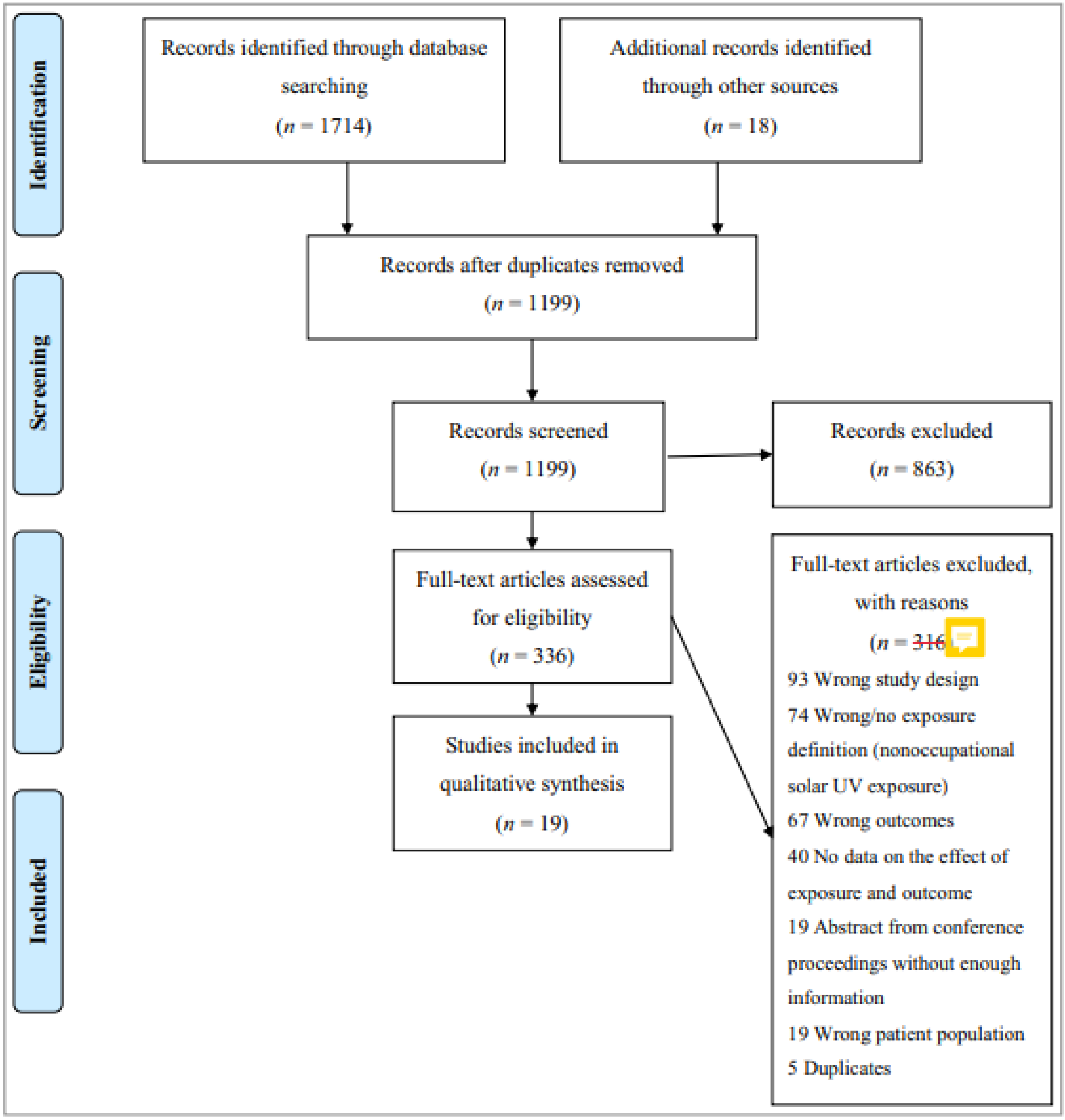

Figure 1. PRISMA flowchart. UV, ultraviolet.

Americas

North America

Three studies were from Canada[22,23,26] and two from the USA.[24,25] Aubry and MacGibbon[22] reported that patients with SCC were nine times more likely to be exposed to occupational sunlight exposure in Montreal; however, the 95% CIs were extremely wide (0·99–84·5) and caution is required when interpreting this risk estimate (Table 1). Gallagher et al.[23,26] did not find a significant relationship between BCC[26] or SCC[23] and mean lifetime occupational sun exposure (thousand hours accumulated) in Alberta (Table 1). Iannacone et al.[24] reported that patients with SCC but not patients with BCC in Florida were 50% more likely to report a job in the sun for ≥ 3 months, although the risk was estimated imprecisely. With regard to prolonged exposure, Iannacone et al.[24] found that patients with BCC or SCC in Florida were 2·0–2·5 times more likely to report a history of working in the sun for ≥ 3 months per year for a duration of at least 10 years compared with clinic-based controls (Table 1). Marehbian et al.[25] found that patients with BCC or SCC in New Hampshire were 3·2–3·3 times more likely to report working as groundkeepers and gardeners and 2·8–3·0 times more likely

Table 1 Study characteristics: North America

Study	KC type	Setting, region, country	n	Data collection period	Exposure ascertainment	OR (95% CI) (most adjusted)		Latitude (UVI)
Aubry 1985[22]	SCC	Multicentre hospital, Montreal, Canada	266	1977–78	SAQ	Occupational sun exposure	RR 9·1 (0·99–84·5)	46° N (5·5)[b]
Gallagher 1995a[26]	BCC	Cancer registry, Alberta, Canada	632	1983–84	SI	Mean occupational sun exposure per year (lifetime) in hours per week[a] 14·0–24·9 ≥ 25·0	 1·3 (0·8–2·3) 1·4 (0·8–2·4)	54° N (5·5)[b]
Gallagher 1995b[23]	SCC	Cancer registry, Alberta, Canada	586	1983–84	SI	Mean occupational sun exposure per year (lifetime) in hours per week[a] 14·0–24·9 ≥ 25·0	 1·5 (0·6–4·2) 1·4 (0·4–4·3)	54° N (5·5)[b]
Iannacone 2012[24]	BCC/SCC	Hospital, Florida, USA	703	2006–08	SAQ	Job in the sun ≥ 3 months per year, > 10 years[a]	BCC 2·1 (1·1–4·3); SCC 2·4 (1·1–5·2)	28° N (6)[c]
Marehbian 2007[25]	BCC/SCC	Population, New Hampshire, USA	1413	1994–95	Job category as proxy using the SOC	Farmers[a] Farm operators[a] Related agriculture occupational[a] Gardeners[a]	BCC 2·2 (0·9–5·1) BCC 2·0 (0·9–4·6) BCC 2·8 (1·4–5·6); SCC 3·0 (1·3–6·8) BCC 3·2 (1·5–6·8); SCC 3·3 (1·4–7·8)	43° N (7)[b]

Additional information is provided in Table S1 (see Supporting Information). All cases were histopathologically confirmed. BCC, basal cell carcinoma; CI, confidence interval; KC, keratinocyte cancer; OR, odds ratio; RR, relative risk; SAQ, self-administered questionnaire; SCC, squamous cell carcinoma; SI, standardized interview; SOC, Standard Occupational Classification; UVI, ultraviolet index (spring–summer average). [a]Selected occupational exposure categories. [b]UVI from the World Health Organization INTERSUN Programme.[16] [c]UVI estimated from World Weather (www.worldweatheronline.com).

to report working in related agricultural occupations (Table 1). Marehbian *et al.*[25] also reported that patients with BCC were 2·0–2·2 times more likely to be farmers (working proprietors) and farm operators or managers; however, the 95% CIs were relatively wide.

Latin America and the Caribbean

There was one study from Brazil[27] and one from Colombia[28] (Figure 2). Maia *et al.*[27] reported that patients with BCC in São Paulo were 4·7 times more likely to be agricultural workers than nonagricultural workers. Sanchez *et al.*[28] did not find a significant relationship between the development of BCC and outdoor occupational activities after the age of 30 years in Colombia (Table 2).

Europe

There were 10 studies from Europe, with one from Northern Europe (Finland),[11] five from Western Europe (Germany[14,15,33,34] and Switzerland)[29] and four from Southern Europe (Italy,[1] Greece,[30] Montenegro[31] and Serbia)[32] (Figure 2 and Table 3).

Northern Europe

Milán 2003[11] conducted a case–control study in disease-discordant twin pairs nested within the Finnish Adult Twin Cohort and did not find a significant relationship between BCC and outdoor workers regardless of sex or zygosity.

Western Europe

Schmitt *et al.*[14,15] conducted a multicentre case–control study in Germany and found that patients with BCC or SCC were twice as likely to have been exposed to high doses of occupational solar UVR during their lifetime compared with population-based controls. Kaskel *et al.*[33] also found that patients with BCC in Germany were nearly two times more likely to be outdoor workers and three to five times more likely to be part-time and full-time farmers (respectively) compared with hospital-based controls. Walther *et al.*[34] reported that patients with BCC in Germany were twice as likely to report frequent or sometimes exposure to occupational solar UVR compared with rare or never, and three to five times more likely to be part-time and full-time farmers compared with hospital-based controls. Rosso *et al.*[29] conducted a cancer-registry-based case–control study in Switzerland and did not find a significant association between SCC and cumulative lifelong occupational exposure to solar UVR (Table 3).

Southern Europe

In Serbia, Vlajinac *et al.*[32] found that patients with BCC were four times more likely to work outside during the summer than

Table 2 Study characteristics: South America and Oceania

Study	KC type	Setting, region, country	n	Data collection period	Exposure ascertainment	OR (95% CI) (most adjusted)		Latitude (UVI)
South America								
Maia 1995[27]	BCC	Hospital, São Paulo, Brazil	777	1991–92	SAQ	Agricultural activity	4·7 (2·7–8·1)	24° S (11)[a]
Sánchez 2012[28]	BCC	Hospital, Bogotá, Colombia	406	2010	SQ	After age of 30 years	1·7 (0·8–3·4)	5° N (4)[a]
Oceania								
Green 1996[10]	BCC/ SCC	Population, Nambour, Queensland, Australia	2049	1985–87	SAQ	Mixed	BCC 1·1 (0·8–1·5) [illegible] 0·8 (0·5–1·4)	27° S (7·3)[b]
						Outdoor	BCC 1·3 (0·9–1·8); SCC 1·4 (0·8–2·3)	
Kricker 1995[35]	BCC	Population, Geraldton, Australia	901	1987–88	SI	Accumulated occupational exposure (thousand h) 09·00–17·00 h from age 15 years		29° S (7·3)[b]
						14·8–27·7	1·23 (0·8–1·9)	
						27·8–49·3	1·2 (0·7–1·9)	
						≥ 49·4	0·9 (0·5–1·5)	

Additional information is provided in Table S1 (see Supporting Information). All cases were histopathologically confirmed. BCC, basal cell carcinoma; CI, confidence interval; KC, keratinocyte cancer; OR, odds ratio; SAQ, self-administered questionnaire; SCC, squamous cell carcinoma; SI, standardized interview; SQ, standardized questionnaire; UVI, ultraviolet index (spring–summer average). [a]UVI estimated from World Weather (www.worldweatheronline.com). [b]UVI from the World Health Organization INTERSUN Programme.[16]

dermatology clinic controls. Jankovic *et al.*[31] reported that patients with BCC in Montenegro were 26% more likely to report outdoor work in the summer than dermatology clinic controls in the univariate analysis (95% CI 1·10–1·44); however, the strength of the association increased and the precision of the estimate decreased in the multivariate analysis (OR 2·73, 95% CI 1·00–7·45) (Table 3). The data presented in the manuscript were not sufficient to determine the cause(s) for this observation, but it is most likely due to confounding and/or different sample sizes used in the univariate vs. the multivariate model (i.e. listwise deletion of participants from the multivariate model with missing covariate data). In Greece, Dessinioti *et al.*[30] reported that patients with BCC were 1·2 times more likely to have been exposed to occupational solar UVR than hospital-based controls. In Italy, Pelucchi *et al.*[1] reported an effect estimate for the association between two clinical variants of BCC (nodular and superficial) and outdoor work. Only patients with nodular BCC were more likely (by 53%) to have a history of occupational solar UVR exposure (Table 3).

Oceania

Australia and New Zealand

There were two studies from Australia (Figure 2). Green *et al.*[10] conducted a prospective study in Nambour, Queensland, and reported no significant association between working indoors and outdoors (mixed) or only outdoors with the development of BCC or SCC (Table 2). Kricker *et al.*[35] conducted a case–control study in Western Australia and reported no significant association between the development of BCC and workers in the groups with low, medium or high exposure based on accumulated thousands of hours of occupational exposure (Table 2).

Study quality

The assessment of study quality using the Newcastle–Ottawa Scale is presented in Table 4. Briefly, the one cohort study adequately described selection of the exposed and unexposed groups and ascertainment that BCC and SCC were not present at the start of the study; however, exposure ascertainment was via a standardized self-reported questionnaire. This cohort study adequately controlled for important confounders, and BCC and SCC were histologically confirmed. All case–control studies provided a clear definition of cases (histopathological confirmation) and controls and employed consecutive sampling, and the majority (78%) recruited hospital-based rather than community-based controls. More than half (55%) of the case–control studies ensured comparability of cases and controls through either design (matching) and/or analysis (controlling for pertinent confounders). The majority (58%) of the studies used a standardized interview-administered questionnaire to ascertain exposure, but only three studies reported blinding of the interviewers to disease status (Table S1; see Supporting Information). A lack of blinding might lead to interviewer bias only in studies where the interviewer has the expertise to identify cases (e.g. physicians or dermatologists). More than one-third (37%) used a self-reported questionnaire, and one study (5%) used job category as a proxy. All studies used the same exposure ascertainment method for both cases and controls.

Table 3 Study characteristics: Europe

Study	KC type	Setting, region, country	n	Data collection period	Exposure ascertainment	OR (95% CI) (most adjusted)		Lat. (UVI)
Milán 2003[11]	BCC	Nationwide Finnish Adult Twin Cohort, Finland	29 MZ twins; 192 DZ twins	1976–99	SAQ	Mainly outside	M 0·7 (0·0–1·8)	62° N (3·8)[c]
							F 0·6 (0·2–2·2)	
						Outside and inside	M 0·8 (0·4–1·6)	
							F 0·9 (0·5–1·7)	
Schmitt 2018a[14]	BCC	Population, multicentre, Germany	1672	2013–15	SI	Occupational UV exposure SED[a]		~48–54° N (5)[b]
						0–532·1	0·9 (0·7–1·3)	
						532·2–5870·4	0·9 (0·7–1·2)	
						≥ 5870·5	1·8 (1·2–2·8)	
Schmitt 2018b[15]	SCC	Population, multicentre, Germany	1264	2013–15	SI	Occupational UV exposure SED[a]		~48–54° N (5)[b]
						12·6–863·9	0·80 (0·6–1·1)	
						864–6834·7	1·0 (0·8–1·4)	
						≥ 6834·8	1·9 (1·2–3·2)	
Kaskel 2015[33]	BCC	Hospital, Ulm and Dresden, Germany	832	1997–99	SI	Occupational UV exposure	1·7 (1·2–2·5)	51° N (5)[b]
						Farming FT	4·8 (3·0–7·7)	
						Farming PT	2·7 (1·7–4·3)	
Walther 2004[34]	BCC	Hospital, Ulm and Dresden, Germany	624	1997–99	SI	Occupational UV exposure	2·4 (1·3–4·7)	48° N (5)[b]
						Farming FT	2·8 (1·8–4·3)	
						Farming PT	4·6 (3·0–7·2)	
Rosso 1999[29]	BCC/SCC	Cancer registry, Sion, Switzerland	290	1994–96	SI	Hours of outdoor work[a]		46° N (4·8)[c]
						< 77 200	BCC 0·8 (0·5–1·2)	
							SCC 2·0 (0·6–6·8)	
						≥ 77 200	BCC 0·9 (0·5–1·6)	
							SCC 1·9 (0·3–11·7)	
Vlajinac 2000[32]	BCC	Hospital, Zagreb and Zrenjanin, Serbia	599	2006–07	SI	Outdoor work during summer	3·9 (1·6–9·7)	43° N (4·8)[c]
Jankovic 2010[31]	BCC	Hospital, Podgorica, Montenegro	200	2006–07	SAQ	Outdoor work during summer	2·7 (1·0–7·5)	43° N (5·6)[c]
Dessinioti 2011[30]	BCC	Hospital, Athens, Greece	399	2006–09	SI	Outdoor work	1·2 (0·8–1·9)	38° N (6·5)[b]
Pelucchi 2007[1]	BCC	Hospital, multicentre, Italy	1040	1995–96	SI	Nodular BCC	1·5 (1·1–2·2)	42° N (6)[c]
						Superficial BCC	0·7 (0·4–1·2)	

Additional information is provided in Table S1 (see Supporting Information). All cases were histopathologically confirmed. BCC, basal cell carcinoma; CI, confidence interval; DZ, dizygotic; F, female; FT, full time; KC, keratinocyte cancer; M, male; MZ, monozygotic; OR, odds ratio; PT, part time; SAQ, self-administered questionnaire; SCC, squamous cell carcinoma; SED, standard erythemal dose; SI, standardized interview; UVI, ultraviolet index (spring–summer average). [a]Selected occupational exposure categories. [b]UVI from the World Health Organization INTERSUN Programme.[16] [c]UVI estimated from World Weather (www.worldweatheronline.com).

Discussion

Our systematic review appraises the current body of evidence on the association between occupational solar UVR exposure and the development of KC. Overall, we found that BCC had a stronger association with occupational exposure to solar UVR than SCC. This finding should be interpreted with caution as there was only a limited number of studies available comparing associations with both BCC and SCC. The power of the BCC studies would be substantially greater to detect an

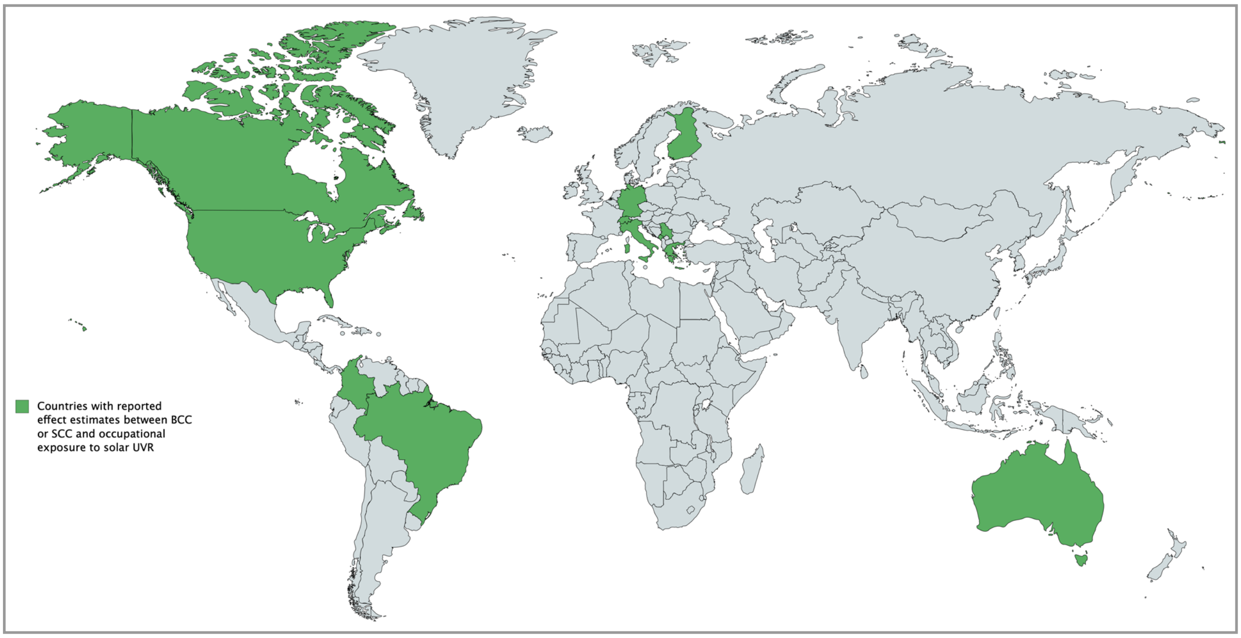

Figure 2. Countries with reported effect estimates for basal cell carcinoma (BCC) or squamous cell carcinoma (SCC) and occupational exposure to solar ultraviolet radiation (UVR).

association with BCC compared with SCC, given that the incidence of BCC is on average double that of SCC.[2] However, from a tumour biological perspective SCC has the stronger association with cumulative UVR exposure,[13] and occupational UVR exposure is typically cumulative.[36]

There was no clear or consistently elevated risk of skin cancer across countries or UN subregions. There was a significantly increased risk of BCC and SCC in individual studies in North America, Latin America and the Caribbean, Western Europe and Southern Europe (USA, Brazil, Colombia, Germany, Italy, Montenegro, Serbia), but the risk was estimated imprecisely as many studies had relatively wide CIs. The current body of evidence from other North American and European countries (Canada, Greece, Switzerland) and from Oceania (Australia) suggests a positive association, but not a statistically increased risk between outdoor work and the development of BCC and/or SCC.

All four studies that reported risk estimates for specific occupations observed a significantly increased risk for agricultural workers, with ORs varying from 1·6 to 4·8 for BCC and 1·9 to 3·3 for SCC. The current body of evidence from Germany showed that patients with BCC or SCC were 1·2–2·8 times more likely to be outdoor workers, and 4·6 times more likely to be farmers. These findings suggest an increased risk for the development of BCC and SCC due to outdoor work, and particularly agricultural-related outdoor occupations.

Our review has highlighted the importance of a systematic approach to estimating the risk of developing occupational KC due to outdoor work. We feel it is crucial to pinpoint the current limitations of the existing data. The majority of the included studies (79%) did not report a sample-size calculation and were probably underpowered to detect modest effect estimates (Table S1; see Supporting Information). Only two studies[14,15] were specifically powered to detect the risk of KC due to occupational solar UVR exposure. Two other studies reported sample sizes for different exposures (i.e. arsenic exposure[25] and skin sensitivity to UVR),[28] and these studies were most likely underpowered to detect a significant relationship between KC and outdoor work.

Adjustment of the reported estimates for the main known confounders for occupational KC (age, sex, skin phototype) might also have played a role in the reported estimates. The majority of the studies accounted for age and sex by matching cases and controls or by adjustment (79% and 58% respectively) for skin colour (73%), nonoccupational solar UVR exposure (26%)[14,15,22,25,28] and history of previous KC (26%)[1,14,15,32,34] (Table S1; see Supporting Information). We noticed that the two studies (Brazil[27] and Germany)[34] that included cases classified as 100% 'white' reported higher effect estimates. Numerous studies had greater proportions of fairer-skinned cases than controls, which might have led to residual confounding even when skin type was adjusted for in the analysis (Table S1; see Supporting Information). We acknowledge that matching cases and controls by skin type might be challenging.

We used rigorous eligibility criteria to screen the studies. We limited inclusion to studies reporting an effect estimate between being chronically or intermittently occupationally exposed to solar UVR and the development of the same KC without occupational solar UVR exposure. Unlike previous reviews,[12,13] we did not include cross-sectional studies as this type of study design does not account for the effect of time between exposure and outcome. Details of the studies that closely met out inclusion criteria but were not included are provided in Table S2 (see Supporting Information).

Table 4 Assessment of study quality using the Newcastle–Ottawa Scale

	Selection				Comparability		Exposure	
Study (cohort studies)	1. Representativeness of the exposed cohort	2. Selection of the nonexposed cohort	3. Ascertainment of exposure	4. Outcome not present at starting	5. Comparability of the cohort(s)	6. Outcome assessment	7. Length of follow-up	8. Adequacy of follow-up
Green 1996[10]	♦	♦		♦	♦	♦		♦
Study (case–control studies)	Selection				Comparability		Exposure	
	1. Adequate case definition	2. Representativeness of the cases	3. Selection of Controls	4. Definition of Controls	5. Comparability of cases and controls	6. Ascertainment of exposure	7. Same method of ascertainment for cases and controls	8. Nonresponse vrate
Aubry 1985[22]	♦	♦		♦	♦		♦	
Dessinioti 2011[30]	♦	♦					♦	
Gallagher 1995a[23]	♦	♦	♦	♦	♦	♦	♦	♦
Gallagher 1995b[26]	♦	♦	♦	♦	♦	♦	♦	♦
Iannacone 2012[24]	♦	♦		♦			♦	
Jankovic 2010[31]	♦	♦					♦	
Kaskel 2015[33]	♦	♦					♦	
Kricker 1995[35]	♦	♦		♦		♦	♦	
Maia 1995[27]	♦	♦		♦	♦		♦	
Marehbian 2007[25]	♦	♦	♦	♦	♦	♦	♦	♦
Milán 2003[11]	♦	♦		♦	♦		♦	
Pelucchi 2007[1]	♦	♦	♦	♦	♦		♦	
Rosso 1999[29]	♦	♦	♦	♦	♦		♦	♦
Sanchez 2012[28]	♦	♦		♦	♦		♦	
Schmitt 2018a[14]	♦	♦	♦	♦	♦	♦	♦	
Schmitt 2018b[15]	♦	♦	♦	♦	♦	♦	♦	
Vlajinac 2000[32]	♦	♦		♦			♦	
Walther 2004[34]	♦	♦		♦			♦	

Following the rating sheet of the scale, we have used the symbol '♦' to identify the questions where the criteria were met in the individual studies.

Despite the rigour of our review, the available evidence has several limitations. There was minimal literature available and the studies were conducted in a limited number of countries, with no data for Africa or Asia. Profound heterogeneity was observed across studies due to a lack of a standard definition of occupational sun exposure. Of the included studies, 95% had case–control designs using self-reported exposure history, which is prone to recall bias. There was a limited body of evidence to permit further analysis of the influence of latitude on the relationship between occupational exposure to solar UVR and KC. From the six studies at a latitude between 43° N and 48° N, two[25,34] reported that patients with BCC or SCC were three to five times more likely to work in agricultural-related occupations. Four studies were conducted at a latitude of 24–29° N/S, and two of these studies[24,27] reported a significant association between the development of BCC and SCC and occupational exposure to solar UVR (Tables 1 and 2). The study with the lowest latitude, 5° N, reported that outdoor workers were 1·8–2·3 times more likely to be diagnosed with BCC.[28] The limited latitude span prevented a more detailed analysis of the variation in risk across latitude and by average annual UV index. We were also not able to quantify precisely the UV index for the specific location and time period where the exposures occurred.

Two earlier systematic reviews and meta-analyses (published nearly 10 years ago) on occupational solar UVR exposure and BCC[12] and SCC[13] reported that the risks of SCC and actinic keratosis were raised by 77%, and the risk of BCC was raised by 43%, for outdoor workers compared with populations not exposed to outdoor work.[12,13] Both systematic reviews included cohorts and case–control studies not focusing primarily on occupationally exposed skin areas. The authors did not take into account individual UVR sensitivity or personal-leisure UVR exposure, but, as discussed previously, this might be due to the lack of data available. Both reviews concluded that there was consistent epidemiological evidence for a positive association between occupational solar UVR exposure and BCC and SCC. The meta-analyses found an increased strength of the association between occupational solar UVR exposure and KC risk with decreasing latitude. Our updated systematic review included six new studies published in the last 9 years and we did not find consistent evidence on the significant relationship between occupational solar UVR exposure and KC.

KC is a recognized occupational disease in eight European countries but is rarely reported.[37–39] As our results and previous studies show,[37,40] Germany is one of the countries reporting a significantly increased risk for outdoor workers to develop KC. Since July 2019, employers in Germany have been specifically required to conduct UVR exposure risk assessment, to provide personal protective equipment, and to offer UVR-exposed employees a consultation by an occupational physician every 3 years.[41] German data (> 9000 new cases reported per year; the second most frequently recognized occupational disease) emphasize the need for better registration of cases on a global scale to enable the required regulatory efforts at the political level (www.svlfg.de).[42] The majority of population-based cancer registries do not report KC or provide detailed information about a patient's profession. If KCs are recorded, then only primary tumours are registered, while consecutive tumours are not. The risk of acquiring further KCs after the first lesion has been diagnosed is about 30% in the first year after diagnosis in the general population, and it is expected to be even higher in outdoor workers due to the substantial actinic damage that many experience, making it a highly chronic disease.[40] Gross under-reporting of cases is the reason why preventive efforts are still lacking in most countries. Therefore, the World Health Organization has implemented a new coding mechanism for occupational causation of skin cancer in the *International Classification of Diseases 11th Revision*, which, if consistently used from 2022, should provide more accurate and reliable estimates of the global incidence of occupational KC.

This review highlights the need for well-designed, adequately powered occupational case–control and prospective cohort studies with standardized methods for exposure and outcome ascertainment. In order to provide an accurate and reliable risk estimate for occupational KC related to outdoor work, it is important to collect precise data on lifelong solar UVR exposure including intermittent and chronic recreational exposure during childhood and adulthood, and to control for these exposures in the analysis. Case–control studies require a harmonized approach collecting detailed historical occupational and nonoccupational solar UVR exposure throughout the life course. Prospective cohort studies need to collect personal solar UVR dosimetric exposure data over extended periods of time (e.g. months and possibly years) to provide accurate aggregate estimates.[40] The crux for prospective studies is the long latency between UVR exposure and occurrence of KC, which may be more than a decade.

An alternative to case–control and long prospective cohort studies in some jurisdictions might be data linkage, where employment records are linked to medical service or pathology records. This provides complete follow-up, although the quality of exposure measures would likely vary across industries and thus the risk estimates would need to be interpreted carefully. In addition, data on important confounders usually obtained by self- or interviewer-administered questionnaires would need to be collected. The dearth of data for many regions and countries, such as South Africa, with a large population of European ancestry, highlights the need for further research. This would be facilitated by an international consortium tasked with harmonizing study designs and reporting across and within countries.

In conclusion, our review appraises and summarizes the latest evidence on occupational KC. Overall, 95% of the studies reported higher risks among outdoor workers, although the increases in risk were statistically significant in just over half of the studies. There was no clear elevated risk of skin cancer across countries, UN subregions, latitude or skin types. This is probably due to the lack of high-quality data from heterogeneous studies. Well-designed and sufficiently powered occupational case–control and prospective cohort studies with adequate adjustment for confounding factors and other risk factors are required to provide more accurate risk estimates for occupational KC.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Table S1 Comprehensive table of the study characteristics.

Table S2 Studies reporting an effect estimate between outdoor work and keratinocyte cancer that closely meet our inclusion criteria.