The effect of occupational exposure to solar ultraviolet radiation on malignant skin melanoma and non-melanoma skin cancer:

a systematic review and meta-analysis from the WHO/ILO Joint Estimates of the Work-related Burden of Disease and Injury

World Health Organization

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List of abbreviations

BCC	basal cell carcinoma
CI	confidence interval
DNA	deoxyribonucleic acid
GATHER	Guidelines for Accurate and Transparent Health Estimates Reporting
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IARC	International Agency for Research on Cancer
ICD-10	International Statistical Classification of Diseases and Related Health Problems 10th Revision
ILO	International Labour Organization
ISIC	International Standard Industrial Classification of All Economic Activities
NIOSH	United States National Institute for Occupational Safety and Health
NMSC	non-melanoma skin cancer
OR	odds ratio
RR	relative risk
SCC	squamous cell carcinoma
SED	standard erythemal dose
USA	United States of America
UVA	ultraviolet A
UVB	ultraviolet B
UVC	ultraviolet B
UVR	ultraviolet radiation
WHO	World Health Organization

Abstract

A systematic review and meta-analysis of studies were conducted reporting on the association between occupational exposure to solar ultraviolet radiation (UVR) and both malignant skin melanoma (melanoma) and non-melanoma skin cancer (NMSC), with the aim of enabling the estimation of the numbers of deaths and disability-adjusted life years from melanoma and NMSC attributable to occupational exposure to solar UVR, for the development of the World Health Organization (WHO)/International Labour Organization (ILO) Joint Estimates of the Work-related Burden of Disease and Injury (WHO/ILO Joint Estimates).

A protocol was developed and published, applying the Navigation Guide as an organizing systematic review framework where feasible. Electronic bibliographic databases were searched for potentially relevant records; electronic grey literature databases and organizational websites were also searched, reference lists of previous systematic reviews and included study records were hand-searched, and additional experts were consulted. Randomized controlled trials and cohort, case–control and other non-randomized studies were included that estimated the effect of any occupational exposure to solar UVR, compared with no occupational exposure to solar UVR, on melanoma (excluding melanoma of the lip or eye) or NMSC prevalence, incidence or mortality. At least two reviewers independently screened titles and abstracts against the eligibility criteria at a first stage and full texts of potentially eligible records at a second stage. Adjusted relative risks were combined using random-effects meta-analysis. Two or more reviewers assessed the risk of bias, quality of evidence and strength of evidence.

Fifty-three (48 case–control, three case–case and two cohort) eligible studies were found, published in 62 study records, including over 457 000 participants in 26 countries of three WHO regions (Region of the Americas, European Region and Western Pacific Region), reporting on the effect on melanoma or NMSC incidence or mortality. No studies on the prevalence of melanoma or NMSC were found. In most studies, exposure was self-reported in questionnaires during interviews and the health outcome was assessed via physician diagnosis based on biopsy and histopathological confirmation. The risk of bias of the body of evidence was judged to be generally "probably low", although there were some concerns regarding risks of exposure misclassification bias, detection bias and confounding.

The main meta-analyses of relevant case–control studies revealed a relative risk (RR) of melanoma and NMSC incidence of 1.45 (95% confidence interval (CI): 1.08–1.94; I^2 = 81%) and 1.60 (95% CI: 1.21–2.11; I^2 = 91%), respectively. No statistically significant differences in risk of melanoma and NMSC incidence were found when conducting subgroup analyses by WHO region, and no differences in risk of NMSC incidence in a subgroup analysis by sex. However, in a subgroup analysis by NMSC subtype, the increased risk of basal cell carcinoma (RR: 1.50; 95% CI: 1.10–2.04; 15 studies) was probably lower (P = 0.05 for subgroup differences) than the

increased risk for squamous cell carcinoma (RR: 2.42; 95% CI: 1.66–3.53; 6 studies). The sensitivity analyses found that effect estimates of NMSC incidence were significantly higher in studies with any risk of bias domain rated as "high" or "probably high" compared with studies with only a "low" or "probably low" risk of bias, and in studies not reporting the health outcome by International Statistical Classification of Diseases and Related Health Problems (ICD) code compared with the two studies reporting ICD codes. The quality of available evidence of the effect of any occupational exposure to solar UVR on melanoma incidence and mortality and on NMSC mortality was rated as "low", and the quality of evidence for NMSC incidence was rated as "moderate".

The strength of the existing bodies of evidence reporting on occupational exposure to solar UVR was judged as "inadequate evidence for harmfulness" for melanoma mortality and NMSC mortality. For the health outcome of melanoma incidence, the strength of evidence was judged as "limited evidence for harmfulness", that is, a positive relationship was observed between exposure and outcome where chance, bias and confounding cannot be ruled out with reasonable confidence. For the health outcome of NMSC incidence, the strength of evidence was judged as "sufficient evidence of harmfulness", that is, a positive relationship is observed between exposure and outcome where chance, bias and confounding can be ruled out with reasonable confidence. The 2009 International Agency for Research on Cancer classification of solar UVR as a Group 1 carcinogen that causes cutaneous melanoma and NMSC is a compelling attribute for the strength of evidence on occupational exposure to solar UVR and skin cancer incidence. Producing estimates for the burden of NMSC attributable to occupational exposure to solar UVR appears evidence-based (while acknowledging the limitations of the bodies of evidence), and the pooled effect estimates can be used as input data for the WHO/ILO Joint Estimates.

Keywords

Systematic review; meta-analysis; ultraviolet radiation; sunlight; outdoor work; occupational risk factors; skin neoplasms; melanoma; non-melanoma skin cancer.

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CHAPTER 1
Introduction

It has been scientifically established that solar ultraviolet radiation (UVR) causes malignant skin melanoma (melanoma) and non-melanoma skin cancer (NMSC), both basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) of the skin, in humans *(1)*. Identification of the patterns of mutations induced by solar radiation in humans, in assays of animals treated with UVR and in human cell line experiments has provided solid evidence of the carcinogenicity of UVR; the International Agency for Research on Cancer (IARC) *Monographs* (volume 100D published in 2012) therefore classified solar radiation as carcinogenic to humans (Group 1), concluding that it induces different types of skin cancer *(2)*. This confirmed an IARC assessment from 1992 *(2, 3)*.

Evidence from mechanistic data suggests that occupational exposure to solar UVR may cause melanoma and NMSC in the population. Sunlight is the main source of UVR exposure in men. Occupations, occupational groups and job tasks that include outdoor work entail exposure to solar UVR, which represents a potential cancer hazard; the effect of this occupational exposure is modified by geographical, climate, genetic and behavioural parameters. However, in the IARC *Monograph* covering solar radiation *(2)*, studies of occupational exposure to natural sunlight and skin cancer were not assigned their own section but discussed jointly with different sources of exposure (i.e. environmental, recreational and occupational) and different cancer types.

One of the aims of the World Health Organization (WHO)/International Labour Organization (ILO) Joint Estimates of the Work-related Burden of Disease and Injury (WHO/ILO Joint Estimates) is to quantify the previously unknown burdens of melanoma and NMSC attributable to occupational exposure to solar UVR, if feasible, as two additional pairs of risk factor and health outcome. To assess the feasibility of the inclusion of this occupational risk factor in the WHO/ILO Joint Estimates, and to ensure that potential estimates of burden of disease are reported in adherence with the *Guidelines for Accurate and Transparent Health Estimates Reporting* (GATHER) *(4)*, a systematic review and meta-analysis were conducted of studies on the association between occupational exposure to solar UVR and the prevalence and incidence of, and mortality from, melanoma and NMSC. The systematic review and meta-analysis were pre-registered in PROSPERO, and followed the relevant pre-published peer-reviewed protocol *(5)*. In conducting the systematic review and meta-analysis, parameters with the best and least biased evidence for the estimation models were selected, and the evidence from observational epidemiological studies up to 2019 on occupational exposure to solar UVR and risk of melanoma and NMSC was presented and summarized.

WHO and the ILO have conducted or are conducting several other systematic reviews and meta-analyses on other additional pairs of risk factor and health outcome *(6–21)*, and have

produced novel systematic review tools for these *(22)*. These are the first systematic reviews and meta-analyses (with a pre-published protocol) conducted specifically for an occupational burden of disease study. An editorial provides an overview of this series of systemic reviews and meta-analyses from the WHO/ILO Joint Estimates and outlines its scientific, methodological, policy and other innovations *(23)*.

The WHO/ILO joint estimation methodology and the WHO/ILO Joint Estimates are separate from these systematic reviews, and are described in more detail and reported elsewhere. The WHO/ILO Joint Estimates are based on existing WHO and ILO methodologies for estimating the burden of disease for selected occupational risk factors *(24–27)*. Population-attributable fractions *(28)* – the proportional reduction in burden from the health outcome achieved by a reduction of exposure to the risk factor to zero – are being calculated for each additional risk factor and outcome pair. These fractions are then being applied to the total disease burden envelopes for the health outcome from the WHO *Global Health Estimates* for the years 2000–2016 *(29)*. WHO/ILO Joint Estimates have recently been published of the global, regional and national burdens of ischaemic heart disease and stroke attributable to exposure to long working hours for 194 countries for the years 2000, 2010 and 2016 *(30)*.

Workers in both the formal economy and the informal economy were considered. Economies defined by level of formality may differ in terms of occupational risk factors and exposure effects. The informal economy is defined as "all economic activities by workers and economic units that are – in law or in practice – not covered or insufficiently covered by formal arrangements" *(31)*. It does not comprise "illicit activities, in particular the provision of services or the production, sale, possession or use of goods forbidden by law, including the illicit production and trafficking of drugs, the illicit manufacturing of and trafficking in firearms, trafficking in persons and money laundering, as defined in the relevant international treaties" *(31)*.

1.1 Previous systematic reviews and meta-analyses

1.1.1 Melanoma

Four existing peer-reviewed systematic reviews and meta-analyses on the effect of occupational exposure to solar UVR on melanoma were identified (Table 1). The 1995 meta-analysis of Nelemans et al. *(32)* reported a reduction in odds of 27% among those exposed to chronic sunlight, which was used as a proxy for occupational exposure (odds ratio (OR): 0.73; 95% confidence interval (CI): 0.60–0.89; 15 studies). Elwood and Jopson's 1997 review *(33)* reported a reduction in odds of 14% among those with occupational exposure to solar UVR (OR: 0.86; 95% CI: 0.77–0.96; 20 studies; 6517 cases of melanoma). Published in 2005, the review by Gandini et al. *(34)* considered the association between melanoma and chronic sun exposure, which "indicated 'a continuous or more continuous pattern of sun exposure' and … was measured essentially entirely as occupational exposure". Gandini et al. found a slight reduction in melanoma risk with occupational exposure to solar UVR (relative risk (RR): 0.95; 95% CI: 0.87–1.04; 40 studies with 42 datasets). The 2015 review by Jiang et al. *(35)* of 10 studies reported that, in the five studies with relevant evidence, "outdoor occupational UVR exposure was significantly associated with incidence of melanoma". A 2006 WHO review that investigated the association between occupational exposure to solar UVR and melanoma found that only one study out of eight reported a statistically significant positive association *(36)*.

Table 1. Previous systematic review or meta-analytic evidence on the effect of occupational exposure to solar ultraviolet radiation on malignant skin melanoma

Author, year	Type of review	No. studies included	No. participants/ cases/ person-years	Summary of review findings	Quality assessment and rating
Nelemans et al., 1995 *(32)*	Meta-analysis	15	Unclear	Pooled OR of 0.73 (95% CI: 0.60–0.89) for chronic sunlight exposure; included studies for chronic exposure reported both positive and negative ORs	Only included published study records; funnel plot suggests there may be publication bias (i.e. studies in which no effect was reported for chronic sunlight exposure on melanoma risk may be underrepresented); all studies that reported an OR with some measure of precision were included, irrespective of judged quality
Elwood & Jopson, 1997 *(33)*	Review and meta-analysis	20	6517 cases	Pooled OR of 0.86 (95% CI: 0.77–0.96) with significant heterogeneity (χ^2 = 70%; 22 degrees of freedom; $P < 0.001$) in individual results; eight studies showed increased ORs (statistically significant in four instances) and 12 studies showed reduced ORs (significant in four)	Unclear
Gandini et al., 2005 *(34)*	Systematic review and meta-analysis	40	Unclear	Pooled RR of 0.95 (95% CI: 0.87–1.04); several studies reported estimates of RR < 1, indicating an inverse association with chronic sun exposure (however, CIs often indicated a non-significant estimate); even if there was a problem with heterogeneity (χ^2 = 96%; 41 degrees of freedom; $P < 0.001$), a general suggestion of a slight inverse association emerged from the analysis but was non-significant	No indication of publication bias was found
Jiang et al., 2015 *(35)*	Systematic review	10	Unclear	Six studies found that outdoor occupational UVR exposure was significantly associated with incidence of melanoma; two studies found indoor occupations were significantly associated with melanoma; two studies found no association	All 10 studies were rated as "B" (on a two-point scale), which indicated "systematic review or meta-analysis with limitations and inconsistent findings, cohort study, case–control study or population-based study"

CI, confidence interval; OR, odds ratio; RR, relative risk; UVR, ultraviolet radiation.

1.1.2 NMSC

At least four reviews have synthesized evidence on the effect of occupational exposure to solar UVR on NMSC (Table 2). A systematic review by Schmitt et al. *(37)* in 2010 reported on both SCC and BCC using 26 studies. Schmitt et al. concluded that, although most studies indicated a positive association between occupational exposure to solar UVR and SCC, results were mixed for BCC. The systematic review and meta-analysis on BCC published by Bauer et al. *(38)* in 2011 included 24 studies and reported a 43% increase in odds of BCC for people employed in outdoor work (OR: 1.43; 95% CI: 1.23–1.66). A similar review on SCC was published in 2011 by Schmitt et al. *(39)*, which included 18 studies and reported a 77% increase in odds of SCC among individuals with occupational exposure to solar UVR (OR: 1.77; 95% CI: 1.40–2.22). Both Bauer et al. *(38)* and Schmitt et al. *(39)* reported substantial heterogeneity, but neither detected evidence of publication bias. Both 2011 reviews included study records previously reported on by the same authors in 2010, assessed quality by the Newcastle–Ottawa scale and reported that no single study met the entire range of criteria. The most recent systematic review on NMSC was published by Loney et al. *(40)* (2020, 19 studies). The reviewers concluded that: "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 [United Nations] subregions, latitude or skin types" *(40)*. No meta-analysis was reported, and the quality of the included studies was assessed by the Newcastle–Ottawa scale *(40)*.

Table 2. Previous systematic (or other) review or meta-analytic evidence on the effect of occupational exposure to solar ultraviolet radiation on non-melanoma skin cancer

Author, year	Type of review	No. studies included	No. participants/ cases/ person-years	Summary of review findings	Quality assessment and rating
Schmitt et al., 2010 (37)	Systematic review	26 studies (reported in 25 study records)	382 575 participants in 25 studies; 2 156 336 person-years for one study	In 12 of the 15 studies on SCC there was a positive association between occupational UVR exposure and SCC; in seven studies the relationship was statistically significant (OR: 1.5–4.3); in three studies there was no association Five of the 16 studies on BCC reported a statistically significant positive relationship between occupational UVR exposure and the risk of BCC; the remaining 11 studies reported no statistically significant association, however, four of these were suggestive of a reduced risk	Newcastle–Ottawa scale; no single study met the entire range of criteria

continues...

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Author, year	Type of review	No. studies included	No. participants/ cases/ person-years	Summary of review findings	Quality assessment and rating
Bauer et al., 2011 (38)	Systematic review and meta-analysis	24 studies (5 cohort, 19 case–control)	144 213 participants in 23 studies; 2 156 336 person-years for one study	Eleven studies showed a significant positive relationship between occupational UVR exposure and the risk of BCC (OR: 1.3–4.7); six studies reported a non-significant risk increase; two studies did not find any effect of occupational UVR exposure on BCC risk; five studies showed a non-significant risk reduction for workers in outdoor occupations (OR: 0.74–0.9) Twenty-three studies reported sufficient data to be included in the meta-analysis; pooled OR for the association between outdoor work and BCC risk was 1.43 (95% CI: 1.23–1.66; P = 0.0001); Q-statistic indicated substantial heterogeneity (Q = 149.9; P = 0.0001 for heterogeneity)	Newcastle–Ottawa scale; no single study met the entire range of criteria Meta-regression analysis on the influence of each single study revealed that none of the studies included significantly influenced the study results (pooled ε coefficient: 3.10; 95% CI: 2.72–3.55); no publication bias detected by regressing the study result (adjusted OR) on sample size for case–control (P = 0.48) or cohort (P = 0.26) studies
Schmitt et al., 2011 (39)	Systematic review and meta-analysis	18 studies (6 cohort, 12 case–control)	488 432 participants in 17 studies; 2 156 339 person-years for one study	Sixteen studies found an increased risk of SCC in individuals with occupational UVR exposure compared with individuals without or with lower exposure; positive association reached statistical significance in 12 studies; two studies found no association between occupational UVR exposure and SCC occurrence; no study found an inverse relationship between occupational UVR exposure and SCC occurrence Meta-analysis indicated that individuals with outdoor occupation/occupational UVR exposure are at significantly increased risk of developing cutaneous SCC; pooled OR including all 18 studies was 1.77 (95% CI: 1.40–2.22; P < 0.001; P < 0.001 for heterogeneity; moment-based estimate of between-studies variance, 0.131)	Newcastle–Ottawa scale; no single study met the entire range of criteria Publication bias was not detected by regressing the study result (OR) on sample size adjusting for study type (P = 0.84)
Loney et al., 2020 (40)	Systematic review	19 studies (1 cohort, 18 case–control)	15 233 participants	There was no clear or consistently elevated risk of skin cancer across countries or United Nations subregions; the current body of evidence suggests a positive (but not statistically significant) association between outdoor work and the development of BCC and/or SCC 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 from 1.9 to 3.3 for SCC	Newcastle–Ottawa scale Cohort study: adequate quality Case–control studies: all provided clear definitions of cases; 78% used hospital-based controls; 55% ensured comparability of controls by matching or adjustment; 58% used a standardized questionnaire completed during interview; interviewers in 17% were blinded to case status

BCC, basal cell carcinoma; CI, confidence interval; NMSC, non-melanoma skin cancer; OR, odds ratio; RR, relative risk; SCC, squamous cell carcinoma; UVR, ultraviolet radiation.

1.2 Definition of risk factor

UVR is part of the spectrum of electromagnetic radiation emitted by the sun. It can be divided into three bands of different wavelengths, namely: (i) ultraviolet A (UVA), 315–400 nm; (ii) ultraviolet B (UVB), 280–315 nm; and (iii) ultraviolet C (UVC), 100–280 nm *(36)*.

UVR from artificial sources (e.g. lamps and welding) can include all three bands. In contrast, solar UVR reaching Earth does not include UVC, which is filtered by the ozone layer. The ozone layer also absorbs the majority (~ 90%) of UVB, but UVA passes through the atmosphere almost unchanged from its source.

UVA and UVB are primarily responsible for skin malignancies. UVA penetrates the skin more deeply, reaching the dermis and generating reactive oxygen species capable of damaging deoxyribonucleic acid (DNA). Radiation in the UVB range is almost completely absorbed by DNA in the epidermis. The subsequent damage to DNA appears to be a key factor in the initiation of carcinogenesis in the skin *(36)*.

Estimation of the burden of disease requires an unambiguous definition of the risk factor, risk factor levels and the theoretical minimum risk exposure level (Table 3). The theoretical minimum risk exposure level is the exposure level that would result in the lowest possible population risk, even if it is not feasible to attain this in practice *(28)*. Occupational exposure to solar UVR is defined here as either exposure to at least 0.33 standard erythemal dose (SED, where 1 SED = 100 J/m^2) per day or by proxy of occupation, occupational group, job task or other variable among workers of working age, compared with the minimum risk exposure level (no occupational exposure, or exposure to UVR at < 0.33 SED/day). All of the studies included in this systematic review have defined occupational exposure to solar UVR using proxy measures. One of the studies estimated UVR exposure dosages using an algorithm and information on occupational exposure to solar UVR *(41, 42)*. The operational definitions used to classify study participants as occupationally "exposed" or "unexposed" to solar UVR are described in detail in Section 2.4.2.

Table 3. Definitions of the risk factor, risk factor levels and the minimum risk exposure level in studies assessing the effect of occupational exposure to solar ultraviolet radiation

Concept	Definition
Risk factor	Occupational exposure to solar UVR, defined as exposure to UVA and UVB from solar radiation that reaches the worker's skin
Risk factor level	Two levels: (i) no (or low) occupational exposure to solar UVR (e.g. as defined by exposure to < 0.33 SED/day or through proxy of occupation, occupational group, job task or other variable); and (ii) any (or high) occupational exposure to solar UVR (e.g. as defined by exposure to ≥ 0.33 SED/day or through proxy of occupation, occupational group, job task or other variable)
Theoretical minimum risk exposure level	No (or low) occupational exposure to solar UVR (e.g. as defined by exposure to < 0.33 SED/day or through proxy of occupation, occupational group, job task or other variable)

SED, standard erythemal dose; UVA, ultraviolet A; UVB, ultraviolet B; UVR, ultraviolet radiation.

Source: Adapted from protocol *(5)*.

1.3 Definition of health outcome

The WHO *Global Health Estimates* group health outcomes into standard burden of disease categories *(43)*, based on the standard codes from the *International Statistical Classification of Diseases and Related Health Problems 10th Revision* (ICD-10) *(44)*. The two relevant WHO *Global Health Estimates* categories for this systematic review are II.A.8.a Malignant skin melanoma (ICD-10 code C43) and II.A.8.b Non-melanoma skin cancer (ICD-10 code C44) *(43)*. In accordance with the WHO *Global Health Estimates*, the health outcomes of melanoma and NMSC are defined as conditions with ICD-10 codes C43 and C44, respectively, and therefore with confirmation by histopathology (Table 4). The standard WHO burden of disease categories exclude all other conditions, as does this systematic review, including in situ melanoma and in situ NMSC. All histological subtypes were eligible, including melanoma subtypes (i.e. superficial spreading, nodular and lentigo maligna melanoma).

Table 4. ICD-10 codes and disease and health problems covered by the WHO Global Health Estimates categories II.A.8a Malignant skin melanoma and II.A.8b Non–melanoma skin cancer and their inclusion in the systematic review

ICD-10 code	WHO *Global Health Estimates* cause category	Included in this review
C43	Malignant skin melanoma	Yes
C44	Non-melanoma skin cancer	Yes

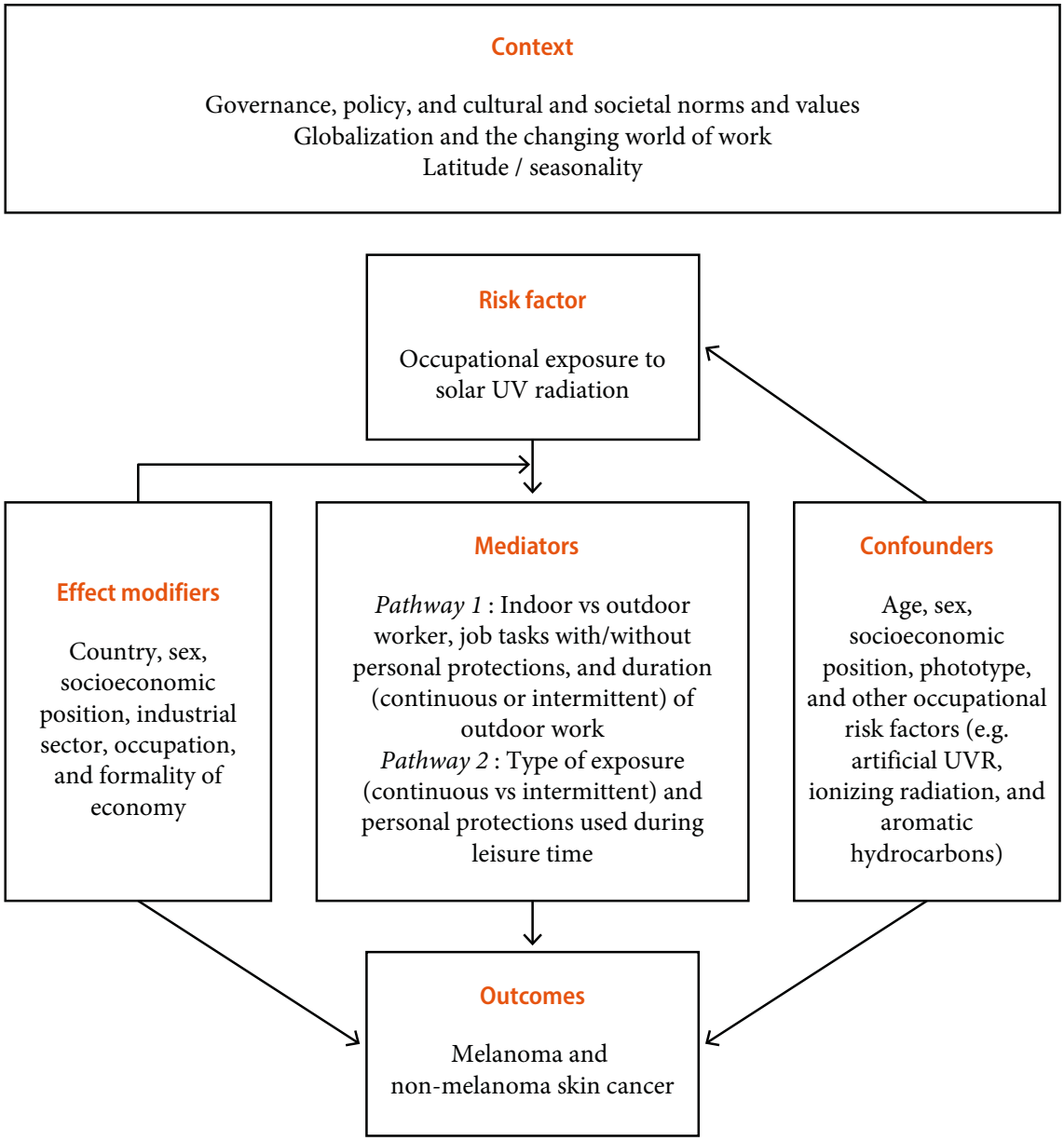
ICD, International Statistical Classification of Diseases and Related Health Problems; WHO, World Health Organization.
Source: Adapted from protocol *(5)*.

1.4 Impact of risk factor on health outcome

Fig. 1 presents the logic model for this systematic review of the causal relationship between occupational exposure to solar UVR and melanoma and NMSC, taken from the published protocol *(5)*. This logic model is an a priori, process-orientated model *(45)* that seeks to capture the complexity of the causal relationship between risk factor and health outcome *(46)*.

Mechanistic or experimental evidence suggests that solar UVR exposure, including in an occupational context, affects the development of melanoma and NMSC through direct (UVB) or indirect (UVA) DNA damage *(47)*. Animal studies support a causal effect of UVR exposure on melanoma and NMSC (see appendix A in the published protocol *(5)*).

Fig. 1. **Logic model of the possible causal relationship between occupational exposure to solar ultraviolet radiation and malignant skin melanoma and non-melanoma skin cancer**



Source: Adapted from protocol (5).

CHAPTER 2
Methods

2.1 Protocol development

The Navigation Guide *(48)* methodology for systematic reviews in environmental and occupational health was applied as the guiding methodological framework, wherever feasible. The guide applies established systematic review methods from clinical medicine, including standard Cochrane methods for systematic reviews of interventions, to the field of environmental and occupational health. The methods ensure systematic and rigorous evidence synthesis on environmental and occupational risk factors that reduces bias and maximizes transparency *(48)*. The need for further methodological development and refinement of the relatively novel Navigation Guide has been acknowledged *(48)*. From the perspective of the Navigation Guide framework, all steps were conducted (i.e. steps 1–6 in fig. 1 in Woodruff et al. *(48)*) for the stream on human data and none of the steps for the stream on non-human data, although the known mechanistic evidence from non-human data was narratively synthesized (Section 1.4 and appendix A of the published protocol *(5)*).

The protocol was registered in PROSPERO under CRD42018094817. The protocol adheres to the preferred reporting items for systematic review and meta-analysis protocols statement (PRISMA-P) *(49, 50)*, with the abstract adhering to the reporting items for systematic reviews in journal and conference abstracts (PRISMA-A) *(51)*. Modifications of the methods stated in the protocol were registered in PROSPERO or reported in the systematic review (Section 6). The systematic review is also reported according to the preferred reporting items for systematic review and meta-analysis statement (PRISMA) *(52)*. Reporting of the parameters for estimating the burdens of melanoma and NMSC attributable to occupational exposure to solar UVR in the systematic review adheres to the requirements of the guidelines for accurate and transparent health estimates reporting (GATHER) *(4)*. The WHO/ILO Joint Estimates to be published following this systematic review must also adhere to these reporting guidelines.

2.2 Literature search

To identify relevant studies for inclusion, several different databases and websites were searched. In some cases, a particular study may have been reported in more than one publication or unpublished document. In this review, "study record" refers to the individual publication or document.

2.2.1 Electronic bibliographic databases

The following electronic bibliographic databases were searched: (i) WHO International Clinical Trials Registry Platform (to 5 October 2020); (ii) Ovid MEDLINE with daily update (1 January 1946–8 August 2018); (iii) PubMed (1 January 1946–8 August 2018, and again to 5 October 2020); (iv) EMBASE (1 January 1947–8 August 2018); and (v) Web of Science (1 January 1945–8 August 2018) with the inclusion of three databases (Science Citation Index Expanded, Social Sciences Citation Index and Arts and Humanities Citation Index).

The original Ovid MEDLINE search strategy is described in the protocol (5). The full search strategies for all databases were revised by an information scientist and are provided in Annex 1. Searches were performed in electronic databases operating in English using a search strategy in English. When completion of the review was imminent, a top-up search of the PubMed database up to 5 October 2020 was conducted to capture the most recent publications (e.g. e-publications ahead of print). Any deviations from the proposed search strategy and the actual search strategy are documented in Section 6.

2.2.2 Electronic grey literature databases

Two electronic grey literature databases were searched in August 2018: OpenGrey (http://www.opengrey.eu) and Grey Literature Report (http://greylit.org).

2.2.3 Internet search engines

Google (www.google.com) and GoogleScholar (www.google.com/scholar) internet search engines were searched and the first 100 hits were screened for potentially relevant records in August 2018, as previously carried out in Cochrane reviews *(53, 54)*.

2.2.4 Organizational websites

The websites of the following international organizations and national government departments were searched in August 2018: (i) ILO (www.ilo.org); (ii) WHO (www.who.int); (iii) European Agency for Safety and Health at Work (https://osha.europa.eu/en); (iv) Eurostat (www.ec.europa.eu/eurostat/web/main/home); (v) China National Knowledge Infrastructure (http://oversea.cnki.net/index); (vi) Finnish Institute of Occupational Health (https://www.ttl.fi/en); and (vii) United States National Institute for Occupational Safety and Health (NIOSH), using the NIOSH data and statistics gateway (https://www.cdc.gov/niosh/data).

2.2.5 Hand-searching and expert consultation

Hand-searches were conducted for potentially eligible studies in: reference lists of previous systematic reviews; reference lists of all study records from all included studies; study records published over the past 24 months in the three peer-reviewed academic journals from which the largest number of included studies were obtained; other study records that cite an already-included study record (identified in Web of Science citation database); and previous publications of the reviewers. The reference list of the IARC *Monograph* volume 100D *(2)* was also hand-searched.

Additional experts were contacted with a list of included studies, with a request to identify further potentially eligible studies.

2.3 Study selection

Study selection was carried out using Covidence software (Veritas Health Innovation, Melbourne, Australia). All study records identified in the search were downloaded, and duplicates were identified and deleted. Two reviewers then independently screened titles and abstracts (step 1) and then screened full texts (step 2) of potentially relevant records. A third reviewer resolved any disagreements between the two reviewers. If a study record identified in the literature search had been authored by a reviewer assigned to study selection, or if an assigned reviewer was involved in the study, the record was reassigned to another reviewer for study selection. The study selection was documented in a flow chart, as per PRISMA guidelines *(52)*.

2.4 Eligibility criteria

The population, exposure, comparator and outcome (PECO) criteria *(55)* are described in the following sections.

2.4.1 Population

Studies of working-age (≥ 15 years) workers in the formal and informal economies were included. Studies of children (aged < 15 years) and unpaid domestic workers were excluded. Studies of participants residing in any Member State of WHO and/or the ILO and any industrial setting or occupational group were included. One occupational or professional group not considered in this report is airplane crew. There are studies that indicate airplane pilots can be exposed to high levels of UVR *(56)*; however, this professional group is exposed to additional sources of radiation and it is difficult to separate the effect of each source on the cancer outcome. In addition, studies investigating the incidence of skin cancers in pilots and other crew personnel often compare the study population with a general population, a comparator that potentially includes people occupationally exposed to solar UVR *(57)*. An overview of the PECO criteria is provided in appendix G of the published protocol *(5)*.

2.4.2 Exposure

Included studies defined solar UVR in accordance with the standard definition used in the systematic review (Table 3). Since only one study *(41, 42)* defined the exposure with reference to exposure limits measured in SED per time unit, the limits considered at the protocol stage *(5)* were found to be insufficient for the systematic review. The most frequently reported exposure definition was exposure via proxy of "outdoor work". In this systematic review, "outdoor work", "being an outdoor worker" or their equivalents are considered as definitive of any occupational exposure to solar UVR or the status of occupationally exposed.

Studies were included that categorized occupational exposure to solar UVR by various proxies: an occupation that was or could be classified as "outdoor worker"; membership of an occupational group categorized as "outdoor workers"; job task categorized as "outdoor worker"; location of work categorized as "outdoor work" or "indoor/outdoor work" (or similar categories such as "mostly outdoor" or "indoor/outdoor"); level of exposure, for example, by the categories "a lot" or "nearly every time"; and lifetime occupational sun exposure categorized as "≥ 50%" or "> 0%, but < 50%".

Cumulative exposure measures were also eligible for inclusion, for example, cumulative dose received (e.g. SED/day) or cumulative duration of exposure (e.g. number of hours, days or

years spent with an occupation or job task classified as "outdoor worker" or as a member of an occupational group classified as "outdoor work").

Studies that defined the exposure purely as one selected occupation (or a small group of occupations only) without prior exposure assignment were excluded. For example, studies that simply described occupation as "farmer" were excluded if the study did not specify which occupations were assigned to the exposed and the unexposed groups. As an illustration, see studies by Marehbian et al. *(58)* or Kachuri et al. *(59)*.

If a study reported two or more exposure categories, then the category that was judged to capture the highest level of exposure was prioritized. For example, if a study reported effect estimates for the exposure categories "mixed indoor/outdoor worker" and "outdoor worker", then the category "outdoor worker" was prioritized because it was assumed that workers exclusively working outdoors are exposed to a higher dose than those exposed to a mixture of indoor and outdoor work.

Studies with objective (e.g. by means of dosimeter) or subjective measurements of occupational exposure to solar UVR were included, including studies that used measurements by experts (e.g. scientists or occupational hygienists with subject matter expertise) or self-reports by the worker, workplace administrator or manager, respectively. If a study presented both objective and subjective measurements, objective measurements were prioritized. Studies with measurements from any data source, including registry data, were included.

2.4.3 Comparator

Studies were included in which the comparator was participants exposed to the theoretical minimum risk exposure level, that is, no (or low) occupational exposure to solar UVR (Table 3). This included studies that categorized such exposure by proxy of: an occupation that was or could be classified as "indoor worker"; membership of an occupational group categorized as "indoor workers"; "indoor work" (e.g. Fortes et al. *(60)*); "mostly indoor" (e.g. Dubin et al. *(61)*); "none/little" (e.g. Nijsten et al. *(62)*); and lifetime occupational sun exposure of "0%" (e.g. Schmitt et al. *(41, 42)*).

Cumulative exposure measures were also eligible for inclusion in the systematic review, for example, no or low cumulative dose received (i.e. Zanetti et al. *(63)*), and no or low cumulative duration of exposure (i.e. Trakatelli et al. *(64)*). For example, if a study assigned exposure based on duration in number of time units (e.g. years), and used a binary exposure definition with a cut-off such as 6 years of working outdoors, working outdoors for ≤ 6 years would be assigned as "unexposed" (comparator) and for > 6 years as "exposed". A study with such a comparator population would be eligible for inclusion in the systematic review.

Studies were only included if their comparators were judged to be reasonably understood as "unexposed". For example, if a cohort study investigated a population over a 40-year period, and compared participants exposed to < 30 years of exposure ("unexposed") with participants exposed to 30–40 years of exposure ("exposed"), this comparator population was not considered to be reasonably unexposed.

Studies with all other types of comparators were excluded. For example, if a study investigated one occupation (e.g. farmer) compared with all other occupations, then it was excluded because the comparator may have had other occupations with outdoor work. In some studies that were excluded (see Annex 2) it was clear that the comparator population did include some exposed study participants or study participants with some level of exposure (including as measured through proxy of duration or intensity of exposure). Studies that used the general

population as the comparator were also excluded, as some members of the general population are very likely to be occupationally exposed to solar UVR.

2.4.4 Health outcomes

This systematic review included studies that investigated one or more of the six health outcomes of melanoma prevalence, incidence and mortality, and NMSC prevalence, incidence and mortality.

Included studies defined melanoma and NMSC in accordance with the standard definitions of these outcomes (Table 4). Studies reporting on melanoma of the lips and ocular melanoma were excluded. For NMSC, studies were included that reported on BCC only, SCC only, both BCC and SCC, or NMSC without specification of subtype. If a study reported effect estimates for two or more body sites or combinations of these, then effect estimates were prioritized in the following order: whole body, head and neck, arm, trunk and other single body sites.

Studies defining the outcome as in situ melanoma only were excluded from the systematic review. If the outcome was defined as a mixture of invasive melanoma and in situ melanoma, the study was included in: (i) the systematic review if the proportion of in situ cases was ≤ 10%; and (ii) the meta-analysis if the proportion of in situ cases amounted to ≤ 5%, or if it reported risk estimates for invasive cancer specifically regardless of the proportion of in situ cases. If the proportion of in situ cases was unclear, the study was included in the systematic review but not in the meta-analysis. Details on the health outcomes of studies included in the systematic review and meta-analysis are provided in Annex 3, including the proportion of histologic subtypes in melanoma and NMSC cases.

Studies with either objective or subjective measurements of melanoma or NMSC were regarded as eligible for inclusion. For example, studies with objective measurements were included, such as diagnosis by a physician, hospital discharge records, other relevant administrative data (e.g. records of sickness absence or disability), registry data of diagnosis or treatment for melanoma and/or NMSC, pathology report or medically certified cause of death. With the exception of studies in which the health outcome was based on death certificate, all other studies included in the systematic review and meta-analysis are based on pathology-confirmed diagnosis, including studies identifying cancer cases through population-based national or regional cancer registries using verification procedures. Not all studies with pathology-confirmed diagnosis reported histology subtypes. Subjective measurements of the outcomes were also eligible, such as self-report by the worker. If a study presented both objective and subjective outcome measurements, then the objective measurements were prioritized. Studies with any other type of outcome measurement were excluded.

2.4.5 Study designs

Included studies investigated the effect of occupational exposure to solar UVR on the risk of melanoma and NMSC for any specific year or over any period of years. Eligible study designs were randomized controlled trials (including parallel-group, cluster, cross-over and factorial trials), cohort studies (both prospective and retrospective), case–control studies and non-randomized intervention studies (including quasi-randomized controlled trials, controlled before–after studies, case–case studies and interrupted time-series studies). A broader set of observational study designs was included than is commonly incorporated because a recent augmented Cochrane review of complex interventions identified valuable additional studies from this approach *(65)*. As the aim was to quantify risk and not to carry out a qualitative assessment

of hazard *(66)*, all other study designs were excluded (e.g. uncontrolled before–after, cross-sectional, qualitative, modelling, case, case–series and non-original studies).

Study records published in any year and in any language were included. The search was conducted using English-language terms, so that records published in other languages that presented essential information (i.e. title and abstract) in English were included. If a study record was published in a language other than those spoken by the contributors to this systematic review, or contributors to other reviews *(6–21)* in the series (i.e. Arabic, Bulgarian, Chinese, Danish, Dutch, English, Finnish, French, German, Hungarian, Italian, Japanese, Norwegian, Portuguese, Russian, Spanish, Swedish and Thai), then it was translated into English. Published and unpublished studies were included, but studies conducted using unethical practices were excluded (e.g. studies that deliberately exposed people to a known risk factor to health).

The aim was to identify and include all study records reporting on any included study. If different records reporting on the same study described effect estimates for different numbers of participants, cases and/or deaths (e.g. due to extended recruitment intervals or the inclusion of extra recruitment sites), the effect estimate that captured the largest number of cancer cases or deaths was prioritized (assuming all other variables remained unchanged).

2.4.6 Effect measurements

Measurements were included of the relative effect of any occupational exposure to solar UVR on the risk of melanoma or NMSC prevalence, incidence or mortality, compared with the theoretical minimum risk exposure level. Relative effect measurements were included such as RRs, ORs and hazard ratios for prevalence, incidence and mortality. Measurements of absolute effects (e.g. mean differences in risks or odds) were converted into relative measures; studies where such conversions were not possible were excluded. To ensure comparability of effect estimates and facilitate meta-analysis, if a study presented an OR it was converted into an RR using the guidance provided in the *Cochrane handbook for systematic reviews of interventions (67)*. To convert an OR to an RR (Section 3.4) the 14-year incidence rate was used of melanoma or of NMSC, as relevant, in the unexposed population from the 2001 Swedish cohort study by Håkansson et al. *(68)* – which reported incidence data in unexposed and exposed male workers – as the baseline risk for the outcome under investigation, and a 95% CI was calculated for each RR *(69)*. The study by Håkansson et al. *(68)* was the only study that could be identified that had such baseline data in the unexposed population available for the conversion.

If a study presented effect estimates for two or more comparisons of exposures measured via proxies (e.g. occupation, occupational group or other relevant variable), the comparison of the largest level of exposure with the lowest level of exposure was prioritized. For example, if a study presented comparisons between (i) "outdoor work" and "indoor work" and (ii) "indoor/outdoor work" and "indoor work", then comparison (i) was prioritized over (ii). If a study presented multiple effect estimates for different levels of cumulative exposure, then the effect estimate of the greatest cumulative exposure compared with the level closest to no cumulative exposure was included. For example, if a study reported effect estimates for participants exposed to 1, 5 and 10 years of being an outdoor worker compared with participants exposed to 0 years of being an outdoor worker, then the comparison between 10 years and 0 years of exposure was selected.

If a study presented estimates of the effect from two or more alternative models that had been adjusted for different variables, then the estimate from the model that included the most appropriate adjustment for the relevant confounders and/or mediators (at a minimum, age and sex) was systematically prioritized. Estimates from models that had adjusted for a larger number of potential confounders were prioritized. For example, if a study presented estimates

from an unadjusted model (Model A), a model adjusted for one potential confounder (e.g. age; Model B) and a model adjusted for two potential confounders (e.g. age and sex; Model C), then the estimate from Model C was prioritized. Estimates from models unadjusted for mediators were prioritized over those from models adjusted for mediators, because adjustment for mediators can introduce bias. For example, if Model A was adjusted for two confounders, and Model B adjusted for the same two confounders and a potential mediator, then the estimate from Model A was selected over that from Model B. Estimates from models that adjusted for time-varying confounders that are also mediators, such as marginal structural models *(70)*, were prioritized over estimates from models that could only adjust for time-varying confounders, such as fixed-effects models *(71)*, and over estimates from models that could not adjust for time-varying confounding. If a study presented effect estimates from two or more potentially eligible models, then the reason/rationale for selecting this model was documented.

If a study reported pooled effect estimates of individual studies, the effect estimates of eligible individual studies were identified and used in the meta-analysis.

2.5 Data extraction

A standard data extraction form was developed and trialled until data extractors reached agreement. At least two reviewers independently extracted data on study characteristics (including study authors, study year, study country, participants, exposure and outcome), study design (including study type, comparator, epidemiological model(s) used and effect estimate measure) and risk of bias (see Section 2.7). A third reviewer resolved data extraction conflicts. Data were recorded and managed with Excel (Microsoft, Redmond, United States of America (USA)).

Data on any potential conflict of interest in included studies were also extracted. Financial disclosures and funding sources were extracted for every author and affiliated organization of every included study record. A modification of a previously published method was used to identify and assess any undisclosed financial interest of authors *(72)*. Where no financial disclosure or conflict of interest statements were available, searches were conducted for the names of authors in other study records included for a particular study, in other research articles published in the prior 36 months and in other publicly available declarations of interests *(73, 74)*.

2.6 Missing data requests

Missing data were requested from the principal author of each study by email or telephone, using the contact details provided in the principal study record. When no positive response was received from the study author, follow-up emails were sent twice at 2 and 4 weeks. Even if requested missing data were not obtained, a study was retained in the systematic review if it fulfilled the eligibility criteria described in Section 2.4. A description of missing data, the study author from whom the data were requested, the date of requests sent, the date on which data were received (if any) and a summary of the responses provided by the study authors is presented in Annex 4.

2.7 Risk of bias assessment

Standard risk of bias tools do not exist for systematic reviews for hazard identification in occupational and environmental health, or for risk assessment. The five methods specifically developed for occupational and environmental health are for hazard identification and/or risk assessment, and differ substantially in the types of studies (randomized, observational and/or simulation stud-

ies) and data (e.g. human, animal and/or in vitro) they seek to assess *(75)*. However, the five methods, including the Navigation Guide *(76)*, assess risk of bias in human studies in a similar way *(75)*.

Consistent with using the Navigation Guide as the organizing framework, its risk of bias tool that builds on the standard risk of bias assessment methods of Cochrane *(67)* and the United States Agency for Healthcare Research and Quality *(77)* was used. Further refinements of the Navigation Guide method may be warranted *(78)*, but it has been successfully applied in several completed and ongoing systematic reviews *(75, 79–83)*. In applying the Navigation Guide method, this systematic review drew heavily on one of its latest versions *(76)*.

Risk of bias was assessed on the individual study level and on the body of evidence overall. The nine risk of bias domains included in the Navigation Guide method for human studies are: (i) selection bias; (ii) performance bias; (iii) exposure misclassification bias; (iv) detection bias; (v) confounding; (vi) incomplete outcome data bias; (vii) reporting bias; (viii) conflict of interest bias; and (ix) other sources of bias. Risk of bias or confounding ratings were "low", "probably low", "probably high", "high" or "not applicable" *(76)*. To judge the risk of bias in each domain, a priori instructions *(5)* were applied that were adopted or adapted from a Navigation Guide systematic review *(76)*. For example, a study assessed as carrying a "low" risk of selection bias would be judged as describing the source population (including eligibility criteria, recruitment, enrolment, participation and loss to follow-up), and the distribution and characteristics of the study sample, in sufficient detail to indicate minimal or no risk of selection effects.

All risk of bias assessors jointly trialled the application of the risk of bias criteria until they had synchronized their understanding and application of these criteria. Two or more reviewers independently judged (or assessed) the risk of bias for each study. Where individual assessments differed, a third reviewer resolved the conflict. For each included study, the risk of bias assessment was reported at the level of the individual study by domain in a standard risk of bias table *(84)*. For the entire body of evidence, the study-level risk of bias ratings were presented by domain in a risk of bias summary figure (or risk of bias matrix) *(84)*.

2.8 Evidence synthesis (including meta-analysis)

Meta-analyses of eligible studies were intended to be conducted separately for the six different health outcomes of melanoma prevalence, incidence and mortality, and NMSC prevalence, incidence and mortality. If two or more studies with an eligible effect estimate were found, two or more reviewers independently investigated the clinical heterogeneity *(85)* of the studies in terms of participants (including country, sex, age, and industrial sector or occupation), risk factor exposure, comparator and health outcomes following the protocol *(5)*. If effect estimates differed considerably across WHO regions, sex and/or age groups, then evidence was synthesized for the relevant populations. If effect estimates were found to be clinically homogenous across WHO regions, sex and age groups, then studies from all of these populations were combined into one pooled effect estimate for application across all population combinations in the WHO/ILO Joint Estimates. It must also be noted that WHO regions differ in latitude, population composition (e.g. in terms of skin types), prevalence of outdoor work and other parameters, potentially modifying the effect of the exposure under investigation and susceptibility to its harmfulness. Further, these regions may differ in incidence of and mortality from skin cancer.

If two or more studies for the relevant combination of WHO region, sex and/or age group were judged to be sufficiently clinically homogenous to be combined quantitatively in meta-analysis, the RRs of the studies were pooled in a quantitative meta-analysis, using the inverse variance method with a random effects model to account for cross-study heterogeneity, and the statistical heterogeneity of the studies was tested using the I^2 statistic *(86)*. "Clinical homogeneity" is the lack of clinical

heterogeneity, which can be defined as "differences in participant characteristics, types or timing of outcome measurements and intervention characteristics" (Chess & Gagnier *(87)*, p. 1). The data were prepared for entry using Excel and the meta-analysis was conducted in RevMan version 5.4.1 (Nordic Cochrane Centre, Copenhagen, Denmark). Relative risks (log–transformed) and the standard error were input into RevMan with a precision of two decimal places. A leave-one-out analysis was performed to weigh the contribution of each individual study to the estimated statistical heterogeneity on the meta-analyses for the health outcomes of melanoma and NMSC incidence, recalculating the pooled RR and corresponding I^2 statistic for each iteration (Section 3.4).

Data from studies of different designs were not quantitatively combined (e.g. cohort studies were not combined with case–control studies), and data from unadjusted and adjusted models were not combined. Only studies that were judged to have at least a minimum acceptable level of adjustment for two of the identified core confounders (sex and age; Fig. 1) were combined.

If it was not possible to conduct a meta–analysis, study findings were synthesized narratively and the estimates that were judged to be the highest-quality evidence available were identified.

2.9 Subgroup and sensitivity analyses

For the outcome of melanoma incidence, a subgroup analysis was conducted for the main meta-analysis by WHO region. For NMSC incidence, subgroup analyses were conducted for the main meta-analysis by WHO region, sex and subtype (SCC versus BCC). It was also planned to conduct subgroup analyses by age group, occupation, industrial sector, socioeconomic status and formality of economy for both outcomes, and also by sex for melanoma, but evidence or data to populate these subgroup analyses were not found.

For both melanoma and NMSC, sensitivity analyses were conducted between:

- studies with a "high" or "probably high" risk of bias rating in any domain, and studies with a "low" or "probably low" risk of bias rating in all domains;
- studies with a "high" or "probably high" risk of exposure misclassification bias, and studies with a "low" or "probably low" risk of bias rating in this domain;
- studies with a "high" or "probably high" risk of confounding, and studies with a "low" or "probably low" rating in this domain;
- studies with a "low" or "probably low" risk of bias for conflict of interest, and studies with a "high" or "probably high" risk of bias in this domain;
- studies with documented or approximated ICD-10 diagnostic codes (e.g. as recorded in administrative health records), and studies without ICD-10 diagnostic codes (e.g. self-reports); and
- studies comparing the highest level of cumulative exposure with the comparator, and studies not employing exposure categories defined by cumulative exposure.

For melanoma, sensitivity analyses were also conducted between:

- studies including the lentigo maligna melanoma subtype, and studies excluding this subtype; and
- studies with in situ cases comprising up to 5% of cases, and studies with no in situ cases.

For NMSC, sensitivity analyses were also conducted between:

- studies defining the outcome as "any NMSC", and studies defining the outcome as either SCC or BCC subtype only.

2.10 Quality of evidence assessment

Quality of evidence was assessed using a modified version of the Navigation Guide quality of evidence assessment tool *(48)*. The tool is based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach *(88)* adapted specifically to systematic reviews in occupational and environmental health *(89)*.

At least two reviewers assessed quality of evidence for the entire body of evidence by outcome, with any disagreements resolved by a third reviewer. The latest Navigation Guide instructions *(76)* for grading the quality of evidence were adapted and these adapted instructions were reported in the protocol *(5)*. The quality of evidence was downgraded for the following five domains: (i) risk of bias; (ii) inconsistency; (iii) indirectness; (iv) imprecision; and (v) publication bias. If the systematic review included 10 or more studies, an Egger's funnel plot was generated to judge publication bias. If the review included nine or fewer studies, this was judged qualitatively.

The quality of the entire body of evidence was graded using the three Navigation Guide standard quality of evidence ratings: "high", "moderate" and "low" *(76)*. Within each of the relevant domains, concern over the quality of evidence was classified as "none", "serious" or "very serious". As per the Navigation Guide, the assessments started with a "high" quality of evidence for randomized studies and a "moderate" quality of evidence for observational studies. Quality of evidence was downgraded for concern classified as "none" by nil levels (0), for "serious" concern by one level (–1) and for "very serious" concern by two levels (–2). The quality of evidence was upgraded along the three domains: (i) large effect; (ii) dose–response; and (iii) plausible residual confounding and bias. There had to be compelling reasons to upgrade or downgrade. If there was a "serious" concern of risk of bias in a body of evidence consisting of observational studies (–1), but no other concerns and no reasons for upgrading, then the quality of evidence was downgraded by one grade from "moderate" to "low".

2.11 Strength of evidence assessment

This systematic review included observational epidemiological studies of human data only, and no other streams of evidence (e.g. no studies of non-human data). The Navigation Guide allows the rating of a single stream of evidence based on the factors described in Section 2.10 above (i.e. risk of bias, inconsistency, indirectness, imprecision, publication bias, large magnitude of effect, dose–response and residual confounding and bias) to arrive at an overall rating of the quality of evidence as "high", "moderate" or "low" (see Section 2.10 above and the protocol *(5)*). The approach of evaluating only the human evidence stream is consistent with the GRADE methodology, which adopts the Bradford–Hill considerations *(90)*; using the method based on the Navigation Guide therefore incorporates the Bradford–Hill considerations (Table 5).

Table 5. Bradford–Hill considerations and their relationship to GRADE and the Navigation Guide in evaluating the overall quality of the evidence for human observational studies

Bradford–Hill	GRADE	Navigation Guide
Strength	Strength of association and imprecision in effect estimate	Strength of association and imprecision in effect estimate
Consistency	Consistency across studies, that is, across different situations (different researchers)	Consistency across studies, that is, across different situations (different researchers)
Temporality	Study design; properly designed and conducted observational studies	Study design; properly designed and conducted observational studies

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Bradford–Hill	GRADE	Navigation Guide
Biological gradient	Dose–response gradient	Dose–response gradient
Specificity	Indirectness	Indirectness
Coherence	Indirectness	Indirectness
Experiment	Study design; properly designed and conducted observational studies	Study design; properly designed and conducted observational studies
Analogy	Existing association for critical outcomes does not lead to a downgrading of the quality; indirectness	Existing association for critical outcomes does not lead to a downgrading of the quality; indirectness; evaluating the overall strength of body of human evidence allows the consideration of other compelling attributes of the data that may influence certainty

GRADE: Grading of Recommendations Assessment, Development and Evaluation *(88, 89)*.
Source: Adapted from Schünemann et al. *(90)*.

There is an additional step described in the protocol *(5)* that integrates (i) the quality of the evidence (Section 2.10) with other elements, including (ii) direction of effect, (iii) confidence in the effect and (iv) other compelling attributes of the data that may influence certainty, allowing for an overall rating of the strength of the body of evidence of "sufficient evidence of harmfulness", "limited evidence of harmfulness", "inadequate evidence of harmfulness" or "evidence of lack of harmfulness" based on human evidence (Table 6). The approach to evaluate only the human evidence has been applied in previous systematic reviews *(76, 82)* and verified by the United States National Academy of Sciences *(91)*. The approach also provides two steps that integrate Bradford–Hill criteria (evaluating both the quality and then the overall strength of the evidence). Finally, the GRADE quality of evidence ratings (which are aligned with the Navigation Guide strength of evidence ratings) are analogous to the final ratings from the Bradford–Hill criteria for causality; interpretation of the strength of evidence is described in Table 6.

Table 6. Interpretation of the GRADE ratings of the overall quality of evidence and the Navigation Guide ratings for strength of evidence

GRADE: quality of evidence		Navigation Guide: strength of evidence	
Rating	**Interpretation**	**Rating**	**Interpretation**
High	There is high confidence that the true effect lies close to that of the estimate of the effect	Sufficient evidence for harmfulness	A positive relationship is observed between exposure and outcome where chance, bias and confounding can be ruled out with reasonable confidence; the available evidence includes results from one or more well designed, well conducted studies, and the conclusion is unlikely to be strongly affected by the results of future studies
		Evidence of lack of harmfulness	The available evidence includes consistent results from well designed, well conducted studies, and the conclusion is unlikely to be strongly affected by the results of future studies; for human evidence, more than one study showed no effect on the outcome of interest at the full range of exposure levels that humans are known to encounter, and bias and confounding can be ruled out with reasonable confidence; the conclusion is limited to the age at exposure and/or other conditions and levels of exposure studied
Moderate	There is moderate confidence in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	Limited evidence for harmfulness	A positive relationship is observed between exposure and outcome where chance, bias and confounding cannot be ruled out with reasonable confidence; confidence in the relationship is constrained by factors such as the number, size or quality of individual studies, or inconsistency of findings across individual studies; as more information becomes available, the observed effect could change and this change may be large enough to alter the conclusion

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GRADE: quality of evidence		Navigation Guide: strength of evidence	
Rating	**Interpretation**	**Rating**	**Interpretation**
Low	The panel's confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect	Inadequate evidence for harmfulness	The available evidence is insufficient to assess the effects of the exposure; evidence is insufficient because of the limited number or size of studies, low quality of individual studies or inconsistency of findings across individual studies; more information may allow an assessment of effects
Very low	There is little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect	–	–

GRADE: Grading of Recommendations Assessment, Development and Evaluation *(88, 89)*.
Source: Adapted from Schünemann et al. *(90)* and Lam et al. *(76)*.

CHAPTER 3
Results

3.1 Study selection

Of the 1891 unique individual study records identified in the database searches and 324 identified through other sources, 53 studies comprising 62 study records fulfilled the eligibility criteria and were included in the systematic review (Fig. 2). Of the 53 included studies, 38 studies (47 study records) were included in the meta-analysis for at least one outcome (Fig. 2). Of the many studies not included in the systematic review, the reasons for the exclusion of the 30 studies that most closely met eligibility criteria are listed in Annex 2.

3.2 Characteristics of included studies

The characteristics of the 53 included studies (62 study records) are presented in Tables 7–10 *(41, 42, 60–64, 68, 92–145)* and summarized in the following sections. Where possible, the number of participants and the breakdowns by sex, cases and controls, and exposed and unexposed in the effective sample size (i.e. for population included in the prioritized model) are provided. For studies for which this was not possible, details of the wider study population are provided if available. Information on age is provided as reported in the study record, although this normally related to the entire study population.

3.2.1 Study type

Of the 53 included studies on melanoma and NMSC (Table 7), 48 (90.6%) were case–control, three were case–case *(114, 134, 137)* and two *(68, 118)* were cohort studies (both prospective). Case–control studies investigate the exposure status of individuals with and without melanoma and NMSC, case–case studies compare one group of cases with another, while cohort studies follow a group of individuals to monitor the development of melanoma and NMSC. The two most commonly reported types of effect estimates were ORs (45 studies) and RRs (eight studies) (Table 8).

A total of 41 studies adjusted effect estimates for at least one of the pre–specified confounders (age, sex and socioeconomic status) and 12 studies did not adjust for any of these confounders (Table 8). Studies that provided completely unadjusted effect estimates were excluded from the meta-analysis; these are reported in Table 11 (melanoma) and Table 12 (NMSC). The confounders most commonly adjusted for were age (39 studies), sex (30 studies) and socioeconomic status (16 studies). Twelve studies adjusted for all three confounders in their statistical models (Table 8).

Fig. 2. **Flow diagram of study selection in systematic review and meta-analysis of the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma and non–melanoma skin cancer**

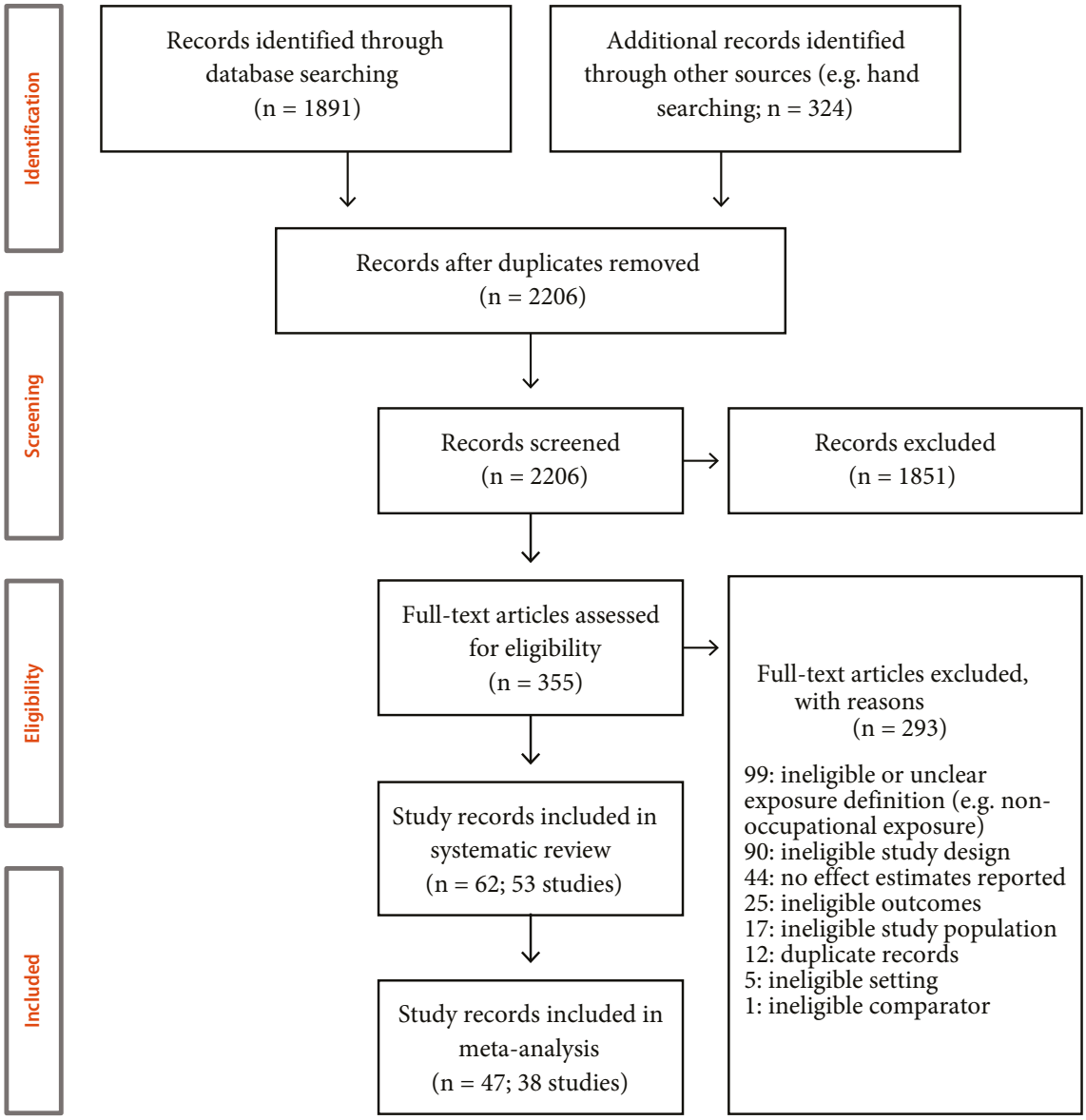

Table 7. **Characteristics of studies and study populations included in systematic review and meta–analyses of effect of occupational exposure to solar ultraviolet radiation on malignant skin melanoma and non-melanoma skin cancer**

Author, year	Study ID	Study design	Country	Study/follow-up period	Effective sample included in prioritized model	Study population (if considered informative)	Age (years)	Industrial sector (ISIC-4 code)	Occupation (ISCO-08 code)	Study context (latitude and/or seasonality)
Klepp & Magnus, 1979 *(92)*	Klepp 1979	Case–control	Norway (regional)	1 Jan 1974–1 May 1975/ unclear	209 (82 F, 127 M) Cases: 78; controls: 131	–	20 to ≥ 70	Unclear	Unclear	Unclear
MacKie & Aitchison, 1982 *(93)*	MacKie 1982	Case–control	United Kingdom (regional)	1978–1980/ unclear	221 (117 F, 104 M) Cases: 109; controls: 112	–	Mean: 54 (range: 18–76)	Unclear	Unclear	Unclear
Aubry & MacGibbon, 1985 *(94)*	Aubry 1985	Case–control	Canada (regional)	1977–1978/ unclear	266 (91 F, 175 M) Cases: 92; controls: 174	–	Mean: 68.1 (M), 72.7 (F)	Unclear	Unclear	45.5088° N
Elwood et al., 1985 *(95, 96)* Gallagher et al., 1987 *(97)*	Elwood 1985	Case–control	Canada (regional)	1 Apr 1979–31 Mar 1981/ lifetime	459 (288 F, 171 M) Cases: 213; controls: 246	–	20–79	Unclear	Unclear	Season of exposure and vacation exposures, including latitude, altitude and type of location, using estimates of relative intensity of solar UVR from published sources
Graham et al., 1985 *(98)*	Graham 1985	Case–control	USA (local)	1974–1980/ unclear	173 M Cases: 84; controls: 89	–	Unclear	Unclear	Unclear	Unclear
Bell et al., 1987 *(99)*	Bell 1987	Case–control	United Kingdom (regional)	1 Jan 1961–28 Feb 1982/unclear	1521 Cases: 224; controls: 1297	1845 (1009 F, 836 M) Cases: 268; controls: 1577	No restriction (< 30 to ≥ 70)	Unclear	Unclear	Unclear
Cristofolini et al., 1987 *(100)*	Cristofolini 1987	Case–control	Italy (regional)	Jan 1983–Dec 1985/unclear	303 Cases: 103; controls: 200	308 Cases: 103 (56 F, 47 M); controls: 205	21–79	Unclear	Unclear	46.0678° N
Østerlind et al., 1988 *(101)*	Østerlind 1988	Case–control	Denmark (regional)	Oct 1982–Mar 1985/NA	Unclear (M only)	1400 Cases: 474; controls: 926	20–79	Unclear	Unclear	Unclear

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Author, year	Study ID	Study design	Country	Study/follow-up period	Effective sample included in prioritized model	Study population (if considered informative)	Age (years)	Industrial sector (ISIC-4 code)	Occupation (ISCO-08 code)	Study context (latitude and/or seasonality)
Zanetti et al., 1988 *(102)*, 1999 *(103)* Rosso et al., 1998 *(104)*, 2008 *(105)*	Zanetti 1988	Extended follow-up of cancer cases from a case–control study to assess survival	Italy (regional)	May 1984–Dec 2005/1–21 years (median: 17 years)	524[a] Cases: 233; controls: 291	–	Average: 56	Unclear	Unclear	Unclear
Dubin et al., 1989 *(106)*, 1990 *(61)*	Dubin 1989	Case–control	USA (local)	Oct 1979–Jan 1982/none	740 Cases: 263; controls: 477	816 (415 F, 401 M) Cases: 289; controls: 527	≥ 20	Unclear	Unclear	Both: birthplace and residential history included latitudes of all places lived
Garbe et al., 1989 *(107)*	Garbe 1989	Case–control	Germany (local)	Jan–Jun 1987/unclear	345 Cases: 169; controls: 176	400 (242 F, 158 M) Cases: 200; controls: 200	20–89	Unclear	Unclear	Unclear
Beitner et al., 1990 *(108)*	Beitner 1990	Case–control	Sweden (local)	Feb 1978–Dec 1983/unclear	1028 (564 F, 464 M) Cases: 523; controls: 505	–	Unclear	Unclear	Unclear	Unclear
Weiss et al., 1991 *(109)*	Weiss 1991	Case–control	Germany (regional)	1984–1987/unclear	200 Cases: 100; controls: 100	404 Cases: 204; controls: 200	Unclear	Unclear	Unclear	Unclear
Nelemans et al., 1993 *(110)*	Nelemans 1993	Case–control	Netherlands (regional)	1998–1990/unclear	324 (156 F, 168 M) Cases: 141; controls: 183	–	≤ 40 to ≥ 60	Unclear	Unclear	Unclear
White et al., 1994 *(111)*	White 1994	Case–control	USA (regional)	Jan 1984–Dec 1987/unclear	379 Cases: 184; controls: 195	529 (272 F, 257 M) Cases: 256; controls: 273	25–65	Unclear	Unclear	Unclear
Gallagher et al., 1995 *(112, 113)*	Gallagher 1995	Case–control	Canada (regional)	1 Jan 1983– 31 Dec 1984/unclear	441 M Cases: 226; controls: 215	–	25–79	Unclear	Unclear	Unclear

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Author, year	Study ID	Study design	Country	Study/follow-up period	Effective sample included in prioritized model	Study population (if considered informative)	Age (years)	Industrial sector (ISIC-4 code)	Occupation (ISCO-08 code)	Study context (latitude and/or seasonality)
Goodman et al., 1995 *(114)*	Goodman 1995	Case–case study where controls are patients with other cancers	USA (regional)	1972–1990/ unclear	38 307 M Cases: 2423; controls: 35 884	–	20–65	Agriculture, forestry and fishing (A)	8332, 7115, 2320, 3334, 7411, 7115, 7126, 7212, 5412, 9313, 4412, 6113, 8343, 7121, 7123, 7112, 6111, 3421	Unclear
Holly et al., 1995 *(115)*	Holly 1995	Case–control	USA (regional)	Jan 1981–Dec 1986/unclear	Unclear (F only)	1382 F Cases: 452; controls: 930	25–59	Unclear	Unclear	Unclear
Kricker et al., 1995 *(116)*	Kricker 1995	Case–control	Australia (local)	Nov 1987–1988/ since 15 years of age[b]	449 Cases: 91; controls: 358	901 Cases: 201; controls: 700	40–64	Unclear	Unclear	Warmer months: Oct–Apr in the Southern Hemisphere and Mar–Aug in the Northern Hemisphere
Chen et al., 1996 *(117)*	Chen 1996	Case–control	USA (local)	Jan 1987–May 1989/unclear	Unclear	1042 (460 F, 582 M) Cases: 548; controls: 494	29% < 45; 41% 45–64; 30% ≥ 65	Unclear	Unclear	Unclear
Green et al., 1996 *(118)*	Green 1996	Cohort study (prospective)	Australia (local)	Dec 1986–Mar 1992/5 years from study baseline	Unclear	2049 (1154 F; 895 M) Cases: 344; controls: 1705	18–69	Unclear	Unclear	Subtropical
Ródenas et al., 1996 *(119)*	Ródenas 1996	Case–control	Spain (regional)	1988–1993/ unclear	199 Cases: 89; controls: 110	243 (158 F, 85 M) Cases: 105; controls: 138	Mean: 51.7 ± 14.7 standard deviation (range: 20–79)	Unclear	Unclear	36° 45' N, 38° 25' S
Rosso et al., 1996 *(120)*, 1998 *(104)*	Rosso 1996	Case–control	France, Italy, Spain (regional)	Nov 1989–Jun 1993/unclear	1966 Cases: 967; controls: 999	3572 Cases: 1777; controls: 1795	Unclear	Unclear	Unclear	Unclear
Suárez-Varela et al., 1996 *(121)*	Suárez-Varela 1996	Case–control	Spain (regional)	1990–1992/ unclear	Unclear	812 (270 F, 542 M) Cases: 260; controls: 552	Mean: 67.8 (cases); 67.7 (controls)	Unclear	Unclear	Unclear

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Author, year	Study ID	Study design	Country	Study/follow-up period	Effective sample included in prioritized model	Study population (if considered informative)	Age (years)	Industrial sector (ISIC-4 code)	Occupation (ISCO-08 code)	Study context (latitude and/or seasonality)
Freedman et al., 1997 *(122)*, 2002 *(123)*	Freedman 1997	Case–control based on death certificates	USA (24 states)	Melanoma: 1984–1991; NMSC: 1984–1995/ unclear (usually from death certificate main occupation)	Melanoma, 19 707 Cases: 6980; controls: 12 727 NMSC, 80 987 Cases: 3398; controls: 77 589	Melanoma, 36 001 (14 490 F, 21 511 M) Cases: 12 156; controls: 23 845 NMSC, 160 067 (72 154 F, 87 913 M) Cases: 6565; controls: 153 502	20 to ≥ 75	Unclear	Farming, other outdoor, indoor work and mixed indoor/ outdoor	Unclear
Espinosa Arranz et al., 1999 *(124)*	Espinosa Arranz 1999	Case–control	Spain (regional)	Jan 1990–Jan 1994/unclear	351 (186 F, 165 M) Cases: 116; controls: 235	–	21–87	Construction of buildings (41); crop and animal production, hunting and related service activities (01)	Building construction labourers (9313); "farmers", without further specifying	Unclear
Rosso et al., 1999 *(125)*	Rosso 1999	Case–control	Switzerland (regional)	Apr 1994–Jun 1996/unclear	167 Cases: 80; controls: 87	289 Cases: 145 (69 F, 76 M); controls: 144	20–75	Unclear	Unclear	Unclear
Walter et al., 1999 *(126)*	Walter 1999	Case–control	Canada (local)	1984–1986/ unclear	1144 Cases: 558; controls: 586	1191 (631 F, 560 M) Cases: 583; controls: 608	20–69	Unclear	Unclear	Unclear
Vlajinac et al., 2000 *(127)*	Vlajinac 2000	Case–control	Serbia (local)	1996–1997/ unclear	599 (236 F, 363 M) Cases: 200; controls: 399	–	32–90	Unclear	Unclear	Unclear
Corona et al., 2001 *(128)*	Corona 2001	Case–control	Italy (regional)	Mar 1995–Jun 1997/unclear	320 Cases: 162; controls: 158	324 (169 F, 155 M) Cases: 166; controls: 158	≥ 18	Unclear	Unclear	Unclear

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Author, year	Study ID	Study design	Country	Study/follow-up period	Effective sample included in prioritized model	Study population (if considered informative)	Age (years)	Industrial sector (ISIC-4 code)	Occupation (ISCO-08 code)	Study context (latitude and/or seasonality)
Håkansson et al., 2001 *(68)*	Håkansson 2001	Cohort study (prospective)	Sweden (national)	1971–1993/22 years maximum	196 025 M Melanoma cases: 30; controls 195 995 NMSC cases 133; controls: 195 892	–	Median (at first examination): 31	Construction of buildings (41)	9313	Significant seasonal variation in solar UVR exposure occurs in Sweden
Loria & Matos, 2001 *(129)*	Loria 2001	Case–control	Argentina (local)	May 1993–Mar 1995/unclear	347 Cases: 101 (46 F, 55 M); controls: 246	–	> 40 to ≥ 70	Unclear	Unclear	No latitude specified
Milán et al., 2003 *(130)*	Milán 2003	Case–control	Finland (national)	1975–1999/unclear	371 (218 F, 153 M) Cases: 188; controls: 183	–	24–89	Unclear	Unclear	Unclear
Bataille et al., 2004 *(131)*	Bataille 2004	Case–control	United Kingdom (regional)	Aug 1989–Jul 1993/unclear	495 Cases: 251; controls: 244	829 Cases: 413; controls: 416	16–75	Unclear	Unclear	Unclear
Fargnoli et al., 2004 *(132)*	Fargnoli 2004	Case–control	Italy (local)	1 Sep 2000–31 Dec 2001/unclear	300 (159 F, 141 M) Cases: 100; controls: 200	–	18–74	Unclear	Unclear	Unclear
Walther et al., 2004 *(133)*	Walther 2004	Case–control	Germany (regional)	1997–1999/unclear	624 (324 F, 300 M) Cases: 213; controls: 411	–	27–90	Unclear	Unclear	Unclear
Nijsten et al., 2005 *(62)*	Nijsten 2005	Case–control	Belgium (regional)	1998–2001/unclear	348 Cases: 119; controls: 229	377 (231 F, 146 M) Cases: 132; controls: 245	Median: 50.6 (cases); 51.8 (controls)	Unclear	Unclear	Unclear
Whiteman et al., 2006 *(134)*	Whiteman 2006	Case–case	Australia (regional)	Jun 2000–Oct 2001/unclear	96 Cases: 30; controls: 66	230 (113 F, 117 M) Cases: 76; controls: 154	50–54	Unclear	Unclear	27° S
Zanetti et al., 2006 *(63)*	Zanetti 2006	Case–control	Argentina, France, Germany, Italy, Portugal, Spain (local)	Autumn 2001–spring 2002/unclear	426 NMSC cases: 168; melanoma cases: 94; controls: 164	917 M Melanoma cases: 214; NMSC cases 354; controls: 349	20–75	Unclear	Unclear	Unclear

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Author, year	Study ID	Study design	Country	Study/follow-up period	Effective sample included in prioritized model	Study population (if considered informative)	Age (years)	Industrial sector (ISIC-4 code)	Occupation (ISCO-08 code)	Study context (latitude and/or seasonality)
Pelucchi et al., 2007 *(135)*	Pelucchi 2007	Case–control	Italy (national)	Mar 1995–Dec 1996/unclear	830 Cases: 384; controls: 446	1040 Cases: 528 (236 F, 292 M); controls: 512	Median: 64	Unclear	Unclear	Unclear
Nikolaou et al., 2008 *(136)*	Nikolaou 2008	Case–control	Greece (regional)	Oct 2000–Mar 2004/unclear	400 (204 F, 196 M) Cases: 200; controls: 200	–	19–84	Unclear	Unclear	Unclear
Radespiel-Tröger et al., 2009 *(137)*	Radespiel-Tröger 2009	Case–case	Germany (regional)	1 Jan 2001–31 Dec 2005/unclear[c]	Melanoma, 125; NMSC, 661	Melanoma cases, 454 (229 F, 225 M) NMSC cases, 2140 (967 F, 1173 M)	All new cases included irrespective of age; analysis had age groupings at 10-year intervals	Unclear	Unclear	Unclear
Janković et al., 2010 *(138)*	Janković 2010	Case–control	Montenegro (local)	2006–2007/unclear	200 (96 F, 104 M) Cases: 100; controls: 100	–	> 40 to < 70	Unclear	Unclear	Unclear
Kenborg et al., 2010 *(139)*	Kenborg 2010	Case–control	Denmark (national)	Cancer diagnosed 1 Jan 1970–1 Jun 2003/unclear	Melanoma, 20 610 M NMSC, 76 156 M	Melanoma, 23 070 M Cases: 7690; controls: 15 380 NMSC, 85 084 M Cases: 42 542; controls: 42 542	Mean age at diagnosis: 54.7 (melanoma), 69.9 (NMSC)	Outdoor/construction (F); agriculture (A); forestry (A); gardening/fishing (A)	Other	Unclear
Dessinioti et al., 2011 *(140)*	Dessinioti 2011	Case–control	Greece (regional)	2006–2009/unclear	399 (194 F, 205 M) Cases: 199; controls: 200	–	Mean: 67 (cases); 53 (controls)	Unclear	Unclear	Unclear
Ferreira et al., 2011 *(141)*	Ferreira 2011	Case–control	Brazil (local)	Jan 2005–Dec 2006/unclear	264 (158 F, 106 M) Cases: 132; controls: 132	–	≥ 25	Unclear	Unclear	Unclear
Iannacone et al., 2012 *(142)*	Iannacone 2012	Case–control	USA (local)	30 Oct 2006–24 Dec 2008/unclear	246 Cases: 168; controls: 78	703 (345 F, 358 M) Cases: 387; controls: 316	18–80	Unclear	Unclear	Unclear

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Author, year	Study ID	Study design	Country	Study/follow-up period	Effective sample included in prioritized model	Study population (if considered informative)	Age (years)	Industrial sector (ISIC-4 code)	Occupation (ISCO-08 code)	Study context (latitude and/or seasonality)
Sanchez et al., 2012 *(143)*	Sanchez 2012	Case–control	Colombia (local)	2010/unclear	406 (256 F, 150 M) Cases: 203; controls: 203	–	Median: 66 (range: 30–97)	Unclear	Unclear	Unclear
Surdu et al., 2013 *(144)*	Surdu 2013	Case–control	Hungary, Romania, Slovakia (eight counties)	Jan 2003–Sep 2004/unclear	1041 Cases: 563; controls: 478	1145 (588 F, 557 M) Cases: 618; controls: 527	30–79 (cases)	Unclear	Unclear	Unclear
Kaskel et al., 2015 *(145)*	Kaskel 2015	Case–control	Germany (local)	1997–1999/unclear	832 (423 F, 409 M) Melanoma cases: 291; NMSC cases: 212; controls: 329	–	Median age at diagnosis: 55; 57 (controls)	Agriculture, forestry and fishing (A)	Unclear	Unclear
Fortes et al., 2016 *(60)*	Fortes 2016	Case–control	Brazil, Italy (local)	Italy: 2001–2003; Brazil: 2007–2013/unclear	676 Cases: 344; controls: 332	–	≥ 18	Unclear	Unclear	Unclear
Trakatelli et al., 2016 *(64)*	Trakatelli 2016	Case–control	Finland, Germany, Greece, Italy, Malta, Poland, Scotland, Spain (other)	Unclear/unclear	2795 Melanoma cases: 326; NMSC cases 919; controls: 1550	2921 Melanoma cases: 360; NMSC cases: 1011; controls: 1550	62–71	Unclear	Unclear	Unclear
Schmitt et al., 2018 *(41, 42)*	Schmitt 2018	Case–control	Germany (national)	2013–2015/NA	902 Cases: 476; controls: 426	1672 (703 F, 969 M) Cases: 836; controls: 836	29–86	Unclear	Unclear	Unclear

F, females; ISCO-08, International Standard Classification of Occupations, version 8; ISIC-4, International Standard Industrial Classification of All Economic Activities, revision 4; M, males; N, north; NA, not applicable; NMSC, non-melanoma skin cancer; S, south; USA, United States of America; UVR, ultraviolet radiation.

[a] The Zanetti 1988 study comprised multiple study records including both melanoma and BCC cases; however, Zanetti et al. 1988 *(102)* contributed solely to melanoma analyses in this systematic review so the effective sample for this study included only melanoma cases.

[b] Solar UVR exposure was recorded on both working days and non-working days from the age of 15 years.

[c] Date of database query was 18 months after cut-off date for case selection.

Table 8. Adjustments of effect estimates and estimates of effect on health outcome in studies included in systematic review and meta–analyses of effect of occupational exposure to solar ultraviolet radiation on malignant skin melanoma and non-melanoma skin cancer

Author, year	Study ID	Adjustments for confounding factors				Interactions adjusted for	Adjustment for clustering	Treatment effect measure type	Exposure–response (or dose–response) analysis conducted
		Age	Sex	SES	Other				
Klepp & Magnus, 1979 *(92)*	Klepp 1979	No	No	No	No	No	No	OR	No
MacKie & Aitchison, 1982 *(93)*	MacKie 1982	Yes	Yes	Yes	Skin type, incidence of severe sunburn	No	No	OR	No
Aubry & MacGibbon, 1985 *(94)*	Aubry 1985	Yes	Yes	No	Eye and hair colour, complexion, descent, non-occupational sunlight exposure	No	No	RR	Yes
Elwood et al., 1985 *(95, 96)* Gallagher et al., 1987 *(97)*	Elwood 1985	Yes	Yes	Yes	Hair colour, skin colour, history of freckles, ethnic origin	Yes	Unclear	OR	Yes
Graham et al., 1985 *(98)*	Graham 1985	No	NA (M only)	No	Burn reaction to sun	No	No	OR	Yes
Bell et al., 1987 *(99)*	Bell 1987	Yes	No	Unclear	No	No	Unclear	RR	Unclear
Cristofolini et al., 1987 *(100)*	Cristofolini 1987	Yes	Yes	Yes	Unclear	No	No	RR	Unclear
Østerlind et al., 1988 *(101)*	Østerlind 1988	Yes	Yes	No	Constitutional factors	No	No	RR	No
Zanetti et al., 1988 *(102)*, 1999 *(103)* Rosso et al., 1998 *(104)*, 2008 *(105)*	Zanetti 1988	Yes	Yes	Yes	Hair colour, skin reaction to sun, sunburn in youth	No	No	OR	No
Dubin et al., 1989 *(106)*, 1990 *(61)*	Dubin 1989	Yes	Yes	Unclear	History of UV recommender/ contraindicated skin conditions	Yes	Unclear	OR	Unclear
Garbe et al., 1989 *(107)*	Garbe 1989	No	No	No	No	No	No	RR	Yes
Beitner et al., 1990 *(108)*	Beitner 1990	Yes	Yes	No	Hair colour	No	No	OR	No
Weiss et al., 1991 *(109)*	Weiss 1991	No	No	No	Skin type, number of naevi	No	No	OR	No

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Author, year	Study ID	Adjustments for confounding factors				Interactions adjusted for	Adjustment for clustering	Treatment effect measure type	Exposure–response (or dose–response) analysis conducted
		Age	Sex	SES	Other				
Nelemans et al., 1993 *(110)*	Nelemans 1993	Yes	Yes	Yes	Unclear	No	No	OR	No
White et al., 1994 *(111)*	White 1994	Yes	Yes	Yes	No	No	No	OR	No
Gallagher et al., 1995 *(112, 113)*	Gallagher 1995	Yes (stratified)	NA (M only)	Unclear	Mother's ethnic origin, skin colour, hair colour	No	No	OR	Yes
Goodman et al., 1995 *(114)*	Goodman 1995	Yes	NA (M only)	Yes	Birthplace, sun exposure, educational level	No	No	OR	No
Holly et al., 1995 *(115)*	Holly 1995	No	NA (F only)	No	No	No	No	OR	No
Kricker et al., 1995 *(116)*	Kricker 1995	Yes	Yes	Yes	Migrant status, age of arrival, ethnic origin, pigmentary characteristics	No	No	OR	No
Chen et al., 1996 *(117)*	Chen 1996	Yes	Yes	No	Skin colour, naevi on arms, skin type, recreational sun exposure	No	No	OR	Yes
Green et al., 1996 *(118)*	Green 1996	Yes	Yes	No	Skin colour	No	No	RR	Yes
Ródenas et al., 1996 *(119)*	Ródenas 1996	Yes	No	No	Skin colour, skin type	Unclear	Unclear	OR	No
Rosso et al., 1996 *(120)*, 1998 *(104)*	Rosso 1996	Yes	Yes	Yes	No	Unclear	Unclear	OR	Yes
Suárez-Varela et al., 1996 *(121)*	Suárez-Varela 1996	Yes	Yes (stratified)	No	No	No	No	OR	No
Freedman et al., 1997 *(122)*, 2002 *(123)*	Freedman 1997	Yes	Yes	Yes	Residential sunlight, race	No	No	Death OR	No
Espinosa Arranz et al., 1999 *(124)*	Espinosa Arranz 1999	Yes	No	No	Skin type, naevi count	No	No	OR	No
Rosso et al., 1999 *(125)*	Rosso 1999	By matching	By matching	No	No	No	No	OR	Yes
Walter et al., 1999 *(126)*	Walter 1999	Yes	Yes	No	Region, non-BCC skin cancers, non-cutaneous cancers	No	No	OR	Unclear

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Author, year	Study ID	Adjustments for confounding factors				Interactions adjusted for	Adjustment for clustering	Treatment effect measure type	Exposure–response (or dose–response) analysis conducted
		Age	Sex	SES	Other				
Vlajinac et al., 2000 *(127)*	Vlajinac 2000	No	No	No	Eye colour, skin reaction to sun, previous BCC, exposure to chemicals	No	No	OR	Unclear
Corona et al., 2001 *(128)*	Corona 2001	Yes	Yes	No	Light hair and eye colour, fair skin, skin phototype, sunlight-related lesions, family history of skin cancer, history of sunburn, lifestyle	No	No	OR	No
Håkansson et al., 2001 *(68)*	Håkansson 2001	Yes	NA (M only)	Yes	Smoking, magnetic field exposure	No	No	RR	No
Loria & Matos, 2001 *(129)*	Loria 2001	No	No	No	Hospital at which treated	No	No	OR	Yes
Milán et al., 2003 *(130)*	Milán 2003	No	No	Yes	Twin study	No	No	OR	No
Bataille et al., 2004 *(131)*	Bataille 2004	Yes	Yes	No	Skin type	No	No	OR	Unclear
Fargnoli et al., 2004 *(132)*	Fargnoli 2004	Yes	Yes	Yes	Hair colour, eye colour, skin type, number of naevi	Yes	Unclear	OR	Unclear
Walther et al., 2004 *(133)*	Walther 2004	Yes	No	No	Skin phototype, hair colour	Unclear	Unclear	OR	No
Nijsten et al., 2005 *(62)*	Nijsten 2005	Yes	Yes	No	Skin phototype, skin phenotypical characteristics	No	No	OR	No
Whiteman et al., 2006 *(134)*	Whiteman 2006	No	No	No	Unclear	Unclear	Unclear	OR	Unclear
Zanetti et al., 2006 *(63)*	Zanetti 2006	Yes	NA (M only)	No	Significant host factors (pigmentary characteristic, naevi and freckles)	No	No	OR	No
Pelucchi et al., 2007 *(135)*	Pelucchi 2007	Yes	Yes	No	Eye, hair and skin colour	No	No	OR	Yes
Nikolaou et al., 2008 *(136)*	Nikolaou 2008	No	No	No	No	No	No	OR	No

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Author, year	Study ID	Adjustments for confounding factors				Interactions adjusted for	Adjustment for clustering	Treatment effect measure type	Exposure–response (or dose–response) analysis conducted
		Age	Sex	SES	Other				
Radespiel-Tröger et al., 2009 *(137)*	Radespiel-Tröger 2009	Yes	Yes (stratified)	No	No	Unclear	Unclear	RR	Yes
Janković et al., 2010 *(138)*	Janković 2010	No	No	No	Naevi, vacations in childhood/ youth/after 40 years, type of tan, skin reaction to sun exposure, lifetime no. sunburns, exposure to sunlight outside of vacation, history of eczema/ previous BCC	No	No	OR	No
Kenborg et al., 2010 *(139)*	Kenborg 2010[a]	No	No	Yes	First year of employment, place of birth, skin colour, SES	No	No	OR	No
Dessinioti et al., 2011 *(140)*	Dessinioti 2011	Yes	Yes	No	Unclear	No	No	OR	Unclear
Ferreira et al., 2011 *(141)*	Ferreira 2011	Yes	Yes	Unclear	Descent, phototype	Yes	Unclear	OR	No
Iannacone et al., 2012 *(142)*	Iannacone 2012	Yes	Yes	Yes	Education level, history of ever smoking	No	No	OR	No
Sanchez et al., 2012 *(143)*	Sanchez 2012	Yes	No	No	Rural residence, recreational sun exposure, family history of skin cancer	No	No	OR	No
Surdu et al., 2013 *(144)*	Surdu 2013	Yes	Yes	No	Arsenic in water, family history of skin cancer	No	No	OR	Unclear
Kaskel et al., 2015 *(145)*	Kaskel 2015	No	No	No	No	No	No	OR	No
Fortes et al., 2016 *(60)*	Fortes 2016	Yes	Yes	Yes	No	Yes	Unclear	OR	Unclear
Trakatelli et al., 2016 *(64)*	Trakatelli 2016	Yes	Yes	No	Skin phototype, smoking	No	No	OR	Unclear
Schmitt et al., 2018 *(41, 42)*	Schmitt 2018	Yes	Yes	No	Phototype, non-occupational UVR exposure	No	No	OR	Yes

BCC, basal cell carcinoma; F, females; M, males; NA, not applicable; OR, odds ratio; RR, relative risk; SES, socioeconomic status; UV, ultraviolet; UVR, ultraviolet radiation.

Table 9. Properties of exposure assessments and models prioritized in studies included in systematic review and meta–analyses of association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma and non-melanoma skin cancer

Author, year	Study ID	Exposure assessment				Co-exposure to other occupational risk factors	Model used in review and/or meta-analysis and reason for prioritization (if relevant)
		Exposure definition	Exposure assessment method	Level/intensity of exposure[a]	No. participants in exposed, unexposed groups		
Klepp & Magnus, 1979 *(92)*	Klepp 1979	At least 3–4 h in fresh air at work daily	Self-completed questionnaire	Yes/no (yes assigned if at least 3–4 h/day in fresh air at work)	51, 158	Unclear	Single model reported; presumably sex-specific risk estimates
MacKie & Aitchison, 1982 *(93)*	MacKie 1982	Total no. hours of occupational sun exposure in winter and summer	In-person interview (questionnaire)	Yes/no (yes assigned if ≥ 16 h/wk spent outdoors in occupation)	44, 177	Unclear	Multiple models reported; model including all cases and adjusted for skin type, severe sunburns, recreational sun exposure and social class prioritized over sex-specific models
Aubry & MacGibbon, 1985 *(94)*	Aubry 1985	Occupational exposure to UVR/sun based on occupational history	Self-completed questionnaire	Classified occupational sunlight exposure as low, medium or high	110, 156	Dichotomous variable for occupational exposure to soot, coal tar, pitch, creosote, asphalt, carbon black, shale oil, crude mineral oils, fuel oil, arsenic, external radiation, chemicals and/or plastics	Single model reported
Elwood et al., 1985 *(95, 96)* Gallagher et al., 1987 *(97)*	Elwood 1985	Occupational exposure per year of working life; hours of WBE to sunlight per year	In-person interview (questionnaire)	< 1, 1–99, 100–199, 200–399 or ≥ 400 equivalent hours of exposure per year	162, 297	Unclear	Multiple models reported; model adjusting for host risk factors (hair colour, skin colour, history of freckles and ethnic origin) prioritized over unadjusted model
Graham et al., 1985 *(98)*	Graham 1985	Cumulative no. hours of occupational sun exposure	In-person interview (questionnaire)	Cumulative occupational sun exposure in hours (< 1, 1–4000, 4001–14 000, 14 001–45 000, > 45 000)	80, 93	Unclear	Single model reported; cumulative hours of outdoor work adjusted for burn reaction to sun

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Author, year	Study ID	Exposure assessment				Co-exposure to other occupational risk factors	Model used in review and/or meta-analysis and reason for prioritization (if relevant)
		Exposure definition	Exposure assessment method	Level/intensity of exposure[a]	No. participants in exposed, unexposed groups		
Bell et al., 1987 *(99)*	Bell 1987	Occupational description as outdoor, indoor or mixed; specific definitions of "keen gardener" and "outdoor sportsman"	In-person interview (questionnaire)	Occupational sun exposure categorized as indoor, outdoor or mixed-type workers	102, 1419	Cutting oils in male participants (no. cases, 21); risk estimate 2.13 ($P = 0.02$; CI: 1.11–3.28), adjusted for age and year of diagnosis	Single model reported
Cristofolini et al., 1987 *(100)*	Cristofolini 1987	Occupational exposure to sunlight (outdoor vs indoor work)	In-person interview (questionnaire)	Main occupation: indoor, outdoor	59, 244	No	Multiple models reported; model in table 2 of the study prioritized as it included adjustments for age and sex
Østerlind et al., 1988 *(101)*	Østerlind 1988	Working outside in the summer for ≥ 6 mo	In-person interview (questionnaire)	Yes, no; duration up to 10 yr cited but no results by duration reported	Unclear	Unclear	Multiple models reported; model for outdoor work in men (adjusted for socioeconomic status) selected over models for specific occupations
Zanetti et al., 1988*(102)*, 1999 *(103)* Rosso et al., 1998 *(104)*, 2008 *(105)*	Zanetti 1988	No. years of outdoor work	In-person interview (questionnaire)	Never, 1–5, 6–16, 17–32, > 32 yr	91, 433	Unclear	Multiple models reported; model adjusted for confounders (age, education level, sunburn in childhood, skin type, hair colour) prioritized over univariate model (only for males)
Dubin et al., 1989 *(106)*, 1990 *(61)*	Dubin 1989	Qualitative occupational sun exposure	In-person interview (questionnaire)	Mostly indoors, mostly indoors/outdoors, mostly outdoors	41, 772	Unclear	Multiple models reported; model for melanoma in Dubin et al. *(106)* adjusted for age and sex, and 95% CI prioritized
Garbe et al., 1989 *(107)*	Garbe 1989	Occupational sun exposure to the upper part of the body and/or the extremities on the occasion of sunshine	In-person interview (questionnaire)	Three categories of occupational sun exposure: none, sometimes, nearly every time	12, 333	Unclear	Multiple models reported; model that adjusted for confounders (no. melanocytic naevi, no. atypical melanocytic naevi, no. actinic lentigines and skin type) was prioritized
Beitner et al., 1990 *(108)*	Beitner 1990	Outdoor or indoor workers	Self-completed questionnaire	Outdoor vs indoor worker	Unclear	Unclear	Single model reported (not for occupational sun exposure)

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Author, year	Study ID	Exposure assessment				Co-exposure to other occupational risk factors	Model used in review and/or meta-analysis and reason for prioritization (if relevant)
		Exposure definition	Exposure assessment method	Level/intensity of exposure[a]	No. participants in exposed, unexposed groups		
Weiss et al., 1991 *(109)*	Weiss 1991	Occupational sun exposure categorized as "full-time most of life, part-time or some years and insignificant"	In-person interview	Almost continuously, part-time, ever (full-time most of life, part-time or for some years, and insignificant)	42, 158	Unclear	Multiple models reported; model presenting all cases of malignant melanoma prioritized over models of specific types of malignant melanoma
Nelemans et al., 1993 *(110)*	Nelemans 1993	Occupational sun exposure (ever vs never)	In-person interview (questionnaire)	Ever vs never outdoor	148, 176	Unclear	Multiple models reported; model adjusting for confounders (age, sex, education level, tendency to burn, hair colour and freckling) prioritized over unadjusted model
White et al., 1994 *(111)*	White 1994	Adult occupation (indoor, indoor/outdoor, outdoor) and duration	Telephone interview (questionnaire)	Years estimated: never, < 50% and ≥ 50% of lifetime occupation	46, 333	Unclear	Single model reported; model adjusted for confounders (age, sex, education level)
Gallagher et al., 1995 *(112, 113)*	Gallagher 1995	Occupational sunlight exposure index: annual WBE	In-person interview (questionnaire)	Annual WBE categories for summer: < 15, 15–59, 60–104 and ≥ 105 WBE/yr for summer; weekly categories < 3.5, 3.5–13.9, 14.0–24.9, ≥ 25 h/wk	272, 169	Unclear	Multiple models reported; model that adjusted for age, skin colour, hair colour and mother's ethnic origin was prioritized
Goodman et al., 1995 *(114)*	Goodman 1995	Job title	Expert (occupational medicine physician) assessment of administrative records	Mainly indoor, indoor/outdoor and mainly outdoor	2436, 35 871	Unclear	Single model reported
Holly et al., 1995 *(115)*	Holly 1995	Time spent outdoors on weekdays with arms and legs exposed to the sun (> 10 occupational years)	In-person interview (questionnaire)	Time spent outdoors on weekdays with arms and legs exposed to the sun (for > 10 occupational years): < 1/4 of time, 1/4 to < 1/2 of time, ≥ 3/4 of time	Unclear	Unclear	Multiple models reported for melanoma, superficial spreading and nodular melanoma; model included cases from all histology types (no adjustment for confounders)

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Author, year	Study ID	Exposure assessment				Co-exposure to other occupational risk factors	Model used in review and/or meta-analysis and reason for prioritization (if relevant)
		Exposure definition	Exposure assessment method	Level/intensity of exposure[a]	No. participants in exposed, unexposed groups		
Kricker et al., 1995 *(116)*	Kricker 1995	Accumulated hours of sun exposure on working days during 09:00–17:00 from age 15 yr	Self-completed questionnaire	0–14.7, 14.8–27.7, 27.8–49.3, ≥ 49.4 h/wk	223, 226	Unclear	Single model reported; risk modelled from cumulative no. hours adjusted for age, sex and ability to tan
Chen et al., 1996 *(117)*	Chen 1996	Ever worked as a lifeguard, construction worker, farmer or in any other outdoor job, and for period; total no. years in outdoor jobs	In-person interview (questionnaire)	Total no. years in outdoor jobs (0, < 5 or ≥ 5)	Unclear	Unclear	Multiple polychotomous logistic regression risk models reported for different anatomical sites of melanoma; models of risk estimates for head and neck prioritized because of greater exposure
Green et al., 1996 *(118)*	Green 1996	Self-report of "mainly outdoors occupation"	Self-completed questionnaire	Mainly indoors, indoors and outdoors, mainly outdoors	456, unclear	Unclear	Single model reported for each of the NMSC subtypes; models for BCC and for SCC adjusted by sex, age and skin colour
Ródenas et al., 1996 *(119)*	Ródenas 1996	Occupational exposure to solar UVR (hours)	In-person interview (questionnaire)	No. hours: 0, 1–11 500, ≥ 11 501	71, 128	Unclear	Single model reported; duration of exposure in hours, adjusted for age, skin type and skin colour
Rosso et al., 1996 *(120)*, 1998 *(104)*	Rosso 1996	No. hours of sun exposure in lifetime	In-person interview (questionnaire)	No. hours over lifetime: < 7200, 7200–12 480, 12 481–54 720, ≥ 54 720	818, 1148	Unclear	Multiple models reported; model that utilized lifetime sun exposure in hours in BCC and in SCC with adjustment for a larger number of confounders (sex, age, centre, hair colour, eye colour and skin reaction to sun exposure) prioritized
Suárez-Varela et al., 1996 *(121)*	Suárez-Varela 1996	Daily no. hours of sun exposure in occupational activity outdoor	In-person interview (questionnaire)	Daily no. hours: < 1.7 (low), 1.7–3.6 (medium), 3.6–4.8 (high), > 4.8 (very high)	Unclear	Unclear	Multiple models reported (for males and for females); sex-specific models by level of daily intensity of exposure adjusted by age
Freedman et al., 1997 *(122)*, 2002 *(123)*	Freedman 1997	Occupational sunlight: indoor, mixed, outdoor non-farmer, farmer	Classification by industrial hygienist of occupation in death certificate	Indoor, indoor/outdoor, outdoor non-farmer, farmer	7833, 92 861	Unclear	Multiple models reported; model that adjusted for age, sex, race, residence, occupational sun exposure and socioeconomic status was prioritized

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Author, year	Study ID	Exposure assessment				Co-exposure to other occupational risk factors	Model used in review and/or meta-analysis and reason for prioritization (if relevant)
		Exposure definition	Exposure assessment method	Level/intensity of exposure[a]	No. participants in exposed, unexposed groups		
Espinosa Arranz et al., 1999 *(124)*	Espinosa Arranz 1999	Occupational exposure definition of place of working as outdoor or indoor	In-person interview (questionnaire)	Indoor or outdoor	109, 242	Building materials such as cement, lead, radon, mercury, wood powder, paints and solvents	Multiple models reported; model in which OR was adjusted for skin type, naevi count and age was prioritized
Rosso et al., 1999 *(125)*	Rosso 1999	No. hours of sun exposure during outdoor work over lifetime	In-person interview (questionnaire)	No. hours over lifetime: never, < 12 000, < 47 900, < 77 200, ≥ 77 200	30, 137	Unclear	Multiple models reported; models by NMSC histology type (both BCC and SCC) adjusted for sex and age prioritized
Walter et al., 1999 *(126)*	Walter 1999	Chronic exposure to sun for > 0 h in the last 5 yr	In-person interview (questionnaire)	Average no. hours spent outdoors during the summer months in jobs held during 5 yr before interview (0 vs > 0)	580, 564	Unclear	Multiple models reported; model adjusted for age, sex and skin reaction to summer sun exposure prioritized over univariate model
Vlajinac et al., 2000 *(127)*	Vlajinac 2000	Outdoor work during summer	In-person interview (questionnaire)	Exposed, not exposed (yes, no)	31, 568	Organic and non-organic dissolvents, and organophosphatic compounds	Single model reported; model adjusted for confounders (brown eyes, freckling at age < 15 yr, skin reaction to sun exposure, weeks per year of seaside vacation, occupational exposure to chemicals, previous BCC in personal history, other)
Corona et al., 2001 *(128)*	Corona 2001	Occupational exposure to sunlight (outdoor work and duration)	In-person interview (questionnaire)	Working outdoors for > 8 yr vs ≤ 8 yr	60, 260	No	Single model reported
Håkansson et al., 2001 *(68)*	Håkansson 2001	Occupational exposure to solar UVR from outdoor work	Expert (industrial hygienist) assessment of administrative records	Low, medium, high levels of occupational sunlight exposure	28 597, 167 428	Extremely low-frequency magnetic fields and polycyclic aromatic hydrocarbons in asphalt and coal tar	Multiple models reported; model that accounted for co-exposure to asphalt and coal tar (table 4 in the study record) was prioritized (result was similar when co-exposed participants were excluded)
Loria & Matos, 2001 *(129)*	Loria 2001	Total no. hours spent outdoors at work (outdoor work: yes, no)	In-person interview (questionnaire)	No. hours spent outdoors: none, > 21 to 9230	111, 236	Unclear	Single model reported; model unadjusted for confounders

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Author, year	Study ID	Exposure assessment				Co-exposure to other occupational risk factors	Model used in review and/or meta-analysis and reason for prioritization (if relevant)
		Exposure definition	Exposure assessment method	Level/intensity of exposure[a]	No. participants in exposed, unexposed groups		
Milán et al., 2003 *(130)*	Milán 2003	Occupational setting: mainly inside, mainly outside, both, never worked	Self-completed questionnaire	Mainly inside, mainly outside, both, never worked	52, 319	Unclear	Multiple models reported; both sex-adjusted models used
Bataille et al., 2004 *(131)*	Bataille 2004	No. hours working outdoors in the summer	In-person interview (questionnaire)	0, 1–2, 3–6, > 6 h	22, 473	Unclear	Single model reported
Fargnoli et al., 2004 *(132)*	Fargnoli 2004	Occupational sun exposure assessed by asking whether occupation was mainly indoors or outdoors for ≥ 6 mo/yr including spring and/or summer	In-person interview (questionnaire)	Occupational (yes/no)	67, 233	Unclear	Multiple models reported; model that generated risk estimates adjusted for confounders (hair colour, eye colour, skin type for pigmentation factors) was prioritized
Walther et al., 2004 *(133)*	Walther 2004	Occupational exposure to solar UVR in general	In-person interview (questionnaire)	Frequently/sometimes vs never/rarely	216, 408	Unclear	Multiple models reported; model adjusted for age, region, smoking, history of skin cancer, history of benign skin conditions, phenotypic attributes and sun exposure during childhood prioritized over univariate model
Nijsten et al., 2005 *(62)*	Nijsten 2005	Occupational sun exposure	In-person interview (questionnaire)	Little or none, moderate, a lot	34, 314	Unclear	Single model reported; model adjusted for age, sex and skin phototype
Whiteman et al., 2006 *(134)*	Whiteman 2006	Occupational exposure to the sun ("how much time did you spend outdoors in the sun in summer on workdays")	In-person interview, at which participant self-completed questionnaire	< 1, 1–4, > 4 hr/day Categories in lifetime hours of outdoor work: low, 209–7311; medium, 7331–20 037; high, ≥ 20 037	43, 53	Unclear	Multiple models reported; model for invasive cancer including all histologies, adjusted for age, age squared, sex and Breslow thickness prioritized over model including all cases (in situ and invasive)

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Author, year	Study ID	Exposure assessment				Co-exposure to other occupational risk factors	Model used in review and/or meta-analysis and reason for prioritization (if relevant)
		Exposure definition	Exposure assessment method	Level/intensity of exposure[a]	No. participants in exposed, unexposed groups		
Zanetti et al., 2006 *(63)*	Zanetti 2006	Outdoor work (no. weighted hours in a lifetime)	In-person interview (questionnaire)	No. lifetime hours of outdoor work: never; low, ≤ 320; medium, ≤ 1128; high, ≤ 3878; very high, > 3878	179, 247	Unclear	Multiple models reported; model adjusted for potential confounders (country of interview, pigmentary characteristics, naevi and freckles) prioritized over univariate models by type of cancer
Pelucchi et al., 2007 *(135)*	Pelucchi 2007	Lifetime occupational sun exposure	In-person interview (questionnaire)	Yes (long or short duration) or no	139, 691	Unclear	Multiple models reported; model by histology of BCC (superficial spreading, nodular) adjusted for age, sex, study centre, education level, and eye, hair and skin colour prioritized
Nikolaou et al., 2008 *(136)*	Nikolaou 2008	Outdoor occupation (yes, no)	In-person interview (questionnaire)	Yes, no	117, 283	Unclear	Single model reported; model adjusted for confounders
Radespiel-Tröger et al., 2009 *(137)*	Radespiel-Tröger 2009	Job title with the longest overall duration used to classify people into outdoor, mixed or indoor worker	Categorical assessment of job title from administrative records, with reference to previously published studies	Indoor, mixed indoor/outdoor and outdoor	Unclear	Unclear	Single model reported; sex-stratified and age-adjusted model by histology type for NMSC and melanoma for all cases combined
Janković et al., 2010 *(138)*	Janković 2010	Outdoor work during the summer	In-person interview (questionnaire)	Yes, no	108, 92	Chemicals including insecticides, herbicides and pesticides	Multiple models reported; model adjusting for confounders (vacations at seaside, type of tan after repeated sun exposure in childhood, skin reaction to sunlight as a child or adolescent, lifetime no. severe and painful sunburns, occupational exposure to chemicals, history of eczema and history of previous BCC) prioritized
Kenborg et al., 2010 *(139)*[b]	Kenborg 2010	Years in outdoor work and years in specific outdoor jobs	Exposure categories in years of employment from pension fund records; Danish job–exposure matrixes	No outdoor work or outdoor work for 1–5, 5–10, > 10 yr	5126, 91 640	Social class determined by job title	Multiple models reported; model comparing time spent in outdoor jobs prioritized over models comparing specific outdoor jobs

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Author, year	Study ID	Exposure assessment				Co-exposure to other occupational risk factors	Model used in review and/or meta-analysis and reason for prioritization (if relevant)
		Exposure definition	Exposure assessment method	Level/intensity of exposure[a]	No. participants in exposed, unexposed groups		
Dessinioti et al., 2011 *(140)*	Dessinioti 2011	Outdoor work for > 5 yr	In-person interview (questionnaire)	Outdoor workers vs no outdoor work, outdoor work for 0–5 yr or > 5 yr	Unclear	No	Multiple models reported; model adjusted for age and sex prioritized although it was not clear which other variables were adjusted while performing multivariate analysis
Ferreira et al., 2011 *(141)*	Ferreira 2011	Exposure to sunlight (mean h/day); period in profession with occupational exposure to sunlight (years)	In-person interview (questionnaire)	< 10 yr = 0; ≥ 11 yr = 1 No. hours of occupational exposure per day (< 5 h, ≥ 6 h)	65, 199	No	Multiple models reported; model that generated risk estimates adjusted for confounders (phenotype, family history of cancer, and non-occupational sun exposure) was prioritized
Iannacone et al., 2012 *(142)*	Iannacone 2012	Having a job in the sunlight for ≥ 3 mo (yes/no), the number of years with a job in the sunlight for ≥ 3 mo	Self-completed questionnaire	No. years with a job in the sunlight for ≥ 3 mo: < 1, 1–5, 6–10 or > 10 yr; < 10 or > 10 yr	98, 148	No	Multiple models reported; models for BCC and SCC with larger number of confounders (including extra variables that adjusted for important risk factors such as eye and hair colour) were prioritized
Sanchez et al., 2012 *(143)*	Sanchez 2012	Lifetime outdoor work activity by age at exposure	Questionnaire, but unclear if self-completed or by interviewer	At age < 15, 15–30 and > 30 yr	132, unclear	Arsenic	Multiple models reported; model adjusted for confounders (family history of skin cancer, history of sunburns, actinic keratosis, rural residence and phototype) prioritized over univariate model
Surdu et al., 2013 *(144)*	Surdu 2013	Occupational exposure to natural UVR	In-person interview and validation by expert in occupational health or hygienist	Never, ever, cumulative life exposure by tertile: ≤ 1225, 1225.5–5075, ≥ 5075 hr	135, 906	Arsenic	Multiple models reported; model with 30-yr lag (ever/never and by tertile of cumulative exposure) prioritized over no lag
Kaskel et al., 2015 *(145)*	Kaskel 2015	Occupational exposure to UVR, farming	In-person interview (questionnaire)	Occupational UVR exposure (sometimes/often vs no/few)	277, 555	No	Single model reported; model unadjusted for confounders
Fortes et al., 2016 *(60)*	Fortes 2016	Sun exposure at occupational level (indoors, outdoors or both)	In-person interview (questionnaire)	Indoor, indoor/outdoor, outdoor	137, 539	Pesticides: percentage, frequency of use (no. times/wk), duration (yr)	Multiple models reported; model that adjusted for sex and age was prioritized

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Author, year	Study ID	Exposure assessment				Co-exposure to other occupational risk factors	Model used in review and/or meta-analysis and reason for prioritization (if relevant)
		Exposure definition	Exposure assessment method	Level/intensity of exposure[a]	No. participants in exposed, unexposed groups		
Trakatelli et al., 2016 *(64)*	Trakatelli 2016	Indoor work (reference), farm/ construction work, other outdoor work	In-person interview, at which participant self-completed questionnaire	Never, < 1, 1–5, ≥ 5 yr	Unclear	Unclear	Multiple models reported; multivariate analysis (by duration of outdoor work and for specific occupations) adjusted for country, sex, age and phototype (plus smoking, sunscreen use, outdoor hobbies), which gave risk estimates by a quantitative metric of exposure
Schmitt et al., 2018 *(41, 42)*	Schmitt 2018	Occupational cumulative solar exposure, measured in SED	Computer-assisted interview of lifetime occupational history; solar UVR exposure estimated by algorithm	0, > 0–532.1, 532.2–5870.4, ≥ 5870.5 SED	167, 735	Unclear	Multiple models reported; model with four levels of exposure and reference 0 SED, with larger number of adjustments (for age, age squared, sex, phototype and non-occupational sun exposure), prioritized over model comparing middle with high exposure

BCC, basal cell carcinoma; CI, confidence interval; h, hour(s); mo, months(s); NMSC, non-melanoma skin cancer; OR, odds ratio; SCC, squamous cell carcinoma; SED, standard erythemal dose; UVR, ultraviolet radiation; vs, versus; WBE, whole-body equivalents; wk, week(s); yr, year(s).

[a] Where multiple exposure levels were included, the comparison between the lowest level (reference group) and highest level of exposure was included in the main analysis.

[b] With the exception of Kenborg et al. *(139)*, in which exposure was assessed at a group level, all studies assessed exposure at an individual level.

Table 10. Properties of health outcome assessments and comparators in studies included in systematic review and meta-analyses on association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma and non-melanoma skin cancer

Author, year	Study ID	Definition/specification of health outcome	ICD code	Diagnostic assessment method	Exposed group: no. cases, no. non-cases	Unexposed group: no. cases, no. non-cases	Definition of comparator group, including specific level of exposure	Included in meta-analysis?
Klepp & Magnus, 1979 *(92)*	Klepp 1979	Melanoma	Unclear	Physician diagnostic record	19, 32	59, 99	< 3–4 h/day in the fresh air at work	No
MacKie & Aitchison, 1982 *(93)*	MacKie 1982	Melanoma	Unclear	Physician diagnostic record	16, 28	93, 84	< 16 h/wk outdoor work	Melanoma incidence
Aubry & MacGibbon, 1985 *(94)*	Aubry 1985	SCC	Unclear	Administrative records	42, 68	50, 106	Non-occupational sun exposure	NMSC incidence
Elwood et al., 1985 *(95, 96)* Gallagher et al., 1987 *(97)*	Elwood 1985	Melanoma	Unclear	Other	72, 90	141, 156	Equivalent WBE hours of exposure < 1, approximate hours of actual exposure with typical clothing = 0	Melanoma incidence
Graham et al., 1985 *(98)*	Graham 1985	Melanoma	Unclear	Physician diagnostic record	34, 46	50, 43	< 1 h of cumulative occupational sun exposure	Melanoma incidence
Bell et al., 1987 *(99)*	Bell 1987	Melanoma	Unclear	Physician diagnostic record	17, 85	207, 1212	No definition of indoor, outdoor or mixed (indoor and outdoor) occupation; the exception was for tropical residence, in which "Indoor Occupation" and "Tropical Residence 1–4 Years" were used as reference groups in determination of relative risk	No
Cristofolini et al., 1987 *(100)*	Cristofolini 1987	Melanoma	Unclear	Administrative records	21, 38	82, 162	Indoor workers	Melanoma incidence
Østerlind et al., 1988 *(101)*	Østerlind 1988	Melanoma	Unclear	Histology	Unclear	Unclear	Not working outdoors in the summer (indoor work)	Melanoma incidence

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Author, year	Study ID	Definition/specification of health outcome	ICD code	Diagnostic assessment method	Exposed group: no. cases, no. non-cases	Unexposed group: no. cases, no. non-cases	Definition of comparator group, including specific level of exposure	Included in meta-analysis?
Zanetti et al., 1988 *(102)*, 1999 *(103)* Rosso et al., 1998 *(104)*, 2008 *(105)*	Zanetti 1988	Melanoma	8720/2, 8720/3, 8721/3, 8722/3, 8730/3, 8740/3, 8741/2, 8742/2, 8742/3, 8743/2, 8743/3, 8772/3 (ICD-O)	Physician diagnostic record; cancer registry	25, 66	208, 225	Never outdoor work	Melanoma incidence (Rosso et al., 1998), melanoma mortality (Rosso et al., 2008)
Dubin et al., 1989 *(106)*, 1990 *(61)*[a]	Dubin 1989	Melanoma	Unclear	Other	21, 19	242, 458	Baseline exposure group for each study factor was either the unexposed category or the category most frequently reported by controls	Melanoma incidence
Garbe et al., 1989 *(107)*	Garbe 1989	Melanoma	Unclear	Physician diagnostic record	10, 2	159, 174	Group without occupational sun exposure	Melanoma incidence
Beitner et al., 1990 *(108)*	Beitner 1990	Melanoma	Unclear	Physician diagnostic record	Unclear	Unclear	Non-outdoor workers	Melanoma incidence
Weiss et al., 1991 *(109)*	Weiss 1991	Melanoma	Unclear	Physician diagnostic record	28, 14	72, 86	Insignificant or no occupational sun exposure	Melanoma incidence
Nelemans et al., 1993 *(110)*	Nelemans 1993	Melanoma	C43 (ICD-10)	Physician diagnostic record	54, 94	87, 89	Never outdoors	No
White et al., 1994 *(111)*	White 1994	Melanoma	8743, 8720, 8771, 8772, 8774 (ICD-O)	Administrative records	16, 30	168, 165	Indoor; never outdoor occupation	Melanoma incidence
Gallagher et al., 1995 *(112, 113)*	Gallagher 1995	BCC and SCC	Unclear	Physician diagnostic record	144, 128	82, 87	Mean occupational sun exposure per year (lifetime), annual WBE < 15 WBE/yr or < 2.8 h/wk (summer)	NMSC incidence

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Author, year	Study ID	Definition/specification of health outcome	ICD code	Diagnostic assessment method	Exposed group: no. cases, no. non-cases	Unexposed group: no. cases, no. non-cases	Definition of comparator group, including specific level of exposure	Included in meta-analysis?
Goodman et al., 1995 *(114)*	Goodman 1995	Melanoma	Unclear	Administrative records	122, 2314	2301, 33 570	Indoor work	No
Holly et al., 1995 *(115)*	Holly 1995	Melanoma	Unclear	Administrative records	Unclear	Unclear	No time spent outdoors on weekdays with arms and legs exposed to the sun (in last 10 yr)	No
Kricker et al., 1995 *(116)*	Kricker 1995	BCC	Unclear	Physician diagnostic record	44, 179	47, 179	Control group	NMSC incidence
Chen et al., 1996 *(117)*	Chen 1996	Melanoma	Unclear	Administrative records (rapid case ascertainment system)	Unclear	Unclear	Never worked in an outdoor job	Melanoma incidence
Green et al., 1996 *(118)*	Green 1996	BCC	Unclear	Physician diagnostic record	Unclear	Unclear	Mainly indoor occupation or mixed (indoor/outdoor occupation)	No
Ródenas et al., 1996 *(119)*	Ródenas 1996	Melanoma	Unclear	Physician diagnostic record	41, 30	48, 80	Zero occupational sun exposure (possibly indoor occupational groups)	Melanoma incidence
Rosso et al., 1996 *(120)*, 1998 *(104)*	Rosso 1996	BCC and SCC	Unclear	Physician diagnostic record	408, 410	559, 589	< 7200 h of cumulative outdoor work	NMSC incidence
Suárez-Varela et al., 1996 *(121)*	Suárez-Varela 1996	NMSC	C44.9 (ICD-10)	Physician diagnostic record	Unclear	Unclear	Group with occupational sun exposure < 1.7 h/day	NMSC incidence
Freedman et al., 1997 *(122)*, 2002 *(123)*	Freedman 1997	Melanoma and NMSC, mortality	172, 173, 154.3, 187.7 (ICD-9)	NIH-NIOSH mortality database (death certificate[b])	Melanoma: 406, 993; NMSC: 374, 6060	Melanoma: 6574, 11 734; NMSC: 3024, 71 529	Indoor work	Melanoma and NMSC mortality
Espinosa Arranz et al., 1999 *(124)*	Espinosa Arranz 1999	Melanoma	Unclear	Other	45, 64	71, 171	Place of work recorded as indoors occupation category; no further definition in text	Melanoma incidence
Rosso et al., 1999 *(125)*	Rosso 1999	BCC and SCC	Unclear	Physician diagnostic record	12, 18	68, 69	Category with lifetime sun exposure "Never" used as reference in table 4 of the study record	No
Walter et al., 1999 *(126)*	Walter 1999	Melanoma	Unclear	Physician diagnostic record	266, 314	292, 272	Rare/never exposed	No

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Author, year	Study ID	Definition/specification of health outcome	ICD code	Diagnostic assessment method	Exposed group: no. cases, no. non-cases	Unexposed group: no. cases, no. non-cases	Definition of comparator group, including specific level of exposure	Included in meta-analysis?
Vlajinac et al., 2000 *(127)*	Vlajinac 2000	BCC	Unclear	Physician diagnostic record	22, 9	178, 390	No outdoor work in summer	NMSC incidence
Corona et al., 2001 *(128)*	Corona 2001	BCC	Unclear	Physician diagnostic	42, 18	120, 140	Outdoor work for 0–8 yr	NMSC incidence
Håkansson et al., 2001 *(68)*	Håkansson 2001	Melanoma and NMSC	190, 191, 192 (ICD-7)	Administrative records	Melanoma: 40, 28 557; NMSC: 14, 28 583	Melanoma: 271, 167 157; NMSC: 119, 167 309	Low exposure category; exposure level "Never or seldom works outdoors"	No
Loria & Matos, 2001 *(129)*	Loria 2001	Melanoma	Unclear	Physician diagnostic record	30, 81	71, 165	No lifelong occupational exposure	No
Milán et al., 2003 *(130)*	Milán 2003	BCC	Unclear	Cancer register	24, 28	164, 155	Control group (co-twin alive at diagnosis of the case)	NMSC incidence
Bataille et al., 2004 *(131)*	Bataille 2004	Melanoma	Unclear	Physician diagnostic record	13, 9	238, 235	Zero hours of outdoor work during the summer	No
Fargnoli et al., 2004 *(132)*	Fargnoli 2004	Melanoma	Unclear	Physician diagnostic record	33, 34	67, 166	No occupational exposure	Melanoma incidence
Walther et al., 2004 *(133)*	Walther 2004	BCC	Unclear	Physician diagnostic record	93, 123	120, 288	Never exposed	NMSC incidence
Nijsten et al., 2005 *(62)*	Nijsten 2005	Melanoma	C43 (ICD-10)	Physician diagnostic record	6, 28	113, 201	Little or no occupational sun exposure	Melanoma incidence
Whiteman et al., 2006 *(134)*	Whiteman 2006	Melanoma	Unclear	Physician diagnostic record	17, 26	13, 40	Low level (209–7331 h over a lifetime) of occupational sun exposure	No
Zanetti et al., 2006 *(63)*	Zanetti 2006	Melanoma, BCC and SCC	Unclear	Physician diagnostic record	Melanoma: 87, 61; NMSC: 31, 61	Melanoma: 81, 103; NMSC: 63, 103	Never exposed to outdoor work	Melanoma and NMSC incidence
Pelucchi et al., 2007 *(135)*	Pelucchi 2007	BCC	C43 (ICD-10)	Physician diagnostic record	65, 74	319, 372	Group without occupational sun exposure	NMSC incidence
Nikolaou et al., 2008 *(136)*	Nikolaou 2008	Melanoma	C43 (ICD-10)	Physician diagnostic record	52, 65	148, 135	No occupational sun exposure	No
Radespiel-Tröger et al., 2009 *(137)*	Radespiel-Tröger 2009	Melanoma, BCC and SCC	Unclear	Administrative records	Melanoma: 23, unclear; NMSC: 104, unclear	Melanoma: 102, unclear; NMSC: 557, unclear	Indoor categorized occupations or job titles	No

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Author, year	Study ID	Definition/specification of health outcome	ICD code	Diagnostic assessment method	Exposed group: no. cases, no. non-cases	Unexposed group: no. cases, no. non-cases	Definition of comparator group, including specific level of exposure	Included in meta-analysis?
Janković et al., 2010 *(138)*	Janković 2010	BCC	Unclear	Physician diagnostic record	51, 57	49, 43	Not working outdoors during summer time	NMSC incidence
Kenborg et al., 2010 *(139)*	Kenborg 2010	Melanoma and NMSC	Unclear	Physician diagnostic record	Unclear	Unclear	Controls matched by sex and year of birth	Melanoma and NMSC incidence
Dessinioti et al., 2011 *(140)*	Dessinioti 2011	BCC	Unclear	Physician diagnostic record	Unclear	Unclear	No outdoor work, 0–5 yr of outdoor work	NMSC incidence
Ferreira et al., 2011 *(141)*	Ferreira 2011	NMSC	Unclear	Patient at dermatology unit, biopsy, histopathology	39, 26	93, 106	< 5 h	NMSC incidence
Iannacone et al., 2012 *(142)*	Iannacone 2012	BCC and SCC	Unclear	Physician diagnostic record	77, 21	91, 57	Control group	NMSC incidence
Sanchez et al., 2012 *(143)*	Sanchez 2012	BCC	Unclear	Physician diagnostic record	84, 48	Unclear	Control group	NMSC incidence
Surdu et al., 2013 *(144)*	Surdu 2013	BCC	C44 (ICD-10)	Physician diagnostic record	78, 57	485, 421	Never occupationally exposed	NMSC incidence
Kaskel et al., 2015 *(145)*	Kaskel 2015	Melanoma, BCC	Unclear	Hospital discharge record	175, 102	328, 227	Controls	No
Fortes et al., 2016 *(60)*	Fortes 2016	Melanoma	Unclear	Other (medical examination at dermatology hospital)	78, 59	266, 273	Indoor and indoor/outdoor activity for occupational sun exposure	No
Trakatelli et al., 2016 *(64)*	Trakatelli 2016	Melanoma, BCC and SCC	Unclear	Physician diagnostic record	Unclear	Unclear	Never outdoor occupation	Melanoma and NMSC incidence
Schmitt et al., 2018 *(41, 42)*	Schmitt 2018	BCC	Unclear	Physician diagnostic record	105, 62	371, 364	0 SED occupational UVR exposure	NMSC incidence

BCC, basal cell carcinoma; h, hour(s); ICD, International Statistical Classification of Diseases and Related Health Problems; NIH, National Institutes of Health; NIOSH, National Institute for Occupational Safety and Health; NMSC, non-melanoma skin cancer; SCC, squamous cell carcinoma; SED, standard erythemal dose; UVR, ultraviolet radiation; WBE, whole-body equivalents; wk, week(s); yr, year(s).

[a] NMSC analysis in Dubin et al. 1990 *(61)* was excluded from the systematic review because of the ineligible health outcome (proportion of in situ cases > 10%).

[b] Health outcome was pathologically assessed in all cases; in Freedman et al. *(122, 123)* outcome was assessed by death certificate.

Table 11. Effect estimates from case–control studies on association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence, excluded from the meta–analysis

Author, year	Study ID	Comparison	Effect estimate	Reason for exclusion from main meta-analysis
Klepp & Magnus, 1979 *(92)*	Klepp 1979	Outdoor occupation, defined as ≥ 3–4 h/day in fresh air at work compared with < 3 h/day	Unadjusted OR: 1.45 (95% CI: 0.65–3.23) for males Unadjusted OR: 1.58 (95% CI: 0.35–7.09) for females	Reported data only allowed calculation of RRs unadjusted for confounding
Bell et al., 1987 *(99)*	Bell 1987	Any occupational exposure to solar UVR compared with no occupational exposure to solar UVR, derived from location of work activity (outdoor, outdoor/indoor, indoor)	Outdoor versus indoor RR: 1.31 (95% CI, unclear)	Only reported an RR unadjusted for confounding and without a measure of precision
Nelemans et al., 1993 *(110)*	Nelemans 1993	Occupational sunlight exposure categorized as "ever outdoors", compared with occupational sunlight exposure categorized as "never outdoors" when aged 15–25 yr	OR: 0.57 (95% CI: 0.33–0.98)	Defined exposure (exclusively in youth) differently from the other studies included in the meta-analysis
Holly et al., 1995 *(115)*	Holly 1995	Time spent outdoors on weekdays with arms and legs exposed to the sun in last 10 yr of work (none; < 1/4 of time ; > 1/4 to < 1/2 of time; ≥ 1/2 of time)	Unadjusted OR: 0.83 (95% CI: 0.46–1.5) for ≥ half of the time	Only reported an OR unadjusted for confounding
Walter et al., 1999 *(126)*	Walter 1999	Any occupational sun exposure during the summer, given by the average number of hours of daylight spent outdoors in any job held during the 5 yr prior to interview, versus no exposure (0 h vs > 0 h)	OR: 0.78 (95% CI: 0.61–0.99)	Defined the outcome differently from the other studies included in the meta-analysis; outcome comprised in situ melanoma for an unclear number of cases
Loria & Matos, 2001 *(129)*	Loria 2001	Lifetime occupational sun exposure for the duration of 21–9230 h, compared with lifetime occupational sun exposure for the duration of 0 h	Unadjusted OR: 0.9[a] (95% CI: 0.5–1.5)	Only reported an OR unadjusted for confounding
Bataille et al., 2004 *(131)*	Bataille 2004	Worked outdoors in the sun during summer for ≥ 1 h/wk, compared with worked outdoors in the sun during summer for < 1 h/wk	OR: 0.88 (95% CI: 0.35–2.22)	Defined the exposure differently from the other studies included in the meta-analysis
Nikolaou et al., 2008 *(136)*	Nikolaou 2008	Any occupational sun exposure, compared with no occupational sun exposure (whether occupation was mainly indoors or outdoors, for a period of > or < 5 yr)	Unadjusted OR: 0.69[a] (95% CI: 0.43–1.10)	Only reported an OR unadjusted for confounding; the outcome comprised in situ melanoma for four cases (2%)
Kaskel et al., 2015 *(145)*	Kaskel 2015	Occupational UVR exposure at a frequency of "sometimes/often", compared with occupational UVR exposure at a frequency of "no/few"	Unadjusted OR: 0.9 (95% CI: 0.6–1.2)	Only reported an OR unadjusted for confounding
Fortes et al., 2016 *(60)*	Fortes 2016	Any occupational exposure to solar UVR compared with no occupational exposure to solar UVR, derived from location of work activity (outdoor, outdoor/indoor, indoor)	OR: 1.34 (95% CI: 0.90–2.0)	Outcome comprised in situ melanoma for 26 cases (6.5% of all cases)

CI, confidence interval; h, hour(s); OR, odds ratio; RR, relative risk; UVR, ultraviolet radiation; vs, versus; wk, week(s); yr, year(s).

[a] Cases and controls were matched by sex and age, but this was judged to be different from adjustment by sex and age.

Table 12. Effect estimates from case–control studies on association between occupational exposure to solar ultraviolet radiation and non-melanoma skin cancer incidence, excluded from the main meta–analysis

Author, year	Study ID	Comparison	Effect estimate	Reason for exclusion
Rosso et al., 1999 *(125)*	Rosso 1999	Risk estimate by level of cumulative hours of sun exposure during outdoor work; univariate OR for > 77 200 h of outdoor work compared with never outdoor work	Unadjusted[a] OR for BCC: 0.9 (95% CI: 0.51–1.59) Unadjusted[a] OR for SCC: 1.9 (95% CI: 0.3–11.7)	Only reported an OR unadjusted for confounding
Kaskel et al., 2015 *(145)*	Kaskel 2015	Sometimes/often occupational UVR exposure, compared with no/few occupational UVR exposure	Unadjusted OR: 1.7 (95% CI: 1.2–2.5)	Only reported an OR unadjusted for confounding

BCC, basal cell carcinoma; CI, confidence interval; h, hour(s); OR, odds ratio; SCC, squamous cell carcinoma; UVR, ultraviolet radiation.

[a] Cases and controls were matched by sex and age, but this was judged to be different from adjustment by sex and age.

3.2.2 Population

The included studies captured more than 457 360 participants (Table 7). In the large population-based study in Bavaria, Germany by Radespiel-Tröger et al. *(137)*, only the number of cases was reported; for five studies, it was not possible to count the effective sample *(101, 115, 117, 118, 121)*. Six studies included only men *(68, 98, 101, 112–114, 139)* and one study included only women *(115)* in their analyses of occupational exposure to solar UVR and skin cancer. It was possible to fully disaggregate the effective samples of 21 studies with 242 199 participants by sex, with 3752 women (1.5%) and 238 447 men (98.5%) included. However, imputing the total study population and sex breakdown for the studies that did not provide a sex breakdown for the effective sample size (resulting in 43 studies, 561 967 participants) suggested 98 387 (17.5%) of participants were female and 463 580 (82.5%) were male.

One case–case study *(137)* reported data on different age groups (0–29, 30–39, 40–49, 50–59, 60–69, 70–79, ≥ 80 years). However, of the 46 included case–control studies reporting on the incidence of melanoma or NMSC, 41 of these reported the age of the sampled workers (which ranged over 18–92 years). Twelve studies reported the mean or median age of the participants.

The majority of studies examined populations in the WHO European Region (33 studies from 20 countries), followed by populations in the WHO Region of the Americas (15 studies from five countries) and populations in the WHO Western Pacific Region (three studies from Australia). Two studies included a combination of seven countries from both the Region of the Americas and the European Region *(60, 63)*. The countries in which studies were most frequently based were Italy (nine studies), Germany (eight studies) and the USA (eight studies). The industrial sectors most commonly studied were agriculture, forestry and fishing (International Standard Industrial Classification of All Economic Activities (ISIC) code A01; three studies) and construction (ISIC code F41; two studies).

3.2.3 Exposure

All 53 included studies measured exposure indirectly. Regarding exposure assessment methods (Table 9), 37 studies assessed exposure to solar UVR using standardized questionnaires completed during interviews by trained personnel either face to face or by telephone (one of which used the interview data in an algorithm to provide an SED *(41, 42)*), eight studies used self-completed questionnaires, two studies used job title as a proxy *(137, 139)*, and three studies *(114, 122, 123, 129)* used job exposure assessment by an expert in industrial hygiene or occupational health.

3.2.4 Comparator

Comparators were defined by the categories reported in the studies; "Was an indoor worker" was used in nine studies, and comparators were defined as "Had no occupational exposure to the sun" or by proxy of occupation group in other studies. Some studies reported that the reference group included people who had worked for less than a certain number of cumulative years as an outdoor worker (e.g. 5 or 8 years). Definitions used for no occupational exposure to solar UVR varied substantially and meaningfully, including definitions with diverse limits and time periods (see Section 2.4.3 for more details), for example: zero hours of working outdoors in the summer as an adult (Bataille et al. *(131)*), outdoor work in the sun for < 3 months (Iannacone et al. *(142)*) or no outdoor work during the summer (Janković et al. *(138)*).

3.2.5 Health outcomes

The 53 studies included in the systematic review and meta-analysis reported on four different health outcomes with some overlap (Table 10), namely melanoma incidence (33 studies) and mortality (two studies) *(102–105, 122, 123)*, and NMSC incidence (25 studies) and mortality (a single study) *(122, 123)*. No studies reported on the prevalence of melanoma or NMSC.

Most case–control studies recruited incident (i.e. newly diagnosed) cases of melanoma and NMSC; two case–control studies reported on mortality from melanoma and NMSC *(102–105, 122, 123)*. Five studies reported on NMSC without distinguishing between BCC and SCC *(68, 121, 139, 141, 144)*, seven studies reported on both types of NMSC *(41, 42, 64, 112, 113, 118, 125, 137, 142)*, and 12 studies *(63, 104, 116, 120, 127, 128, 130, 133, 135, 138, 140, 143, 145)* and a single study *(94)* presented results on only BCC and only SCC, respectively. Seven out of the 53 studies reported data for both melanoma and NMSC *(63, 64, 68, 122, 123, 137, 139, 145)*.

The outcome was most commonly assessed through histopathologically confirmed diagnosis. In one study the outcome ascertainment was by death certificate.

3.3 Risk of bias within studies

For studies with two or more study records, risk of bias assessments considered all study records. Even if a particular study record did not report on the health outcome being discussed (e.g. of the four study records for the Zanetti 1988 study, only Rosso et al. *(105)* reported on NMSC mortality), the study records included populations from the same study.

3.3.1 Melanoma incidence

For the outcome of melanoma incidence, the risk of bias ratings are presented in Fig. 3 and the justifications for these ratings are reported in Table A5.1 in Annex 5. Citations of all study records are included, even though a particular effect estimate used in the main meta–analyses may only have been reported in a single study record. The systematic review of studies reporting on melanoma incidence included 29 incident case–control studies *(60–64, 92, 93, 95–111, 115, 117, 119, 120, 124, 126, 129, 131, 132, 136, 139, 145)*, three case–case studies *(114, 134, 137)* and a single prospective cohort study *(68)*. The risk of bias was assessed in the complete body of evidence for this outcome by study design.

Fig. 3. Summary of risk of bias in studies reporting on the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence

Risk of bias domain \ Study ID	Klepp 1979[a]	Mackie 1982[b]	Elwood 1985[c]	Graham 1985[d]	Bell 1987[e]	Cristofolini 1987[f]	Østerlind 1988[g]	Zanetti 1988[h]	Dubin 1989[i]	Garbe 1989[j]	Beitner 1990[k]	Weiss 1991[l]	Nelemans 1993[m]	White 1994[n]	Goodman 1995[o]	Holly 1995[p]	Chen 1996[q]	Ródenas 1996[r]	Espinosa Arranz 1999[s]	Walter 1999[t]	Håkansson 2001[u]	Loria 2001[v]	Bataille 2004[w]	Fargnoli 2004[x]	Nijsten 2005[y]	Whiteman 2006[z]	Zanetti 2006[aa]	Nikolau 2008[ab]	Radespiel-Tröger 2009[ac]	Kenborg 2010[ad]	Kaskel 2015[ae]	Fortes 2016[af]	Trakatelli 2016[ag]
Selection bias	PH	PH	L	PH	PH	L	PL	PL	L	PL	PL	PH	PL	PL	PH	PL	PL	PL	PL	L	L	PL	PL	L	PL	PL	PL	PL	PL	PL	PL	L	PH
Performance bias	PL	PL	PL	PL	PL	PL	L	PL	PL	PL	PL	PL	PL	PL	L	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL
Exposure misclassification bias	PH	PH	PL	PL	PH	PH	PH	PH	PH	PH	PH	H	PH	PH	PH	PH	PH	PL	PH	H	PL	H	H	PH	PH	PL	PL	H	PH	PL	PH	PH	PH
Detection bias	PL	H	H	L	L	L	H	L	L	L	L	L	H	H	PL	L	L	L	L	L	L	L	L	L	H	L	L	L	L	L	L	L	L
Confounding	H	PH	L	PH	PH	L	L	PL	L	PL	PL	H	PL	PL	PH	H	PL	PL	L	PL	PH	PH	L	L	PL	PL	L	PH	PH	PL	PH	PL	PL
Incomplete outcome data	PL	L	PL	PL	L	PL	L	PL	PL	PL	PL	PL	PL	PL	PH	PL	L	L	PL	L	PL	PL	PL	L	PL	L	PL	PL	PL	L	PL	PL	L
Reporting bias	PL	L	PL	PL	L	PL	PL	L	PL	PL	PL	PL	PL	L	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	L	L	PL	PL	L	PL	PL	L
Conflict of interest bias	L	PL	L	L	L	PL	L	L	L	PL	PL	PL	PL	L	L	L	L	PL	PL	L	L	L	L	L	L	L	L	L	PL	L	PL	L	H
Other bias	PH	PL	PL	PH	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PH	PH	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PH	PL	PL	PL	PL

Legend

L Low risk of bias

PL Probably low risk of bias

PH Probably high risk of bias

H High risk of bias

Notes: studies with grey shading were included in a meta-analysis. [a] Klepp & Magnus, 1979 ***(92)***; [b] MacKie & Aitchison, 1982 ***(93)***; [c] Elwood et al., 1985 ***(95, 96)***, Gallagher et al., 1987 ***(97)***; [d] Graham et al., 1985 ***(98)***; [e] Bell et al., 1987 ***(99)***; [f] Cristofolini et al., 1987 ***(100)***; [g] Østerlind et al., 1988 ***(101)***; [h] Zanetti et al., 1988 ***(102)***, 1999 ***(103)***, Rosso et al., 1998 ***(104)***, 2008 ***(105)***; [i] Dubin et al., 1989 ***(106)***, 1990 ***(61)***; [j] Garbe et al., 1989 ***(107)***; [k] Beitner et al., 1990 ***(108)***; [l] Weiss et al., 1991 ***(109)***; [m] Nelemans et al., 1993 ***(110)***; [n] White et al., 1994 ***(111)***; [o] Goodman et al., 1995 ***(114)***; [p] Holly et al., 1995 ***(115)***; [q] Chen et al., 1996 ***(117)***; [r] Ródenas et al., 1996 ***(119)***; [s] Espinosa Arranz et al., 1999 ***(124)***; [t] Walter et al., 1999 ***(126)***; [u] Håkansson et al., 2001 ***(68)***; [v] Loria & Matos, 2001 ***(129)***; [w] Bataille et al., 2004 ***(131)***; [x] Fargnoli et al., 2004 ***(132)***; [y] Nijsten et al., 2005 ***(62)***; [z] Whiteman et al., 2006 ***(134)***; [aa] Zanetti et al., 2006 ***(63)***; [ab] Nikolaou et al., 2008 ***(136)***; [ac] Radespiel-Tröger et al., 2009 ***(137)***; [ad] Kenborg et al., 2010 ***(139)***; [ae] Kaskel et al., 2015 ***(145)***; [af] Fortes et al., 2016 ***(60)***; [ag] Trakatelli et al., 2016 ***(64)***.

(a) Selection bias

Of the 29 case–control studies reporting results on melanoma incidence, selection bias was rated in six studies as "low", 17 as "probably low" and six as "probably high". For the three case–case studies reporting results on melanoma incidence, two were rated as "probably low" *(134, 137)* and the third was rated as "probably high" *(114)* for selection bias. The single cohort study *(68)* reporting the risk of melanoma incidence was judged to have a "low" risk of bias for selection of study participants (i.e. selection bias). The majority of studies were representative of the target population and, for case–control studies, cases and matched controls were mostly, but not exclusively, recruited from the same hospital, clinic or geographical jurisdictions and therefore likely to have come from the same catchment populations. Response rates to participation or detailed study participant selection were not systematically reported in the included studies.

(b) Performance bias

Performance bias occurs in observational studies when researchers are aware of the exposure and/or outcome status of the participants due to a lack of blinding. For the case–control studies, one study was rated as "low" *(101)* and 28 studies were rated as "probably low". Of the three case–case studies, one was judged as "low" *(114)* and two were judged as "probably low" *(134, 137)* for performance bias. The cohort study reporting on the risk of melanoma incidence was judged as "probably low" for risk of performance bias *(68)*. Although study personnel were not

blinded to disease status (cases) or population characteristics of the study participants, or to the aims or hypotheses under study, it was judged unlikely that their knowledge of disease or the characteristics of study participants, or of the study hypotheses, led study personnel to introduce bias at the time of data collection, classification, analyses or reporting of results.

(c) Exposure misclassification bias

Of the 29 case–control studies, five studies were judged to have a "probably low", 19 studies were judged to have a "probably high" and five studies were judged to have a "high" risk of exposure misclassification bias. Of the three case–case studies, one was judged as "probably low" *(134)* and two were judged as "probably high" *(114, 137)* for risk of exposure misclassification bias. The cohort study reporting on the risk of incident melanoma was judged to have a "probably low" risk of bias for exposure assessment (i.e. exposure misclassification bias) *(68)*. Exposure was measured by self-completed questionnaires or in–person interviews in the majority of the studies in the systematic review using occupational exposure to solar UVR via proxy of outdoor work, often defined dichotomously without reference to duration or intensity of exposure and not always described in detail. In a few studies, the fact that the reference group (comparator) may also have experienced some occupational exposure to solar UVR may have introduced bias attenuating reported effect estimates, most likely towards the null.

(d) Detection bias

Of the case–control studies, 22 studies were rated as "low", a single study was rated as "probably low" *(92)* and six studies were rated as "high" for risk of detection bias; the "high" risk of detection bias for these six case–control studies was because they excluded a priori melanoma subtypes of interest in the study of chronic sun exposure (i.e. occupational) and risk of melanoma (i.e. lentigo maligna melanoma), potentially introducing bias towards the null hypothesis (see Annex 3). Two of the three case–case studies were judged as "low" *(134, 137)* and one as "probably low" *(114)* for risk of detection bias. The cohort study reporting on the risk of incident melanoma was judged as "low" for risk of detection bias (i.e. bias in outcome assessment) *(68)*. The outcome was measured by histopathological confirmation in the overwhelming majority of these studies.

(e) Confounding

Of the case–control studies, eight studies were rated as "low", 12 studies were rated as "probably low", six studies were rated as "probably high" and three studies were rated as "high" for risk of confounding. Of three case–case studies, a single study was classified as "probably low" *(134)* and two were classified as "probably high" *(114, 137)* for risk of confounding. The cohort study reporting on the risk of incident melanoma was judged as "probably high" for risk of confounding *(68)*. The judgement on this domain was based on the number and type of variables that the effect estimate in the study was adjusted for. A small number of studies only reported unadjusted effect estimates that did not take important confounders into account, very likely introducing bias that could have gone towards or against the null hypothesis.

(f) Incomplete outcome data bias

Of the case–control studies, nine studies were rated as "low" and 20 studies were rated as "probably low" for risk of bias from incomplete outcome data. The three case–case studies were judged as "low" *(134)*, "probably low" *(137)* and "probably high" *(114)* for risk of bias for this domain.

The cohort study reporting on the risk of incident melanoma was judged to have a "probably low" risk of bias from incomplete outcome data *(68)*.

(g) Reporting bias

Of the case–control studies, seven studies were rated as "low" and 22 studies were rated as "probably low" for risk of reporting bias. One case–case study was classified as "low" *(134)* and two case–case studies as "probably low" *(114, 137)* for risk of reporting bias. The cohort study that reported on the risk of incident melanoma was judged to have a "probably low" risk of reporting bias *(68)*. The majority of the included studies did not have a published or publicly available protocol stating the variables a priori to be analysed; however, it was judged unlikely that this would have introduced a noteworthy risk of bias.

(h) Conflict of interest bias

Of the case–control studies, 19 studies were rated as "low", nine studies were rated as "probably low" and a single study was rated as "high" *(64)* for risk of conflict of interest bias. The risk of conflict of interest bias among the case–case studies was judged to be either "low" *(114, 134)* or "probably low" *(137)*. The cohort study reporting on the risk of incident melanoma was judged to have a "low" risk of conflict of interest bias *(68)*. The majority of studies reported conflict of interest statements and/or funding source. Some authors of the study rated as "high" for risk of bias from a conflict of interest *(64)* received financial support from a pharmaceutical company to study the association between occupational exposure to solar UVR and skin cancer.

(i) Other biases

Of the case–control studies, 26 studies were judged as "probably low" and three studies were judged as "probably high" for risk of other biases. Possible recall bias (differential in case–control studies) was considered in this domain. One case–case study was classified as "probably low" *(134)* and two case–case studies were judged as "probably high" *(114, 137)* for risk of other biases. The cohort study reporting on the risk of incident melanoma was judged to have a "probably low" risk of other biases *(68)*. Studies focusing on younger adults might have excluded the aetiologically relevant age group of older adults, in which melanoma or NMSC associated with chronic sun exposure is often diagnosed (at least for certain histology types). Selection of a younger study population could have introduced bias towards the null value.

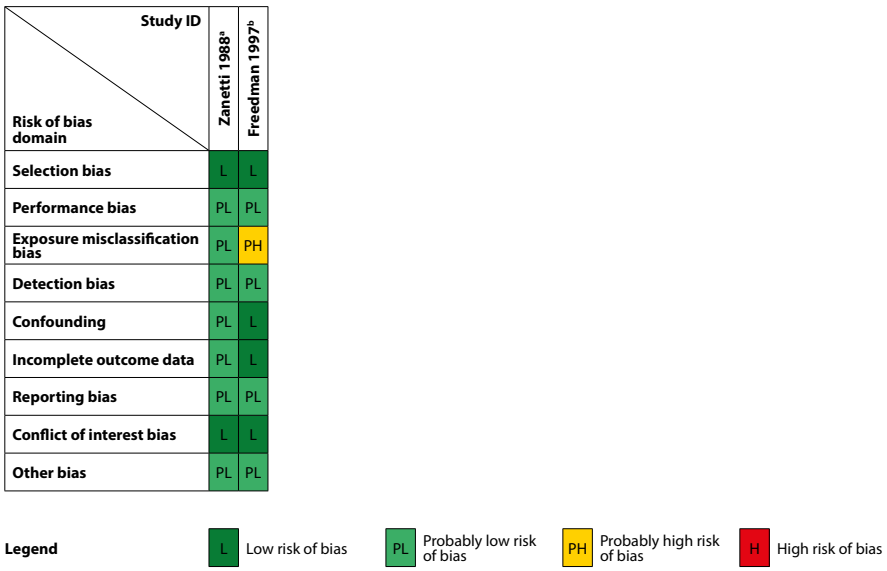
3.3.2 Melanoma mortality

The risk of bias ratings for the two studies investigating determinants of mortality from melanoma – a case–control study in which both melanoma and NMSC mortality were determined from death certificates (Freedman et al. *(122, 123)*), and an extended follow-up of another case–control study originally on melanoma incidence (Rosso et al. *(105)*, part of the Zanetti 1988 study *(102–105)*) – are provided in Fig. 4. Justifications for these ratings are provided in Table A5.2 in Annex 5 and in the following sections.

(a) Selection bias

Both studies were judged as "low" for risk of selection bias. In the study by Freedman et al. *(122, 123)*, all cases and controls were identified from the same nationally representative databases (United States National Institute for Occupational Safety and Health and the National Center

Fig. 4. Summary of bias in studies reporting on the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma mortality (both studies) and non-melanoma skin cancer mortality (Freedman et al. only)



Notes: [a] Zanetti et al., 1988 ***(102)***, 1999 ***(103)***, Rosso et al., 1998 ***(104)***, 2008 ***(105)***; [b] Freedman et al., 1997 ***(122)***, 2002 ***(123)***.

for Health Statistics). In the study including Rosso et al. *(105)*, the majority of melanoma cases originally enrolled in the Turin case–control study *(102–105)* were actively followed up to ascertain determinants of survival, and were considered representative of the source population.

(b) Performance bias

The Freedman et al. *(122, 123)* study was judged as "probably low" for risk of performance bias; although there was no clear indication of the blinding status of the researchers, this would probably not have influenced the study. In the study *(102–105)* including Rosso et al. *(105)*, blinding was not applicable as case status and exposure classification had been revealed at the start of follow-up; therefore the risk of bias was considered to be "probably low".

(c) Exposure misclassification bias

The Freedman et al. *(122, 123)* study based on death certificates was judged as "probably high" for risk of exposure misclassification bias. Although exposure was classified by an industrial hygienist from occupation reported in the death certificates of cases and controls, reporting of occupation at the source was limited to "usual" or last occupation; this could misrepresent the true occupational lifetime history and concomitant deduction of occupational exposure to solar UVR (probably affecting cases and controls that had died non-differentially). In the study *(102–105)* including Rosso et al. *(105)*, we assigned a "probably low" rating. Baseline information at the time of diagnosis included a complete occupational history. Validated methods were used

in structured questionnaires to aid recall, from which participants were classified as outdoor or indoor workers, and by more detailed characterization of exposure.

(d) Detection bias

The Freedman et al. *(122, 123)* study was judged as "probably low" for risk of detection bias, as the outcome was recorded by death certificate. The study *(102–105)* including Rosso et al. *(105)* was also judged as "probably low" for risk of detection bias; ascertainment was performed by active follow-up of cancer cases over a long period, and the specific cause of death was undetermined in a fraction of cases only.

(e) Confounding

The Freedman et al. *(122, 123)* study was judged as "low" for risk of confounding, as the effect estimates were adjusted for the variables age, sex, race, residential sun exposure and socioeconomic status in the statistical model. Socioeconomic status was derived from the occupation reported on the death certificate. The study *(102–105)* including Rosso et al. *(105)* received a rating of "probably low" as the adjustment set was reduced.

(f) Incomplete outcome data bias

The Freedman et al. *(122, 123)* study was judged as "low" for risk of bias from incomplete outcome data, as all included cases had complete outcome information. The study *(102–105)* including Rosso et al. *(105)* was assigned a "probably low" rating to risk of bias from incomplete outcome data, as the cause of death was unknown in a fraction of study participants.

(g) Reporting bias

Although both studies on melanoma mortality discussed in this section did not have pre-published protocols, no evidence of reporting bias and both studies were judged as "probably low" for risk of bias in this domain.

(h) Conflict of interest bias

Both studies were assessed as "low" for risk of conflict of interest bias; the authors declared no conflict of interest in each study and no conflicting interests were identified.

(i) Other biases

Both studies were judged as "probably low" for risk of other biases.

3.3.3 NMSC incidence

The risk of bias ratings for the 25 studies reporting on the outcome of NMSC incidence are described in the following sections and in Table A5.3 in Annex 5, and summarized in Fig. 5. The systematic review included 22 incident case–control studies *(41, 42, 63, 64, 94, 104, 112, 113, 116, 120, 121, 125, 127, 128, 130, 133, 135, 138–145)*, a single case–case study *(137)* and two prospective cohort studies *(68, 118)*.

Fig. 5. Summary of risk of bias in studies reporting on the association between occupational exposure to solar ultraviolet radiation and non-melanoma skin cancer incidence

Risk of bias domain \ Study ID	Aubry 1985[a]	Gallagher 1995[b]	Kricker 1995[c]	Green 1996[d]	Rosso 1996[e]	Suárez-Varela 1996[f]	Rosso 1999[g]	Vlajinac 2000[h]	Corona 2001[i]	Håkansson 2001[j]	Milán 2003[k]	Walther 2004[l]	Zanetti 2006[m]	Pelucchi 2007[n]	Radespiel-Tröger 2009[o]	Janković 2010[p]	Kenborg 2010[q]	Dessintoti 2011[r]	Ferreira 2011[s]	Iannacone 2012[t]	Sanchez 2012[u]	Surdu 2013[v]	Kaskel 2015[w]	Trakatelli 2016[x]	Schmitt 2018[y]
Selection bias	PL	PL	PL	L	L	PH	PL	PH	PH	L	PL	PL	PL	L	PL	PH	PL	PL	PH	PL	PL	PL	PL	PH	PL
Performance bias	L	L	L	PL	L	PL	L	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL	L	PL	PL	L
Exposure misclassification bias	PH	PL	PL	PH	PL	PH	PL	H	H	PL	PH	PH	PL	PH	PH	H	PL	H	H	PL	PH	PH	PH	PH	L
Detection bias	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	L	PL	L	L	L
Confounding	PL	PL	PL	PL	L	PH	PH	PH	L	PH	PH	PL	L	L	PH	PL	PL	PL	PL	L	PL	L	PH	PL	PL
Incomplete outcome data	PL	PL	PL	PL	L	PL	L	PL	PL	PL	L	L	PL	L	PL	L	PL	PL	PL	L	PH	PL	PL	L	PL
Reporting bias	PL	PL	PL	L	PL	PH	L	PL	L	PL	PL	PL	L	PL	PL	PL	L	L	PL	PL	PL	PL	PL	L	PL
Conflict of interest bias	L	L	L	L	L	PL	L	L	L	L	L	PH	L	L	PL	L	L	L	L	L	L	L	PL	H	L
Other bias	PL	PL	PL	PL	L	PH	PL	PL	PL	PL	PL	PH	PL	PL	PH	PL	PL	PL	PL	PL	PL	PL	PL	PL	PL

Legend: L Low risk of bias; PL Probably low risk of bias; PH Probably high risk of bias; H High risk of bias

Notes: studies with grey shading were included in a meta–analysis. [a] Aubry & MacGibbon, 1985 *(94)*; [b] Gallagher et al., 1995 *(112, 113)*; [c] Kricker et al., 1995 *(116)*; [d] Green et al., 1996 *(118)*; [e] Rosso et al., 1996 *(120)*, 1998 *(104)*; [f] Suárez-Varela et al., 1996 *(121)*; [g] Rosso et al., 1999 *(125)*; [h] Vlajinac et al., 2000 *(127)*; [i] Corona et al., 2001 *(128)*; [j] Håkansson et al., 2001 *(68)*; [k] Milán et al., 2003 *(130)*; [l] Walther et al., 2004 *(133)*; [m] Zanetti et al., 2006 *(63)*; [n] Pelucchi et al., 2007 *(135)*; [o] Radespiel-Tröger et al., 2009 *(137)*; [p] Janković et al., 2010 *(138)*; [q] Kenborg et al., 2010 *(139)*; [r] Dessinioti et al., 2011 *(140)*; [s] Ferreira et al., 2011 *(141)*; [t] Iannacone et al., 2012 *(142)*; [u] Sanchez et al., 2012 *(143)*; [v] Surdu et al., 2013 *(144)*; [w] Kaskel et al., 2015 *(145)*; [x] Trakatelli et al., 2016 *(64)*; [y] Schmitt et al., 2018 *(41, 42)*.

(a) Selection bias

For the 22 case–control studies reporting results on NMSC incidence, two studies were rated as "low", 14 studies as "probably low" and six studies as "probably high" for risk of selection bias. The single case–case study was rated as "probably low" for risk of selection bias *(137)*. Both cohort studies were judged as "low" for risk of bias for selection of participants into the study *(68, 118)*. In the majority of studies, the sample of study participants was representative of the target population and, for case–control studies, cases and matched controls were recruited from the same hospital or clinic. Study response rates and study participant selection were not reported comprehensively in the studies included for this health outcome.

(b) Performance bias

Of the 22 case–control studies reporting on this health outcome, seven studies reporting use of blinded study personnel were rated as "low" for risk of performance bias and 15 studies not specifying this attribute as "probably low" for risk of performance bias. In the case–case study *(137)* based on cancer registry information and exposure assigned based on title of longest-held job, the risk of bias from use of blinding was considered as being "probably low". The two cohort

studies reporting on the risk of NMSC incidence were considered to have a "probably low" *(68, 118)* risk of performance bias.

(c) Exposure misclassification bias

Of the 22 case–control studies reporting the risk of NMSC incidence, a single study was rated as "low", seven studies as "probably low", nine studies as "probably high" and five studies as "high" for risk of exposure misclassification bias. The case–case study *(137)* was rated as "probably high" for risk of exposure misclassification bias. Of the two cohort studies reporting the risk of NMSC incidence, one study was judged to have a "probably low" *(68)* and the other to have a "probably high" *(118)* risk of exposure misclassification bias. Exposure was measured by self-reported questionnaires or in–person interviews in the majority of these studies, with widely varying definitions of exposure, exposure metrics employed, degrees of detail collected on outdoor work and comparators used.

(d) Detection bias

Twenty-one of the case–control studies were rated as "low" and a single case–control study as "probably low" for risk of detection bias. The case–case study was assessed as "low" for risk of detection bias *(137)*. Both cohort studies reporting the risk of NMSC incidence were judged as "low" *(68, 118)* for risk of bias for outcome assessment (i.e. detection bias). The health outcome was pathology-confirmed in all studies, including histopathology subtype specification in the majority of studies.

(e) Confounding

Of the 22 case–control studies, six studies were rated as "low", 11 studies as "probably low" and five studies as "probably high" for risk of confounding. The case–case study was rated as "probably high" *(137)* for risk of confounding, based on the number and types of variables that the study adjusted for in its statistical models. One of the cohort studies reporting the risk of NMSC incidence was judged as "probably low" *(118)* and the other as "probably high" *(68)* for risk of confounding.

(f) Incomplete outcome data bias

Of the 22 case–control studies, eight studies were rated as "low", 13 studies as "probably low" and a single study as "probably high" for risk of bias from incomplete outcome data. The case–case study was rated as "probably low" *(137)* for risk of bias in this domain. Both cohort studies reporting the risk of NMSC incidence were judged as "probably low" *(68, 118)* for risk of bias from incomplete outcome data.

(g) Reporting bias

Of the 22 case–control studies, six studies were rated as "low", 15 studies as "probably low" and a single study as "probably high" for risk of reporting bias. The single case–case study was rated as "probably low" *(137)* for this domain. One of the two cohort studies reporting the risk of NMSC incidence was judged as "low" *(118)* and the other as "probably low" *(68)* for risk of reporting bias. Although most studies did not provide a published or publicly available protocol in which they had previously stated the variable to be analysed, it was judged unlikely to carry noteworthy bias into the studies.

(h) Conflict of interest bias

Of the 22 case–control studies, 18 studies were rated as "low", two studies as "probably low", one study as "probably high" and one study as "high" for risk of conflict of interest bias. The case–case study *(137)* was rated as "probably low" for risk of conflict of interest bias. Both cohort studies reporting the risk of NMSC incidence were judged as "low" *(68, 118)* for risk of conflict of interest bias. The majority of studies disclosed any potential conflict of interest and funding source. Selected authors in the case–control study rated "high" for risk of bias due to conflict of interest reported receiving financial support from a pharmaceutical company to study the association between occupational exposure to solar UVR and melanoma and NMSC.

(i) Other biases

Of the 22 case–control studies, one study was judged as "low", 19 studies were judged as "probably low" and two studies were judged as "probably high" for risk of other biases. The single case–case study *(137)* was rated as "probably high" for risk of bias in this domain. Both cohort studies reporting on the risk of NMSC incidence were judged as "probably low" *(68, 118)* for risk of other biases.

3.3.4 NMSC mortality

The only study included in the systematic review reporting on the association between occupational exposure to solar UVR and NMSC mortality (Freedman et al. *(122, 123)*) also reported on the association between occupational exposure to solar UVR and melanoma mortality. The risk of bias in this study was identical for the two health outcomes of melanoma mortality and NMSC mortality. The reader is therefore referred to Section 3.3.2 (*a*)–(*i*) and Table A5.2 in Annex 5 for risk of bias ratings for this study reporting on NMSC mortality, also summarized in Fig. 4.

3.4 Evidence synthesis

3.4.1 Melanoma incidence

A total of 33 studies (29 case–control studies, three case–case studies and a single cohort study) with over 268 603 participants (counting effective sample sizes; Table 7) reported estimates on the effect of any (or high) occupational exposure to solar UVR on the outcome of melanoma incidence, compared with no (or low) occupational exposure to solar UVR. Occupational exposure to solar UVR was generally assessed via the proxy of outdoor work, which was commonly defined by occupation, job title, work task or a combination of these (Section 3.2.3; Table 10). Evidence from different study designs was meta-analysed separately (as per the pre-published protocol). In the risk of bias assessment for the outcome of melanoma incidence (Section 3.3.1), the case–control studies, case–case studies and cohort study were judged to have a comparable risk of bias across domains. Case–control studies have the advantage over cohort studies of being able to assess the effect of a risk factor when the lag time between exposure and health outcome may be long, as is the case for melanoma *(146)*. Case–control studies also have an advantage over case–case studies, in that they are very frequently based on controls sampled from the general population (and not only from the population with the disease). The main meta-analysis for this outcome is consequently that of the relevant case–control studies. The evidence from the case–case studies and the cohort study is considered as supporting evidence.

(a) Case–control studies

Of the 29 case–control studies reporting on melanoma incidence included in the systematic review, 19 with over 28 314 study participants from two WHO regions (Region of the Americas and the European Region) were judged to be sufficiently clinically homogeneous to be combined in meta–analysis (Table 13). These 19 studies reported a total of 34 eligible individual effect estimates. These studies were still somewhat heterogeneous regarding: population, such as local versus regional versus national geographical locations, different scope and type of industrial sectors, and different scope and type of occupations; exposure definition and/or measurement, such as self-reported number of years of occupational exposure to solar UVR versus occupational group categorized as "outdoor worker" versus average number of hours of occupational exposure to solar UVR per year; and comparator definition and/or measurement, such as number of years of occupational exposure to solar UVR equal to "0" or a small number of years, versus occupational group categorized as "indoor worker", versus the exposure category that controls most frequently reported.

Table 13. Effect estimates (odds ratios converted to relative risks) of association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence reported in 19 case–control studies included in meta–analysis (median baseline risk, 0.000 011)

Author, year	Study ID	Location	Effective sample	Odds ratio (95% CI)	Converted relative risk (95% CI)	Included in main meta-analysis (i.e. does not exclude LMM cases)
MacKie & Aitchison, 1982 *(93)*	MacKie 1982	Scotland	221	0.52 (0.23–1.16)	0.52 (0.23–1.17)	No
Elwood et al., 1985 *(95, 96)* Gallagher et al., 1987 *(97)*	Elwood 1985	Canada	459	0.9 (0.6–1.5)	0.90 (0.57–1.42)	No
Graham et al., 1985 *(98)*	Graham 1985	USA	173	0.67 (0.34–1.33)	0.67 (0.34–1.33)	Yes
Cristofolini et al., 1987 *(100)*	Cristofolini 1987	Italy	303	1.65 (0.93–2.90)	1.65 (0.93–2.91)	Yes
Østerlind et al., 1988 *(101)*	Østerlind 1988	Denmark	Unclear	0.7 (0.5–0.9)	0.70 (0.52–0.94)	No
Zanetti et al., 1988 *(102)*, 1999 *(103)* Rosso et al., 1998 *(104)*, 2008 *(105)*	Zanetti 1988	Italy	524	1.4 (0.6–2.2)	1.40 (0.73–2.68)	Yes
Dubin et al, 1989 *(106)*, 1990 *(61)*	Dubin 1989	USA	740	2.51 (1.1–6.0)	2.51 (1.07–5.86)	Yes
Garbe et al., 1989 *(107)*	Garbe	Germany	345	11.62 (2.13–63.33)	11.61 (2.13–63.35)	Yes
Beitner et al., 1990 *(108)*	Beitner 1990	Sweden	1028	0.6 (0.4–1.0)	0.60 (0.38–0.95)	Yes
Weiss et al., 1991 *(109)*	Weiss 1991	Germany	200	2.1 (1.2–3.8)	2.10 (1.18–3.74)	Yes
White et al., 1994 *(111)*	White 1994	USA	379	0.64 (0.33–1.23)	0.64 (0.33–1.24)	No

continues...

...continued

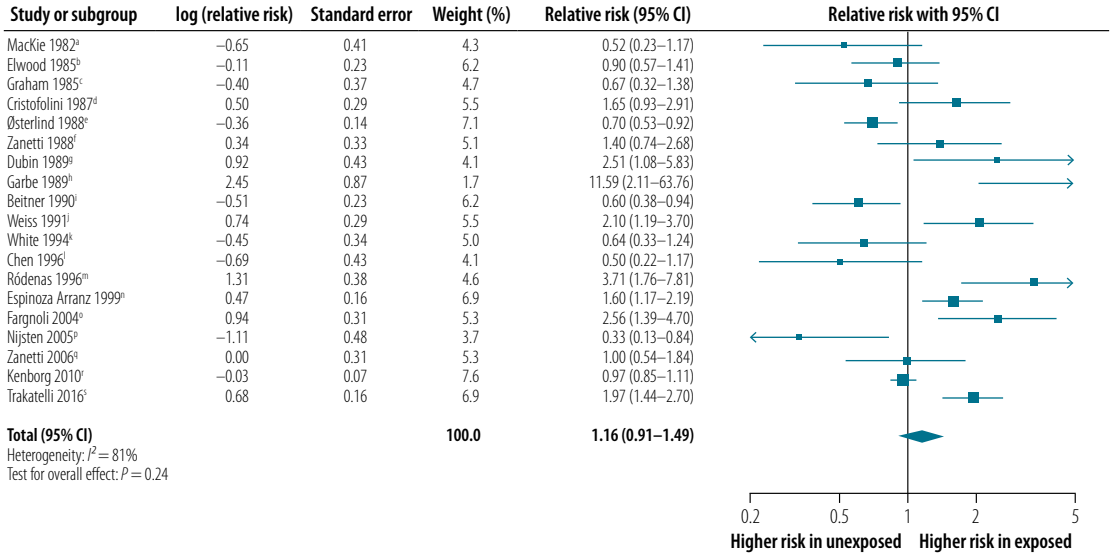
Author, year	Study ID	Location	Effective sample	Odds ratio (95% CI)	Converted relative risk (95% CI)	Included in main meta-analysis (i.e. does not exclude LMM cases)
Chen et al., 1996 *(117)*	Chen 1996	USA	Unclear	0.5 (0.2–1.1)	0.50 (0.21–1.17)	Yes
Ródenas et al., 1996 *(119)*	Ródenas 1996	Spain	199	3.7 (1.7–7.5)	3.70 (1.76–7.77)	Yes
Espinosa Arranz et al., 1999 *(124)*	Espinoza Arranz 1999	Spain	351	1.6 (1.1–2.1)	1.60 (1.16–2.21)	Yes
Fargnoli et al., 2004 *(132)*	Fargnoli 2004	Italy	300	2.57 (1.40–4.73)	2.57 (1.40–4.72)	Yes
Nijsten et al., 2005 *(62)*	Nijsten 2005	Belgium	348	0.33 (0.13–0.86)	0.33 (0.13–0.85)	No
Zanetti et al., 2006 *(63)*	Zanetti 2006	Argentina, France, Germany, Italy, Portugal, Spain	258	1.00 (0.57–1.95)	1.00 (0.54–1.85)	Yes
Kenborg et al., 2010 *(139)*	Kenborg 2010	Denmark	20 610	0.97 (0.84–1.11)	0.97 (0.84–1.12)	Yes
Trakatelli et al., 2016 *(64)*	Trakatelli 2016 (> 5 years of outdoor work versus never)	Finland, Germany, Greece, Italy, Malta, Poland, Scotland, Spain	1876	1.97 (1.43–2.71)	1.97 (1.43–2.71)	Yes

CI, confidence interval; LMM, lentigo malignant melanoma; USA, United States of America.

ORs were converted to RRs using the only baseline risk in the unexposed population (i.e. 11 cases per 100 000 person-years) reported for this outcome in the cohort study included in this systematic review *(68)*, and present the conversions in Table 13. For Østerlind et al. *(101)*, the effect estimate for males was included in the meta-analysis but the effect estimate for females (RR: 1.0) could not be included because no confidence interval was reported. Chen et al. *(117)* reported effect estimates of total number of years of outdoor work (> 0 to 5, ≥ 5 years) compared with 0 years by anatomical location of the melanoma (four locations: head and neck, trunk, upper limbs and lower limbs); the effect estimates corresponding to the head and neck (OR: 0.5; 95% CI: 0.2–1.1) for ≥ 5 years was prioritized, because this was the effect estimate for the most relevant site and highest exposure category (as per the eligibility criteria). For the study by Trakatelli et al. *(64)*, only one of three eligible effect estimates was entered, corresponding to > 5 years of outdoor work compared with never outdoor work, as opposed to estimates for farmers and construction workers combined compared with indoor workers (OR: 1.37; 95% CI: 0.95–1.96), or other outdoor work compared with indoor work (OR: 1.11; 95% CI: 0.79–1.55).

The meta-analysis revealed that, compared with no (or low) occupational exposure to solar UVR, any (or high) occupational exposure to solar UVR led to an increase in the risk of melanoma incidence by an estimated 16% when followed up over the lifetime (or an unclear period) (RR: 1.16; 95% CI: 0.91–1.49; 19 studies; > 28 314 participants; I^2 = 81%; Fig. 6).

Fig. 6. Meta-analysis of prioritized evidence (case–control studies) pooling all eligible studies reporting on the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence



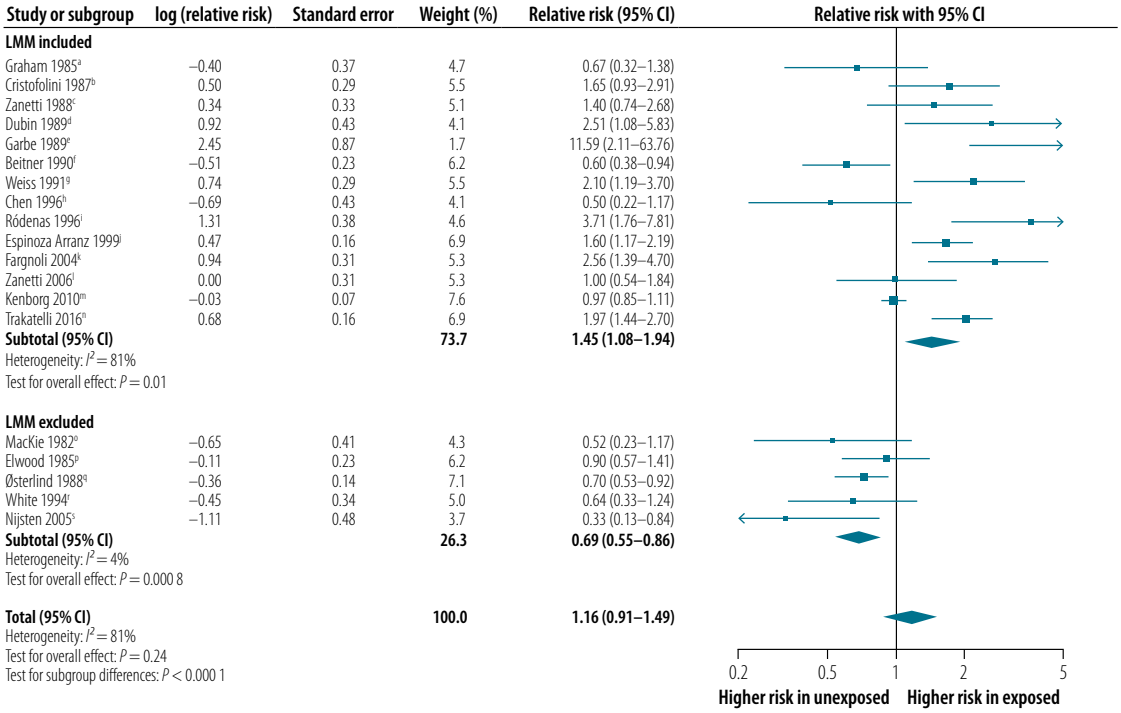
CI, confidence interval.

Notes: [a] MacKie & Aitchison, 1982 ***(93)***; [b] Elwood et al., 1985 ***(95, 96)***, Gallagher et al., 1987 ***(97)***; [c] Graham et al., 1985 ***(98)***; [d] Cristofolini et al., 1987 ***(100)***; [e] Østerlind et al., 1988 ***(101)***; [f] Zanetti et al., 1988 ***(102)***, 1999 ***(103)***, Rosso et al., 1998 ***(104)***, 2008 ***(105)***; [g] Dubin et al., 1989 ***(106)***, 1990 ***(61)***; [h] Garbe et al., 1989 ***(107)***; [i] Beitner et al., 1990 ***(108)***; [j] Weiss et al., 1991 ***(109)***; [k] White et al., 1994 ***(111)***; [l] Chen et al., 1996 ***(117)***; [m] Ródenas et al., 1996 ***(119)***; [n] Espinosa Arranz et al., 1999 ***(124)***; [o] Fargnoli et al., 2004 ***(132)***; [p] Nijsten et al., 2005 ***(62)***; [q] Zanetti et al., 2006 ***(63)***; [r] Kenborg et al., 2010 ***(139)***; [s] Trakatelli et al., 2016 ***(64)***.

In sensitivity analyses, statistically significant differences were observed in pooled RR estimates, in magnitude and direction, between studies including the melanoma subtype lentigo maligna melanoma and studies excluding this subtype. In particular, the point estimate for the 14 out of 19 studies that included the melanoma subtype lentigo maligna melanoma was larger than that for the five out of 19 studies that excluded this subtype (1.45 compared with 0.69), and the test for subgroup differences had a P value of < 0.000 01 (Fig. 7). Because lentigo maligna melanomas are included in the eligible ICD codes for melanoma that were included in the definition of eligible outcome (see Table 4) as per the protocol *(5)*, the pooled effect estimate from studies that included the melanoma subtype lentigo maligna melanoma was prioritized. In this analysis, which becomes the main meta–analysis for melanoma incidence, any (or high) occupational exposure to solar UVR (compared with no (or low) occupational exposure to solar UVR) led to an increase in the risk of melanoma incidence by an estimated 45% when followed up over the lifetime (or an unclear period) (RR: 1.45; 95% CI: 1.08–1.94; 14 studies; > 26 907 participants; $I^2 = 81\%$; Fig. 7).

This was an unexpected result; lentigo maligna melanoma typically represents a small proportion of melanoma cases (< 13% *(147–149)*) and is therefore unlikely to drive the observed difference in pooled estimates between subgroups (the proportion of lentigo maligna melanoma cases in the studies included in the meta-analysis, when reported, varied between 1.5% and 22%;

Fig. 7. Sensitivity analysis (of meta-analysis depicted in Fig. 6) of studies reporting on the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence, comparing studies that included cases of lentigo maligna melanoma with studies that excluded cases of lentigo maligna melanoma



CI, confidence interval; LMM, lentigo maligna melanoma.

Notes: [a] Graham et al., 1985 ***(98)***; [b] Cristofolini et al., 1987 ***(100)***; [c] Zanetti et al., 1988 ***(102)***, 1999 ***(103)***, Rosso et al., 1998 ***(104)***, 2008 ***(105)***; [d] Dubin et al., 1989 ***(106)***, 1990 ***(61)***; [e] Garbe et al., 1989 ***(107)***; [f] Beitner et al., 1990 ***(108)***; [g] Weiss et al., 1991 ***(109)***; [h] Chen et al., 1996 ***(117)***; [i] Ródenas et al., 1996 ***(119)***; [j] Espinosa Arranz et al., 1999 ***(124)***; [k] Fargnoli et al., 2004 ***(132)***; [l] Zanetti et al., 2006 ***(63)***; [m] Kenborg et al., 2010 ***(139)***; [n] Trakatelli et al., 2016 ***(64)***; [o] MacKie & Aitchison, 1982 ***(93)***; [p] Elwood et al., 1985 ***(95, 96)***, Gallagher et al., 1987 ***(97)***; [q] Østerlind et al., 1988 ***(101)***; [r] White et al., 1994 ***(111)***; [s] Nijsten et al., 2005 ***(62)***.

Annex 3). However, this melanoma subtype is associated with chronic solar UVR exposure and the majority of lentigo maligna melanomas are detected in body parts exposed to sunlight, particularly the head and the neck *(150)*. Further, in men aged > 60 years, this histology group can represent a sizable proportion of diagnosed invasive melanoma *(147)*. This is interpreted as evidence that the effect of any occupational exposure to solar UVR on melanoma including the subtype lentigo maligna melanoma is elevated and between a low and moderate increased risk; for studies limited to melanoma subtypes excluding lentigo maligna melanoma, any occupational exposure to solar UVR is associated with a moderate reduction in the effect estimate.

The 10 case–control studies that were included in the systematic review but excluded from the first meta-analysis are listed in Table 11. The main reasons for their exclusion were either: some studies defined and/or measured the exposure, comparator and/or outcome too differently from other studies that we included in the meta-analysis *(60, 110, 126, 131)*; or some studies reported only unadjusted effect estimates (*(92, 99, 115, 129, 136, 145)* and, as per the protocol, adjusted and unadjusted effect estimates were not combined to avoid introducing a risk of confounding.

The point estimates of these 10 excluded case–control studies were generally close to 1. Using vote counting based on direction of effect *(151)*, seven of the 10 studies reported point estimates that indicated a reduction in odds or risk; the point estimates of the remaining three studies indicated increased odds or risk (Table 11). Overall, the results from these excluded case–control studies were judged to be somewhat dissimilar (when comparable) to the pooled effect estimate from the main meta-analysis (Fig. 7), and consequently these studies were judged to provide little support to the evidence presented in the main meta-analysis.

A pooled analysis by Chang et al. *(152)* of 5700 cases of melanoma and 7216 controls on occupational exposure to solar UVR by latitude was identified. Although two of the individual studies from this pooled analysis were included in the current systematic review and meta-analysis *(96, 101)*, the other studies included in the Chang et al. pooled analysis *(152)* were not eligible based on the descriptions reported in individually published study records. For the pooled analysis, the confidence intervals around effect estimates from individually included studies (often previously unpublished) were only included in graphs and not numerically reported (see fig. 2 of Chang et al. *(152)*), meaning that they could not be included in the meta-analysis. Chang et al. *(152)* reported fully adjusted, pooled ORs of 1.1 (95% CI: 0.8–1.5) and 1.7 (95% CI: 1.0–3.0) for high levels of occupational exposure to solar UVR in low-latitude countries for all melanomas and head and neck melanoma, respectively, and ORs of 0.9 (95% CI: 0.7–1.1) and 1.2 (95% CI: 0.8–1.7) for high levels of occupational exposure to solar UVR in high-latitude countries for all melanomas and head and neck melanoma, respectively.

In view of the high statistical heterogeneity obtained in the main meta-analysis (81%), the impact of each study on the heterogeneity indicator was explored in a leave-one-out analysis (Table 14). Leaving Kenborg et al. *(139)* out registered the largest reduction in statistical heterogeneity from 81% to 75%, a moderate decrease. Further, it increased the pooled RR moderately from 1.45 (95% CI: 1.08–1.94) to 1.52 (95% CI: 1.10–2.10), with the lower limit of the 95% CI indicating a 10% increased risk. Leaving out Beitner et al. *(108)* increased the pooled RR by the largest amount from 1.45 to 1.56 (95% CI: 1.16–2.11; I^2 = 79%), while exclusion of Ródenas et al. *(119)* generated the lowest pooled RR of 1.35 (95% CI: 1.02–1.81; I^2 = 79%).

Table 14. Change in pooled effect estimate of association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence in case–control studies, when each study is omitted from the meta-analysis in turn

Study excluded from meta-analysis		Pooled relative risk estimate (95% CI)	I^2(%)
Author, year	Study ID		
None excluded (all studies)	–	1.45 (1.08–1.94)	81
Graham et al., 1985 *(98)*	Graham 1985	1.53 (1.13–2.07)	81
Cristofolini et al., 1987 *(100)*	Cristofolini 1987	1.43 (1.05–1.95)	82
Zanetti et al., 1988 *(102)*, 1999 *(103)* Rosso et al., 1998 *(104)*, 2008 *(105)*	Zanetti 1988	1.45 (1.07–1.98)	82
Dubin et al., 1989 *(106)*, 1990 *(61)*	Dubin 1989	1.40 (1.04–1.89)	81
Garbe et al., 1989 *(107)*	Garbe 1989	1.38 (1.04–1.83)	80
Beitner et al., 1990 *(108)*	Beitner 1990	1.56 (1.16–2.11)	79
Weiss et al., 1991 *(109)*	Weiss 1991	1.40 (1.04–1.90)	81
Chen et al., 1996 *(117)*	Chen 1996	1.54 (1.14–2.07)	81
Ródenas et al., 1996 *(119)*	Ródenas 1996	1.35 (1.02–1.81)	79
Espinosa Arranz et al., 1999 *(124)*	Espinoza Arranz 1999	1.44 (1.04–1.99)	81
Fargnoli et al., 2004 *(132)*	Fargnoli 2004	1.38 (1.03–1.86)	80

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Study excluded from meta-analysis		Pooled relative risk estimate (95% CI)	I^2(%)
Author, year	**Study ID**		
Zanetti et al., 2006 *(63)*	Zanetti 2006	1.49 (1.09–2.03)	82
Kenborg et al., 2010 *(139)*	Kenborg 2010	1.52 (1.10–2.10)	75
Trakatelli et al., 2016 *(64)*	Trakatelli 2016	1.40 (1.03–1.91)	79

CI, confidence interval; UVR, ultraviolet radiation.

(b) Case–case studies

Three case–case studies with more than 59 556 participants (one study only reported number of cases) from three WHO regions (Region of the Americas, European Region and Western Pacific Region) reported evidence on the effect of any (or high) occupational exposure to solar UVR on melanoma incidence, compared with no (or low) occupational exposure to solar UVR (Table 15). However, they were judged to be too heterogeneous to be combined in a quantitative meta-analysis. Although all three reported on melanoma cases, definitions of exposure (e.g. via proxies of job titles versus cumulative duration of exposure) and of comparators (e.g. melanoma cases with a melanoma at a different site versus cases of other cancers) varied between the studies.

Table 15. Effect estimates from case–case studies of association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence, excluded from the main meta–analysis

Author, year	Study ID	Comparison	Effect estimate
Goodman et al., 1995 *(114)*	Goodman 1995	Sun exposure during work categorized as "Mainly outdoors", compared with sun exposure during work categorized as "Mainly indoors"	OR: 1.15 (95% CI: 0.94–1.40)
Whiteman et al., 2006 *(134)*	Whiteman 2006	Cumulative occupational exposure to the sun for a duration of ≥ 20 037 h, compared with the reference category defined by cumulative occupational exposure to the sun for a duration of 209–7331 h (least exposed)	OR: 3.26 (95% CI: 1.01–10.5)
Radespiel-Tröger et al., 2009 *(137)*	Radespiel-Tröger 2009	Occupational exposure to solar UVR categorized (via proxy of job title with the longest duration) as "Mixed indoor/outdoor workers" or "Outdoor workers", compared with occupational exposure to solar UVR categorized (via proxy of job title) as "Indoor workers"	RR for females: 1.1 (95% CI: 0.4–3.6) RR for males: 1.5 (95% CI: 0.9–2.5)

CI, confidence interval; h, hour(s); OR, odds ratio; RR, relative risk; UVR, ultraviolet radiation.

All three case–case studies had an increased point estimate, but two *(114, 137)* of the three included the null value in their 95% CI. The third study *(134)* found a large increased risk among those with high cumulative exposure, but it was limited to invasive melanoma at one body site only (head and neck, using melanoma cases with tumours in the trunk as comparison). This body of evidence was judged as somewhat supportive of the findings from the main meta-analysis (Section 3.4.1 (*a*) above; Fig. 7) that any (or high) occupational exposure to solar UVR, compared with no (or low) occupational exposure to solar UVR, was found to lead to a moderate increase in the risk of melanoma incidence.

(c) Cohort study

The population-based, prospective cohort study by Håkansson et al. *(68)* (323 860 male participants) investigated the effect of occupational exposure to solar UVR, compared with no (or low) occupational exposure to solar UVR, on melanoma incidence. Exposure categories were defined as "Works outdoors to some extent during the workday, some shade from for example

buildings and trees occurs" (medium-level exposure) or "Works outdoors almost the whole work day, all through the year or in the summertime, mostly unprotected from sunlight" (high-level exposure; assigned by an occupational hygienist via proxy of occupation and job tasks), and the comparator was defined as "Never or seldom works outdoors" (low-level exposure) *(68)*. The authors reported that high-level occupational exposure to solar UVR increased the risk of melanoma incidence by an estimated 10%, compared with no (or low) occupational exposure to solar UVR, but the 95% CI included the null value (RR: 1.1; 95% CI: 0.8–1.6).

(d) Synthesis across study designs

The prioritized body of evidence of case–control studies revealed that, compared with no (or low) occupational exposure to solar UVR, any (or high) occupational exposure to solar UVR led to an estimated increase in the risk of melanoma incidence when exposure was assessed with a mixture of metrics including lifetime cumulative number of hours of outdoor work (highest exposure level versus comparator; seven of 14 studies included in the main meta-analysis) or just differentiating broader categories (ever exposed). In the main meta-analysis, the RR was 1.45 (95% CI: 1.08–1.94; 14 studies, > 26 907 participants, I^2 = 81%; Fig. 7). The evidence from the 10 case–control studies that could not be included in the meta-analysis provided marginal support to the findings from the main meta-analysis. The evidence from the three case–case studies and single cohort study was supportive of the findings from the main meta-analysis.

3.4.2 Melanoma mortality

The two case–control studies of Freedman et al. *(122, 123)* and Zanetti et al. *(102–105)*, comprising a total of 20 231 participants from two WHO regions (Region of the Americas and European Region), reported estimates of the effect of any (or high) occupational exposure to solar UVR on melanoma mortality, compared with no (or low) occupational exposure to solar UVR. These two studies were sufficiently similar in population, exposure and outcome to be combined in a meta-analysis, but it was not possible to convert the OR effect estimate from one of the studies *(122, 123)* into an RR because it did not report a suitable baseline risk in the unexposed in the general population; therefore the effect estimates were synthesized narratively. The results reported by these studies are summarized in Table 16.

Table 16. Effect estimates from case–control studies on the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma mortality, excluded from the main meta–analysis

Author, year	Study ID	Comparison	Effect estimate
Zanetti et al., 1988 *(102)*, 1999 *(103)* Rosso et al., 1998 *(104)*, 2008 *(105)*	Zanetti 1988	Occupational exposure to solar UVR categorized (via proxy of occupation) as "Any outdoor work", compared with occupational exposure to solar UVR categorized (via proxy of occupation) as "No outdoor work"	OR: 1.3[a] (95% CI: 0.6–2.5)
Freedman et al., 1997 *(122)*, 2002 *(123)*	Freedman 1997[b]	Occupational exposure to solar UVR categorized (via proxy of occupation) as "Outdoor (nonfarmer)",[c] compared with occupational exposure to solar UVR categorized (via proxy of occupation) as "Indoor"	OR: 0.99 (95% CI: 0.87–1.12)

CI, confidence interval; OR, odds ratio; UVR, ultraviolet radiation.

[a] Refers to data presented in associated study record Rosso et al. (105).

[b] Prioritized study for the outcome.

[c] This exposure category was prioritized over the categories of "mixed" (or mixed indoor/outdoor work) and "Farmer" because we judged it to be the highest exposure category and because it included a larger set of occupations. The effect estimate for melanoma mortality among the category "Farmer" was an OR of 1.31 (95% CI: 1.14–1.52).

Freedman et al. *(122, 123)* reported an OR close to 1 with the 95% CI including the null value (95% CI: 0.87–1.12). Zanetti et al. *(102–105)* reported an OR of 1.3, also with the 95% CI including the null value (95% CI: 0.6–2.5). The 95% CIs were wide for both studies, particularly in the survival study *(102–105)* where the lower and upper limits of the 95% CI indicated that the effect may range between a large decrease and a large increase in the risk of mortality.

The study by Freedman et al. *(122, 123)* was prioritized because it reported on mortality and the effect estimate was less imprecise, whereas Zanetti et al. *(102–105)* studied the effect on or survival of a reduced number of cases (n = 260) after melanoma diagnosis (survival analysis of a case–control study).

3.4.3 NMSC incidence

A total of 25 studies (22 case–control studies, a single case–case study and two cohort studies) with over 286 131 participants from three WHO regions (i.e. Region of the Americas, European Region and Western Pacific Region) reported estimates on the effect of occupational exposure to solar UVR, compared with no (or low) occupational exposure to solar UVR, on NMSC incidence. Evidence from case–control studies and from cohort studies was pooled separately. In the risk of bias assessment for NMSC incidence (Section 3.3.3), both study designs were judged to have a comparable and overall "probably low" risk of bias. Case–control studies have the advantage of being able to assess the effect of a risk factor when the lag time between exposure and incident health outcome is long, as is the case for NMSC *(146)*. The main meta-analysis for this outcome is consequently that of the included case–control studies.

(a) Case–control studies

Of the 22 case–control studies included in the systematic review, 20 studies (listed in Table 17) that were judged to be sufficiently clinically homogenous were combined in the meta-analysis. These studies reported a total of 28 eligible individual effect estimates from three different WHO regions (i.e. Regions of the Americas, European Region and Western Pacific Region). Studies that defined the outcome as BCC, SCC or NMSC were combined. If a study reported effect estimates separately by population characteristics (e.g. sex) and/or by NMSC subtype, the individual effect estimates were included separately in the meta-analysis (as reported in the original study records).

Table 17. Effect estimates (odds ratios converted to relative risks) of association between occupational exposure to solar ultraviolet radiation and non-melanoma skin cancer incidence reported in case–control studies included in meta-analysis (median baseline risk, 0.000 005 8)

Author, year	Study ID	Location	Effective sample	Odds ratio (95% CI)	Converted relative risk (95% CI)
Aubry & MacGibbon, 1985 *(94)*	Aubry 1985	Canada	266	9.12 (0.99–84.47)	9.12 (0.99–84.24)
Gallagher et al., 1995 *(112, 113)*	Gallagher 1995	Canada	441 (BCC: 339; SCC: 317)	BCC: 1.4 (0.8–2.4); SCC: 1.4 (0.4–4.3)	BCC: 1.40 (0.81–2.42); SCC: 1.40 (0.43–4.59)
Kricker et al., 1995 *(116)*	Kricker 1995	Australia	449	0.86 (0.50–1.51)	0.86 (0.49–1.49)
Rosso et al., 1996 *(120)*, 1998 *(104)*	Rosso 1996	France, Italy, Spain	1966	BCC: 0.84 (0.65–1.10); SCC: 1.60 (0.93–2.75)	BCC: 0.84 (0.65–1.09); SCC: 1.60 (0.93–2.75)
Suárez-Varela et al., 1996 *(121)*	Suárez-Varela 1996	Spain	Unclear (total study population 812)	NMSC F: 0.8 (0.1–8.2); M: 5.3 (3.1–9.2)	NMSC F: 0.80 (0.09–7.24); M: 5.30 (3.08–9.13)

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Author, year	Study ID	Location	Effective sample	Odds ratio (95% CI)	Converted relative risk (95% CI)
Vlajinac et al., 2000 *(127)*	Vlajinac 2000	Serbia	599	BCC: 3.95 (1.61–9.66)	BCC: 3.95 (1.61–9.68)
Corona et al., 2001 *(128)*	Corona 2001	Italy	320	BCC: 1.7 (0.7–4.1)	BCC: 1.70 (0.70–4.11)
Milán et al., 2003 *(130)*	Milán 2003	Finland	371	BCC F: 0.57 (0.15–2.21); M: 0.74 (0.30–1.79)	BCC F: 0.57 (0.15–2.19); M: 0.74 (0.30–1.81)
Walther et al., 2004 *(133)*	Walther 2004	Germany	624	BCC: 2.4 (1.3–4.7)	BCC: 2.40 (1.26–4.56)
Zanetti et al., 2006 *(63)*	Zanetti 2006	Argentina, France, Germany, Italy, Portugal, Spain	332	BCC: 1.20 (0.70–2.13); SCC: 2.20 (1.13–4.08)	BCC: 1.20 (0.69–2.09); SCC: 2.20 (1.16–4.18)
Pelucchi et al., 2007 *(135)*	Pelucchi 2007	Italy	830	BCC Nodular: 1.35 (0.85–2.14); superficial: 0.50 (0.25–1.00)	BCC Nodular: 1.35 (0.85–2.14); superficial: 0.50 (0.25–1.00)
Janković et al., 2010 *(138)*	Janković 2010	Montenegro	200	2.73 (1.00–7.45)	2.73 (1.00–7.45)
Kenborg et al., 2010 *(139)*	Kenborg 2010	Denmark	76 156	NMSC: 0.83 (0.77–0.88)	NMSC: 0.83 (0.78–0.89)
Dessinioti et al., 2011 *(140)*	Dessinioti 2011	Greece	339	BCC: 2.3 (1.2–4.3)	BCC: 2.30 (1.22–4.35)
Ferreira et al., 2011 *(141)*	Ferreira 2011	Brazil	264	NMSC: 1.76 (1.04–2.99)	NMSC: 1.76 (1.04–2.98)
Iannacone et al., 2012 *(142)*	Iannacone 2012	USA	246	BCC: 2.12 (1.05–4.27); SCC: 2.36 (1.07–5.20)	BCC: 2.12 (1.05–4.28); SCC: 2.36 (1.07–5.20)
Sanchez et al., 2012 *(143)*	Sanchez 2012	Colombia	406	BCC: 1.67 (0.82–3.44)	BCC: 1.67 (0.82–3.42)
Surdu et al., 2013 *(144)*	Surdu 2013	Hungary, Romania, Slovakia	1041	NMSC: 0.47 (0.27–0.80)	NMSC: 0.47 (0.27–0.81)
Trakatelli et al., 2016 *(64)*	Trakatelli 2016 (BCC) (> 5 years of outdoor work versus never)	Finland, Germany, Greece, Italy, Malta, Poland, Scotland, Spain	2469	BCC: 3.32 (2.55–4.33); SCC: 3.67 (2.63–5.11)	BCC: 3.32 (2.55–4.33); SCC: 3.67 (2.63–5.12)
Schmitt et al., 2018 *(41, 42)*	Schmitt 2018	Germany	902	BCC: 1.84 (1.19–2.83)	BCC: 1.84 (1.19–2.84)

BCC, basal cell carcinoma; CI, confidence interval; F, females; M, males; NMSC, non-melanoma skin cancer; SCC, squamous cell carcinoma.

ORs were converted to RRs using the only total baseline risk in the unexposed population (i.e. 5.8 cases per 100 000 person-years) reported for this outcome in an included cohort study (i.e. Håkansson et al. *(68)*) and present the conversions in Table 17. Schmitt et al. *(41, 42)* reported an adjusted OR for risk of SCC of 1.95 (95% CI: 1.19–3.18), but since it was based on a mix of in situ (n = 224) and invasive tumours (n = 408) this study was excluded from the meta-analysis. Studies by Ferreira et al. *(141)* (Brazil) and Sanchez et al. *(143)* (Colombia) were somewhat different in their exposure definitions (≥ 6 hours daily outdoor work or occupationally exposed to sunlight at age > 30 years, respectively), but they were considered similar enough to be retained in the meta-analysis. This limitation was acknowledged in the risk of bias domain of exposure misclassification (Fig. 5). Further, the pooled effect estimates were not meaningfully changed by either removing both these studies from the analysis (pooled RR based on 18 out of 20 studies: 1.59; 95% CI: 1.19–2.13; I^2 = 91%) or by removing either one of these two studies (Table 18).

Table 18. Change in effect estimate of association between occupational exposure to solar ultraviolet radiation and non-melanoma skin cancer incidence in case–control studies when each study is omitted from the meta-analysis in turn

Study excluded from meta-analysis		Pooled relative risk estimate (95% CI)	I^2(%)
Author, year	Study ID		
None excluded (complete analysis)	–	1.60 (1.21–2.11)	91
Aubry & MacGibbon, 1985 *(94)*	Aubry 1985	1.57 (1.19–2.07)	91
Gallagher et al., 1995 *(112, 113)*	Gallagher 1995	1.62 (1.21–2.16)	91
Kricker et al., 1995 *(116)*	Kricker 1995	1.64 (1.23–2.19)	91
Rosso et al., 1996 *(120)*, 1998 *(104)*	Rosso 1996	1.65 (1.21–2.26)	91
Suárez-Varela et al., 1996 *(121)*	Suárez-Varela 1996	1.53 (1.17–2.02)	90
Vlajinac et al., 2000 *(127)*	Vlajinac 2000	1.55 (1.18–2.06)	91
Corona et al., 2001 *(128)*	Corona 2001	1.60 (1.20–2.12)	91
Milán et al., 2003 *(130)*	Milán 2003	1.68 (1.26–2.25)	91
Walther et al., 2004 *(133)*	Walther 2004	1.58 (1.19–2.09)	91
Zanetti et al., 2006 *(63)*	Zanetti 2006	1.60 (1.19–2.15)	91
Pelucchi et al., 2007 *(135)*	Pelucchi 2007	1.69 (1.26–2.27)	91
Janković et al., 2010 *(138)*	Janković 2010	1.58 (1.19–2.09)	91
Kenborg et al., 2010 *(139)*	Kenborg 2010	1.66 (1.26–2.17)	82
Dessinioti et al., 2011 *(140)*	Dessinioti 2011	1.58 (1.19–2.10)	91
Ferreira et al., 2011 *(141)*	Ferreira 2011	1.59 (1.20–2.12)	91
Iannacone et al., 2012 *(142)*	Iannacone 2012	1.56 (1.17–2.08)	91
Sanchez et al., 2012 *(143)*	Sanchez 2012	1.60 (1.20–2.13)	91
Surdu et al., 2013 *(144)*	Surdu 2013	1.68 (1.27–2.24)	91
Kenborg et al., 2010 *(139)*	Kenborg 2010	1.66 (1.26–2.17)	82
Dessinioti et al., 2011 *(140)*	Dessinioti 2011	1.58 (1.19–2.10)	91
Trakatelli et al., 2016 *(64)*	Trakatelli 2016	1.47 (1.16–1.86)	83
Schmitt et al., 2018 *(41, 42)*	Schmitt 2018	1.59 (1.19–2.12)	91

CI, confidence interval.

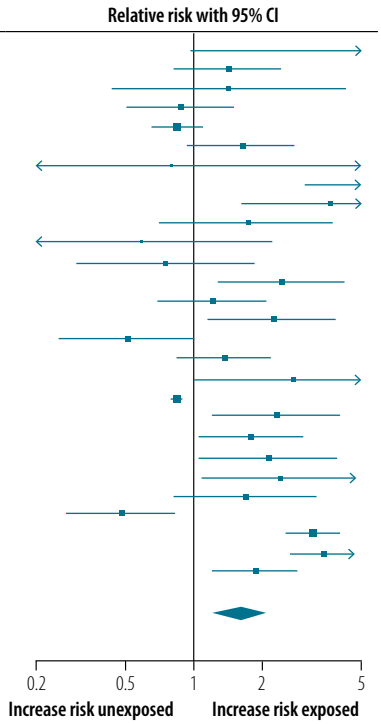
In the main meta-analysis, the evidence from these case–control studies showed that, compared with no (or low) occupational exposure to solar UVR, any (or high) occupational exposure to solar UVR increased the risk of NMSC incidence by an estimated 60% when followed up over an unclear period (RR: 1.60; 95% CI: 1.21–2.11; 20 studies; > 88 448 participants; I^2 = 91%; Fig. 8).

In view of the high statistical heterogeneity obtained in this meta-analysis (I^2 = 91%), the impact each study had on the heterogeneity indicator was explored in a leave-one-out analysis. Excluding Kenborg et al. *(139)* or Trakatelli et al. *(64)* reduced the I^2 estimate for the pooled RR by about 10% (decreasing to 82% and 83%, respectively), with the point risk estimate remaining comparable (Table 18).

Although the case–control studies by Rosso et al. *(125)* and Kaskel et al. *(145)* (effectively comprising 708 participants from the WHO European Region) were included in the systematic review, they were excluded from the meta-analysis (Table 12) because they only reported unadjusted effect estimates (or the data to calculate these). For example, the Rosso et al. *(125)* study matched cases and controls by sex and age (arguably some level of adjustment for confounding by these variables), but reported unadjusted RR estimates for BCC and SCC.

Fig. 8. Meta-analysis of prioritized case–control studies reporting on the association between occupational exposure to solar ultraviolet radiation and non-melanoma skin cancer incidence

Study or subgroup	log (relative risk)	Standard error	Weight (%)	Relative risk (95% CI)
Aubry 1985[a]	2.21	1.14	1.2	9.12 (0.98–85.15)
Gallagher 1995 (BCC)[b]	0.34	0.28	4.0	1.40 (0.81–2.43)
Gallagher 1995 (SCC)[b]	0.34	0.61	2.5	1.40 (0.43–4.64)
Kricker 1995[c]	−0.15	0.28	4.0	0.86 (0.50–1.49)
Rosso 1996 (BCC)[d]	−0.17	0.13	4.6	0.84 (0.65–1.09)
Rosso 1996 (SCC)[d]	0.47	0.28	4.0	1.60 (0.92–2.77)
Suárez-Varela 1996 (F)[e]	−0.22	1.12	1.2	0.80 (0.09–7.21)
Suárez-Varela 1996 (M)[e]	1.67	0.28	4.0	5.31 (3.07–9.20)
Vlajinac 2000[f]	1.37	0.46	3.2	3.94 (1.60–9.69)
Corona 2001[g]	0.53	0.45	3.2	1.70 (0.70–4.10)
Milán 2003 (F)[h]	−0.56	0.69	2.2	0.57 (0.15–2.21)
Milán 2003 (M)[h]	−0.30	0.46	3.2	0.74 (0.30–1.83)
Walther 2004[i]	0.88	0.33	3.8	2.41 (1.26–4.60)
Zanetti 2006 (BCC)[j]	0.18	0.28	4.0	1.20 (0.69–2.07)
Zanetti 2006 (SCC)[j]	0.79	0.33	3.8	2.20 (1.15–4.21)
Pelucchi 2007 (Nodular BCC)[k]	−0.69	0.35	3.7	0.50 (0.25–1.00)
Pelucchi 2007 (Superficial BCC)[k]	0.30	0.24	4.2	1.35 (0.84–2.16)
Janković 2010[l]	1.00	0.51	2.9	2.72 (1.00–7.39)
Kenborg 2010[m]	−0.19	0.03	4.7	0.83 (0.78–0.88)
Dessinioti 2011[n]	0.83	0.33	3.8	2.29 (1.20–4.38)
Ferreira 2011[o]	0.57	0.27	4.0	1.77 (1.04–3.00)
Iannacone 2012 (BCC)[p]	0.75	0.36	3.6	2.12 (1.05–4.29)
Iannacone 2012 (SCC)[p]	0.86	0.4	3.4	2.36 (1.08–5.18)
Sanchez 2012[q]	0.51	0.37	3.6	1.67 (0.81–3.44)
Surdu 2013[r]	−0.75	0.28	4.0	0.47 (0.27–0.82)
Trakatelli 2016 (BCC)[s]	1.20	0.14	4.5	3.32 (2.52–4.37)
Trakatelli 2016 (SCC)[s]	1.30	0.17	4.4	3.67 (2.63–5.12)
Schmitt 2018[t]	0.61	0.22	4.3	1.84 (1.20–2.83)
Total (95% CI)			**100.0**	**1.60 (1.21–2.11)**
Heterogeneity: $I^2 = 91\%$				
Test for overall effect: $P = 0.000\,9$				



BCC, basal cell carcinoma; CI, confidence interval; F, females, M, males; SCC, squamous cell carcinoma.

Notes: [a] Aubry & MacGibbon, 1985 ***(94)***; [b] Gallagher et al., 1995 ***(112, 113)***; [c] Kricker et al., 1995 ***(116)***; [d] Rosso et al., 1996 ***(120)***, 1998 ***(104)***; [e] Suárez-Varela et al., 1996 ***(121)***; [f] Vlajinac et al., 2000 ***(127)***; [g] Corona et al., 2001 ***(128)***; [h] Milán et al., 2003 ***(130)***; [i] Walther et al., 2004 ***(133)***; [j] Zanetti et al., 2006 ***(63)***; [k] Pelucchi et al., 2007 ***(135)***; [l] Janković et al., 2010 ***(138)***; [m] Kenborg et al., 2010 ***(139)***; [n] Dessinioti et al., 2011 ***(140)***; [o] Ferreira et al., 2011 ***(141)***; [p] Iannacone et al., 2012 ***(142)***; [q] Sanchez et al., 2012 ***(143)***; [r] Surdu et al., 2013 ***(144)***; [s] Trakatelli et al., 2016 ***(64)***; [t] Schmitt et al., 2018 ***(41, 42)***.

(b) Case–case study

The case–case study by Radespiel-Tröger et al. *(137)*, based on an unclear number of participants (contributing a total of 2.2 million person-years to the analysis in Germany), reported estimates of the effect of any (or high) occupational exposure to solar UVR, compared with no (or low) occupational exposure to solar UVR, on NMSC incidence when followed up for 4 years. The study reported four eligible individual effect estimates, one each for females and males for both BCC and SCC (Table 19). Compared with no occupational exposure to solar UVR, any occupational exposure to solar UVR led to a large increase in the risk of NMSC incidence, with the 95% CIs indicating a moderate to large increase for each estimate (Table 19).

Table 19. Results from the case–case study on the association between occupational exposure to solar ultraviolet radiation and non-melanoma skin cancer incidence, considered as supporting evidence

Auhor, year	Study ID	Comparison	Effect estimate (95% CI)
Radespiel-Tröger et al., 2009 *(137)*	Radespiel-Tröger 2009	Occupational exposure to solar UVR categorized (via proxy of longest occupation) as "Outdoor", compared with occupational exposure to solar UVR categorized (via proxy of occupation) as "Indoor"	BCC: RR for females: 2.7 (95% CI: 1.8–4.1) RR for males: 2.9 (95% CI: 2.2–3.9) SCC: RR for females: 3.6 (95% CI: 1.6–8.10) RR for males: 2.5 (95% CI: 1.4–4.7)

BCC, basal cell carcinoma; CI, confidence interval; RR, relative risk; SCC, squamous cell carcinoma.

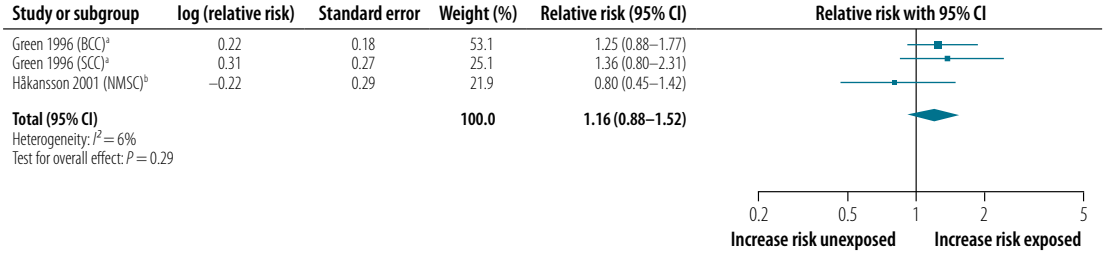
(c) Cohort studies

Two cohort studies comprising 196 481 participants from two WHO regions (European Region and Western Pacific Region) reported estimates of the effect of any (or high) occupational exposure to solar UVR, compared with no (or low) occupational exposure to solar UVR, on NMSC incidence *(68, 118)*. The studies were judged to be sufficiently clinically homogenous across population, exposure, comparator and outcome to be combined in a quantitative meta-analysis. For Green et al. *(118)*, the two eligible effect estimates (one for each of BCC and SCC) were entered separately in the forest plot (Fig. 9). Compared with no (or low) occupational exposure to solar UVR, any (or high) occupational exposure to solar UVR led to an increase in the risk of NMSC incidence by an estimated 16% when followed up by a period of 6–14 years (RR: 1.16; 95% CI: 0.88–1.52; 2 studies; 196 481 participants; I^2 = 6%; Fig. 9). However, the 95% CI included the null value, ranging from a small decrease to a moderate increase in the risk among the exposed compared with the unexposed.

(d) Synthesis across study designs

The prioritized body of evidence from case–control studies revealed that, compared with no (or low) occupational exposure to solar UVR, any (or high) occupational exposure to solar UVR led to an estimated increase in the risk of NMSC incidence when followed up over the lifetime

Fig. 9. Meta-analysis of cohort studies (supporting evidence) reporting on the association between occupational exposure to solar ultraviolet radiation and non-melanoma skin cancer incidence



BCC, basal cell carcinoma; CI, confidence interval; NMSC, non-melanoma skin cancer; SCC, squamous cell carcinoma.

Notes: [a] Green et al., 1996 ***(118)***, comparing occupational exposure to solar UVR categories "mainly outdoors" and "mainly indoors"; [b] Håkansson et al., 2001 ***(68)***, comparing occupational exposure to solar UVR categories "high" and "low".

(or over an unclear period). The evidence from the two case–control studies that could not be included in the main meta-analysis were unadjusted effect estimates only (with risk of confounding), and therefore not directly comparable with the evidence in the main analysis that pooled only adjusted effect estimates. With regards to the supporting evidence, the case–case study indicated larger and statistically significant increased risks among the exposed compared with the unexposed, and the pooled estimate from the two included cohort studies suggested an increased risk among the exposed population but of a lesser magnitude (16%) and with the 95% CI including the null value. The additional evidence from the case–case study and from the two cohort studies was judged to be generally supportive of the findings from the main meta-analysis.

3.4.4 NMSC mortality

The case–control study by Freedman et al. *(122, 123)* reported estimates on the effect of occupational exposure to solar UVR, compared with no (or low) occupational exposure to solar UVR, on NMSC mortality (effective sample size, 80 987). The authors analysed data from death certificates spanning the period 1985–1995 from 24 states in the USA, and reported effect estimates of occupational exposure to solar UVR on NMSC mortality for (i) mixed (indoor/outdoor) workers, (ii) outdoor workers excluding farmers and (iii) farmers, always as compared with indoor workers (comparator). For the highest exposure categories, effect estimates were reported for both (ii) outdoor workers excluding farmers (OR: 1.30; 95% CI: 1.14–1.47) and (iii) farmers (OR: 1.15; 95% CI: 1.00–1.32). The effect estimate for (ii) was prioritized because this population of workers was considered to be broader in scope. Compared with no (or low) occupational exposure to solar UVR, any (or high) occupational exposure to solar UVR increased the risk of NMSC mortality by 30%.

3.5 Subgroup analyses

Quantitative subgroup analyses were performed for the main meta-analyses for the health outcomes of melanoma incidence and NMSC incidence, and the forest plots are provided in Annex 6.

3.5.1 Melanoma incidence

The subgroup analysis by WHO region found no statistically significant subgroup differences (based on 14 studies; $P = 0.29$; Table 20; Annex 6, Fig. A.6.1). None of the studies included for this outcome reported effect estimates disaggregated by sex, age group, occupation, industrial sector, socioeconomic status or formality of the economy; it was therefore not possible to produce subgroup analyses by these variables.

Table 20. Summary of results of subgroup analyses of main meta-analysis of studies reporting on the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma and/or non-melanoma skin cancer incidence, by WHO region, sex and subtype (see also forest plots in Annex 6)

	RR (95% CI)	*I*²(%)
Melanoma incidence		
WHO region (14 studies; $P = 0.29$)		
Region of the Americas	0.94 (0.37–2.39)	76
European Region	1.59 (1.16–2.18)	83

continues...

...continued

	RR (95% CI)	I^2(%)
NMSC incidence		
WHO region (20 studies, $P = 0.07$)		
Region of the Americas	1.78 (1.36–2.35)	0
European Region	1.56 (1.11–2.20)	93
Western Pacific Region	0.86 (0.50–1.49)	–
Sex (two studies; $P = 0.30$)		
Men	2.05 (0.30–14.13)	93
Women	0.63 (0.20–1.98)	0
Subtype (16 studies; $P = 0.05$)		
BCC	1.50 (1.10–2.04)	81
SCC	2.43 (1.64–3.62)	47

BCC, basal cell carcinoma; CI, confidence interval; RR, relative risk; SCC, squamous cell carcinoma; WHO, World Health Organization.

3.5.2 NMSC incidence

In the subgroup analysis by WHO region for the health outcome of NMSC incidence, no evidence of differences in relative risks were found (Table 20; Annex 6, Fig. A6.2). In subgroup analyses by sex, no evidence was found of differences by subgroups with available data (i.e. $P = 0.30$). In subgroup analysis by subtype, based on 16 of the 20 studies included in the main meta-analysis, the point estimate for BCC (RR: 1.50; 15 studies) was lower than that for SCC (RR: 2.42; 6 studies), although both estimates indicated a statistically significant ($P < 0.05$) increased risk. The test for subgroup differences had a P value of 0.05. This result is interpreted as some evidence that the effect of any occupational exposure to solar UVR on BCC incidence may perhaps be less elevated than that on SCC incidence; however, more evidence is required, particularly considering the moderate to high heterogeneity observed among studies including BCC risk estimates, and the lower number of studies reporting SCC risk estimates separately. None of the studies included for this health outcome reported effect estimates disaggregated by age group, occupation, industrial sector, socioeconomic status or formality of the economy; subgroup analyses by these variables were therefore not feasible.

3.6 Sensitivity analyses

Sensitivity analyses of the main meta-analysis were performed for the health outcomes of melanoma incidence and NMSC incidence, and are provided in the forest plots in Annex 7.

3.6.1 Melanoma incidence

In terms of pooled effect estimates of risk of melanoma incidence, no evidence of differences was found between:

- studies with a "high" or "probably high" risk of bias rating in any domain and studies with a "low" or "probably low" risk of bias rating in all domains;
- studies with a "high" or "probably high" and studies with a "low" or "probably low" risk of bias rating for exposure misclassification;
- studies with a "high" or "probably high" and studies with a "low" or "probably low" rating for risk of confounding;
- studies with a "high" or "probably high" and studies with a "low" or "probably low" risk of bias rating for conflict of interest;

- studies without ICD-10 diagnostic codes reported and studies with documented or specified ICD-10 diagnostic codes;
- studies with the exposed group definition based on cumulative exposure compared with studies with the exposed group definition not based on cumulative exposure; and
- studies with in situ cases representing up to 5% of cases and studies with no in situ cases included or reported (Table 21).

Table 21. Summary of sensitivity analyses of studies reporting on the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma and/or non-melanoma skin cancer incidence (see also forest plots in Annex 7)

Melanoma incidence	RR (95% CI)	I^2(%)	NMSC incidence	RR (95% CI)	I^2(%)
Risk of bias (14 studies; *P* = 0.94)			**Risk of bias (20 studies; *P* = 0.005)**		
Any "high" or "probably high"	1.47 (1.04–2.08)	76	Any "high" or "probably high"	1.98 (1.44–2.72)	76
Only "low" or "probably low"	1.43 (0.71–2.87)	83	Only "low" or "probably low"	1.11 (0.86–1.43)	76
Risk of exposure misclassification bias (14 studies; *P* = 0.40)			**Risk of exposure misclassification bias (20 studies; *P* = 0.20)**		
"High" or "probably high"	1.58 (1.11–2.25)	75	"High" or "probably high"	1.75 (1.23–2.47)	82
"Low" or "probably low"	1.20 (0.69–2.06)	77	"Low" or "probably low"	1.31 (0.98–1.74)	80
Risk of confounding (14 studies; *P* = 0.73)			**Risk of confounding (20 studies; *P* = 0.88)**		
"High" or "probably high"	1.21 (0.40–3.70)	83	"High" or "probably high"	1.70 (0.61–4.70)	81
"Low" or "probably low"	1.49 (1.08–2.04)	82	"Low" or "probably low"	1.56 (1.17–2.08)	91
Risk of conflict of interest bias (14 studies; *P* = 0.13)			**Risk of conflict of interest bias (20 studies;*P* = 0.00001)**		
"High" or "probably high"	1.97 (1.44–2.70)	–	"High" or "probably high"	3.34 (2.73–4.08)	0
"Low" or "probably low"	1.40 (1.03–1.91)	79	"Low" or "probably low"	1.43 (1.13–1.82)	82
ICD code (14 studies; *P* = 0.73)			**ICD code (20 studies; *P* = 0.001)**		
No ICD code reported	1.42 (1.03–1.97)	75	No ICD code reported	1.75 (1.35–2.27)	81
ICD code specified	1.80 (0.49–6.67)	92	ICD code specified	0.67 (0.39–1.14)	75
Exposed group definition (14 studies; *P* = 0.22)			**Exposed group definition (20 studies; *P* = 0.46)**		
Not based on cumulative exposure	1.80 (1.12 to 2.87)	78	Not based on cumulative exposure	1.81 (1.20, 2.74)	73
Based on cumulative exposure	1.22 (0.81 to 1.82)	82	Based on cumulative exposure	1.48 (1.06, 2.07)	92
In situ cases (14 studies; *P* = 0.92)			**Outcome definition (20 studies; *P* = 0.56)**		
No in situ cases	1.46 (1.07–1.98)	82	BCC or SCC	1.67 (1.28–2.19)	80
5% in situ cases	1.40 (0.74–2.68)	–	Any NMSC	1.30 (0.59–2.88)	93

BCC, basal cell carcinoma; CI, confidence interval; ICD, International Statistical Classification of Diseases and Related Health Problems; NMSC, non-melanoma skin cancer; RR, relative risk; SCC, squamous cell carcinoma.

Considering the relatively high statistical heterogeneity found in the main meta-analysis of studies including lentigo maligna melanoma (I^2 = 81%; Fig. 7), the impact of each study on the heterogeneity indicator was explored in a leave-one-out analysis. The most substantial reduction of statistical heterogeneity (from 81% to 75%) was observed by excluding Kenborg et al. *(139)*, although this was a modest decrease (Table 14). Excluding Kenborg et al. *(139)* increased the pooled RR modestly, from 1.45 (95% CI: 1.08–1.94) to 1.52 (95% CI: 1.10–2.10), with the lower limit of the 95% CI indicating a 10% increased risk. Exclusion of the study by Beitner et al. *(108)* yielded the largest increase in pooled RR from 1.45 to 1.56 (95% CI: 1.16–2.11; I^2 = 79%),

while exclusion of Ródenas et al. *(119)* resulted in the lowest pooled RR of 1.35 (95% CI: 1.02–1.81; I^2 = 79%) (Table 14).

3.6.2 NMSC incidence

For pooled effect estimates of the risk of NMSC incidence, the sensitivity analyses revealed the following differences (Table 21):

- studies with a "high" or "probably high" risk of bias ratings in any domain had a higher pooled effect estimate than studies with a "low" or "probably low" risk of bias ratings in all domains;
- studies with a "high" or "probably high" risk of conflict of interest bias had a higher pooled effect estimate than studies with a "low" or "probably low" risk of conflict of bias; and
- studies without ICD-10 diagnostic codes reported had a higher pooled effect estimate than studies with reported or approximated (e.g. as recorded in administrative health records) ICD-10 diagnostic codes.

No evidence of differences in pooled effect estimates of the risk of NMSC incidence was found between:

- studies with a "high" or "probably high" and studies with a "low" or "probably low" risk of bias rating for exposure misclassification bias;
- studies with a "high" or "probably high" and studies with a "low" or "probably low" risk of confounding rating;
- studies that measured the exposure without a cumulative exposure metric and those that did not; and
- studies that defined the outcome as any NMSC, and studies that defined the outcome as either SCC or BCC subtype only.

3.7 Quality of evidence

3.7.1 Melanoma incidence

There were some concerns regarding risk of bias in two aspects of the body of evidence on the effect of occupational exposure to solar UVR on melanoma incidence. The first concern was the "probably high" or "high" risk of exposure misclassification bias (i.e. bias in exposure assessment) as a result of exposure being assigned via proxy of occupation, occupational group, job task or other variables, rather than assessed with direct measurements, in 19 and five of the 29 case–control studies included, respectively. However, the sensitivity analysis by cumulative versus non-cumulative exposure measurements provided no evidence for differences, suggesting that cruder exposure measurements and more refined (cumulative) measurements resulted in similar effect estimates (Table 22).

The second concern was the potential for risk of detection bias (i.e. bias in outcome assessment), in particular when comparing studies by subtypes of melanoma excluded a priori by study design. Specifically, the six case–control studies that excluded clinically relevant lentigo maligna melanoma (i.e. can metastasize), which is known to be associated with chronic sun exposure (e.g. occupational exposure), were judged to have a "high" risk of detection bias. The study by Nelemans et al. *(110)* was excluded from the first meta-analysis (because the authors'

Table 22. Effect estimates from studies included in main meta-analysis reporting on association between occupational exposure to solar ultraviolet radiation, in terms of cumulative exposure, and malignant skin melanoma incidence

Author, year	Study ID	Exposure definition	Level of exposure	Adjusted OR (95% CI)	*P* value for trend	Comment
Graham et al., 1985 *(98)*	Graham 1985	Cumulative no. hours spent per week outdoors (winter and summer)	> 45 000 h/wk 14 001–45 000 h/wk 4001–14 000 h/wk 1–4000 h/wk < 1 h/wk	0.67 (0.34–1.33) 0.88 (0.33–2.34) 1.39 (0.11–2.04) 0.84 (0.36–1.95) 1.0 (–)	NR	Estimates for male study participants
Zanetti et al., 1988 *(102)*, 1999 *(103)* Rosso et al., 1998 *(104)*, 2008 *(105)*	Zanetti 1988	Lifetime hours of sun exposure during outdoor work; adjusted for sex and age in decades, using the melanoma set of controls	> 22 000 h/lifetime 7001–22000 h/lifetime 5001–7000 h/lifetime < 5000 h/lifetime	1.4 (0.6–2.2) 0.9 (0.5–1.8) 0.5 (0.2–1.0) 1.0 (–)	0.07 (No evidence of a trend)	
Chen et al., 1996 *(117)*	Chen 1996	Duration in years of outdoor job compared with no outdoor work	≥ 5 yr > 0 to < 5 yr 0 yr	0.5 (0.2–1.1) 0.8 (0.4–1.5) 1.0 (–)	NR	Estimates for the head and neck
Ródenas et al., 1996 *(119)*	Ródenas 1996	Lifetime hours of occupational exposure to sun	≥ 11 501 h/lifetime 1–11 500 h/lifetime 0 h/lifetime	3.7 (1.7–7.5) 1.1 (0.5–2.5) 1.0 (–)	0.03 (Increase in risk with higher level of cumulative exposure)	
Zanetti et al., 2006 *(63)*	Zanetti 2006	No. weighted hours of outdoor work in a lifetime	> 3878 weighted h/lifetime 1128–3878 weighted h/lifetime 320–1128 weighted h/lifetime 1–320 weighted h/lifetime Never	1.00 (0.57–1.95) 1.10 (0.63–2.06) 1.10 (0.62–1.99) 1.10 (0.70–1.87) 1.0 (–)	0.94 (No evidence of a trend)	
Kenborg et al., 2010 *(139)*	Kenborg 2010	Lifetime years of outdoor occupation from records of pension plan	> 10 yr/lifetime 5–10 yr/lifetime 1–5 yr/lifetime No outdoor work or < 1 yr/lifetime	0.97 (0.84–1.11) 0.88 (0.75–1.02) 0.81 (0.72–0.91) 1.0 (–)	0.01 (Increase in risk with higher level of cumulative exposure)	
Trakatelli et al., 2016 *(64)*	Trakatelli 2016	Self-reported duration of outdoor work	> 5 yr 1–5 yr < 1 yr Never outdoor work	1.97 (1.43–2.71) 1.68 (1.00–2.81) 0.77 (0.31–1.88) 1.0 (–)	NR	Outcome definition limited to invasive melanoma

CI, confidence interval; h, hour(s); NR, not reported; OR, odds ratio; wk, week(s); yr, year(s).

[a] All studies of case–control design, except for Håkansson et al. *(68)* (cohort) and Whiteman et al. *(134)* (case–case).

definition of exposure was not consistent with other studies; Table 11), but the other five studies *(62, 93, 95, 101, 111)* were included. The sensitivity analyses then revealed that studies excluding lentigo maligna melanoma generated a pooled statistically significant decreased risk and that studies including the subtype generated a pooled statistically significant increased risk, indicating that definition of the outcome impacts the direction of the effect estimate. However, because it was possible to estimate a pooled RR based on 14 of the 19 studies free from this detection bias because the outcome definition excluded lentigo maligna melanoma, and designated it as the main pooled effect estimate (RR: 1.45; 95% CI: 1.08–1.94; 14 studies; Fig. 7), there were no serious concerns and therefore the quality of evidence was not downgraded for this consideration.

There were no serious concerns regarding inconsistency, despite acknowledgment of some issues arising from clinical heterogeneity among pooled studies. There was a concern about pooling studies that defined the cancer outcome differently (i.e. inclusion versus exclusion of an eligible histology subtype). Studies were therefore grouped according to this outcome-related criterion rather than pooling all 19 original available studies (main analysis; see Fig. 7). However, the degree of statistical heterogeneity (I^2) remained at the same high value of 81% when pooling studies by outcome as when pooling all available studies. The potential inconsistency between case–control studies included in the main meta-analysis (Fig. 7) and those excluded from the main meta–analysis (Table 11) was also noted; excluded studies appear to have indicated a lower increased risk or even no increased risk. The high degree of statistical heterogeneity in the main meta-analysis was considered to be expected as the analysis included studies from diverse countries with different latitudes (Table 13), as well as populations with different susceptibilities to melanoma incidence. Additional sources of heterogeneity may have been the extent of adjustment for potential confounders, differences in exposure definition and possible variations in risk of tumours with different anatomical location, suggesting divergent aetiologies, information not available in all studies. Lastly, as described in Section 3.6.1, leaving Kenborg et al. *(139)* out modestly reduced the statistical heterogeneity from 81% to 75% (Table 14) and increased the pooled RR from 1.45 (95% CI: 1.08–1.94) to 1.52 (95% CI: 1.10–2.10) (also raising the lower bound of the confidence interval). Other individual temporary exclusions changed the I^2 marginally (i.e. from 81% to 75–82%), the effect estimate (from 1.45 to 1.38–1.56) and the lower limit of the 95% CI (from 1.08 to 1.02–1.16, i.e. always above the null value) (Table 14). The quality of evidence was therefore not downgraded for inconsistency.

There were serious concerns for indirectness of the body of evidence, so the quality of evidence was downgraded for this by one level (–1). Evidence was limited to studies from just two WHO regions (Region of the Americas and European Region), and the pooled RR from the main analysis (Fig. 7) was based on three studies from the USA and 11 studies from Europe, that is, studies of populations of mostly European ancestry and based in countries within a limited range of latitudes. Although these regions register important incidence rates of melanoma worldwide (Region of the Americas Age Standardized Incidence Rate, 2020, 8.3 per 100 000 people; European Region, 9.9 per 100 000) (IARC Global Cancer Observatory, https://gco.iarc.fr), the available evidence did not include studies from low-incidence regions (African Region, 1.1 per 100 000; Eastern Mediterranean Region, 0.43 per 100 000; South-East Asian Region, 0.34 per 100 000; Western Pacific Region, 0.99 per 100 000) or from countries with very high incidence (Australia, 36.6 per 100 000; New Zealand, 31.6 per 100 000) (IARC Global Cancer Observatory, https://gco.iarc.fr).

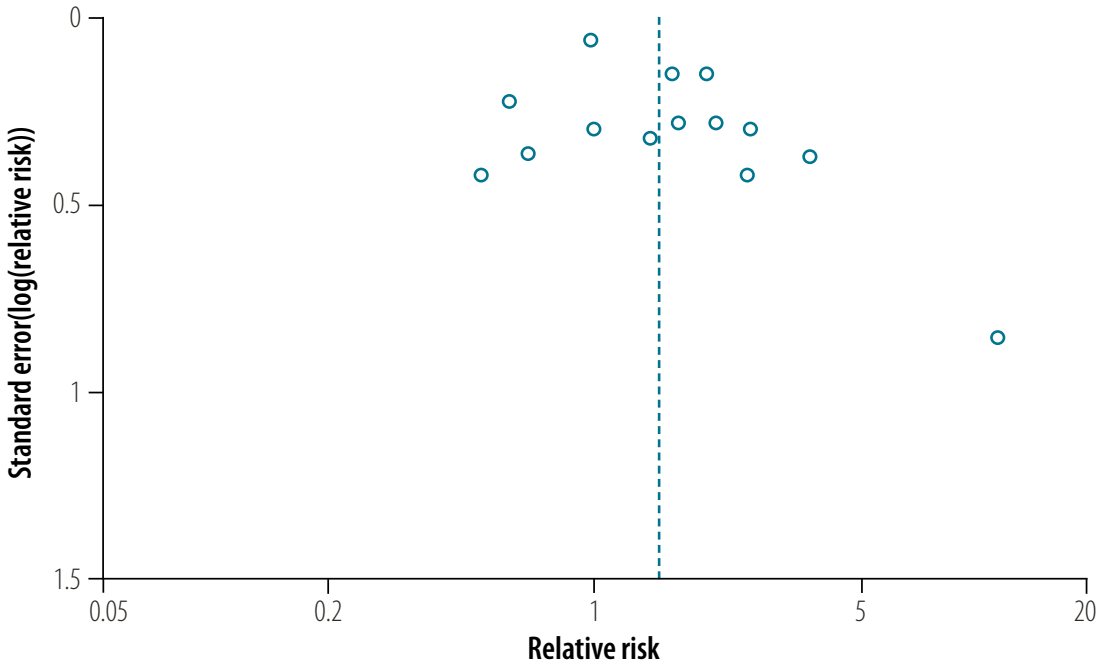
There was also some concern for imprecision, given that the 95% CI of the pooled effect estimate in the main meta-analysis (Fig. 7) ranged from a low increase in risk (8%) to an almost

doubling of the risk (94%). However, the leave-one-out analysis (Table 14) showed that the lower bound of the pooled effect estimate always remained above the null value and the upper bound was always close to a doubled risk. The quality of evidence was therefore not downgraded for imprecision.

There were no serious concerns for reporting bias, as the funnel plot was judged to be symmetric (Fig. 10). Quality of evidence was not upgraded for a large effect estimate, for evidence of a dose–response relationship, or for evidence that all plausible residual confounders or biases would reduce the demonstrated effect. Regarding assessment of evidence of a dose–response relationship, seven of the 14 case–control studies included in the main meta-analysis reported effect estimates by cumulative exposure levels or duration of exposure categories (Table 22). Of these, four studies (with one individual analysis each) reported a formal statistical test for trend in risk by cumulative exposure level. Of these, two studies reported an increase in risk with a higher level of cumulative exposure *(119, 139)*, and two studies found no evidence of a statistically significant trend *(63, 102–105)*; none reported a decrease in risk with higher level of cumulative exposure (Table 22).

In conclusion, from a starting point of a "moderate" grading for quality of evidence from observational studies, quality of evidence was downgraded by one level (–1) for indirectness; therefore the quality of evidence of an association between occupational exposure to solar UVR and melanoma incidence was assigned a final rating of "low".

Fig. 10. Funnel plot for studies reporting on any (or high) occupational exposure, compared with no (or low) exposure, to solar ultraviolet radiation and malignant skin melanoma incidence



3.7.2 Melanoma mortality

There were no serious concerns regarding risk of bias in the body of evidence for or inconsistency in the association between occupational exposure to solar UVR and melanoma mortality, and therefore the quality of evidence was not downgraded for these considerations. However, there were serious concerns regarding indirectness and the quality of evidence was downgraded by one level (–1). Evidence was limited to two studies from just two WHO regions (Region of the Americas and European Region), that is, populations of mostly European ancestry and countries of a limited range of latitudes (USA and Italy). There were also serious concerns for imprecision, and therefore the quality of evidence was downgraded for this consideration by one level (–1). For the prioritized study (122, 123) for this outcome, the 95% CI was rather wide (Table 16), indicating that the estimated effect may range between a modest decrease and a modest increase in risk of melanoma mortality. There were no serious concerns of reporting bias, and the quality of evidence was not upgraded for either a large effect estimate, evidence for a dose–response relationship, or evidence that all plausible residual confounding or bias would have reduced the effect estimate.

In conclusion, from a starting point of a "moderate" grading for the quality of evidence from observational studies, quality of evidence was downgraded by one level each for indirectness (–1) and imprecision (–1); the quality of evidence of an association between occupational exposure to solar UVR and melanoma mortality was assigned a final rating of "low".

3.7.3 NMSC incidence

There were serious concerns regarding risk of bias in the body of evidence of the association between occupational exposure to solar UVR and NMSC incidence. In the sensitivity analysis, it was noted that a greater increased risk was reported by studies judged to have any "probably high" or "high" risk of bias (RR: 1.98; 95% CI: 1.44–2.72) than by studies with only "low" or "probably low" ratings (RR: 1.11; 95% CI: 0.86–1.43), with these differences being statistically significant ($P = 0.005$ for subgroup differences). The main concern was the domain of exposure misclassification bias, as a result of exposure being assigned via proxy of occupation, occupational group, job task or other variables rather than assessed with direct measurements. A "probably high" rating was assigned for risk of exposure misclassification bias to eight case–control studies and one cohort study, and a "high" exposure misclassification bias rating to five case–control studies; these studies reported a higher increased risk of NMSC incidence (RR: 1.75; 95% CI: 1.23–2.47) compared with studies assigned a "low" or "probably low" risk of bias in all domains (RR: 1.31; 95% CI: 0.98–1.74) (Table 21), but this difference was not statistically significant ($P = 0.20$; Table 21). Effect estimates were also higher in studies considered to have a "probably high" compared with a "low" or "probably low" risk of confounding, but this difference was also not statistically significant ($P = 0.88$; Table 21). There were also some concerns that studies judged to have a "probably high" or "high" risk of conflict of interest bias reported a relatively higher increased risk, and studies that reported the outcome using ICD codes had substantially reduced effect estimates compared with those that did not. In summary, the quality of evidence was downgraded by one level (–1) for risk of bias considerations.

There were no serious concerns regarding inconsistency, and therefore the quality of evidence was not downgraded for this consideration. Statistical heterogeneity in the main meta-analysis was very high (RR: 1.60; 95% CI: 1.21–2.11; $I^2 = 91\%$), but this was expected considering that the analysis included studies from diverse countries with a wide range of latitudes, a range of NMSC subtypes and populations with different susceptibilities to NMSC incidence, and varying degrees of adjustment for potential confounding. In the leave-one-out analysis (Table 18),

excluding one study did not change the fact that the lower limit of the 95% CI was always above the null value (1.16–1.27).

There were no serious concerns for indirectness of the body of evidence; evidence was available from three WHO regions (Region of the Americas, European Region and Western Pacific Region), a relatively diverse and large number of countries and, although most studies were of populations of mostly European ancestry, some studies of more diverse populations were included (i.e. Australia, Brazil, Colombia and Greece). There were no serious concerns for either imprecision (the 95% CI indicated an increase in the relative risk that was judged as moderate to large in size) or reporting bias (the funnel plot was considered to be symmetric; Fig. 11). Quality of evidence was not upgraded for large effect size, or plausible residual confounding or bias. However, it was upgraded by one level (+1) for evidence of a dose–response relationship in studies with cumulative exposure estimates (Table 23). Eleven of the 20 case–control studies included in the main meta–analysis reported effect estimates by cumulative exposure levels or duration of exposure categories. Of these, six studies with nine individual analyses reported a formal statistical test for trend in risk by cumulative exposure level. Of these, five analyses from four studies reported an increase in risk with a higher level of cumulative exposure *(63, 104, 112, 113, 120, 142)*; three analyses from three studies reported no evidence of a statistically significant trend *(104, 116, 120, 142)*; and one analysis reported a decrease in risk with a higher level of cumulative exposure *(139)* (Table 23).

In conclusion, from a "moderate" grading for quality of evidence from observational studies, and downgrading for risk of bias by one level (–1) and upgrading for dose–response relation-

Fig. 11. Funnel plot for studies reporting on any (or high) occupational exposure, compared with no (or low) exposure, to solar ultraviolet radiation and non-melanoma skin cancer incidence

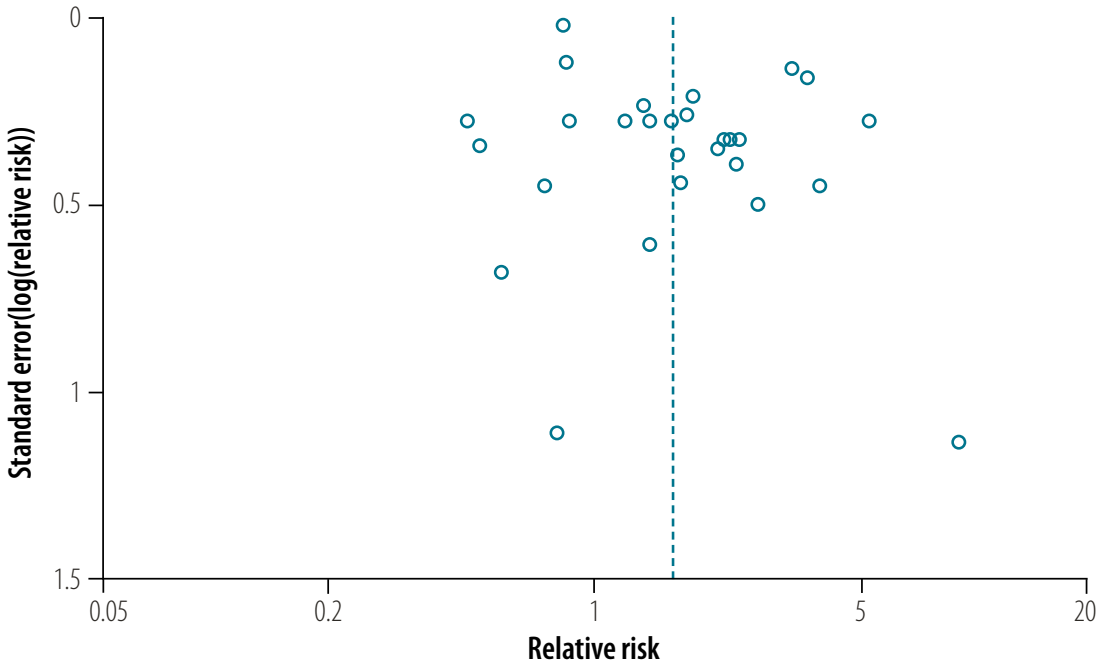


Table 23. Effect estimates from studies included in the main meta-analysis reporting on association between occupational exposure to solar ultraviolet radiation, in terms of cumulative exposure, and non-melanoma skin cancer incidence

Author, year	Study ID	Exposure definition	Level of exposure	Adjusted OR (95% CI)	*P* value for trend (as reported)
Gallagher et al., 1995 *(112)*	Gallagher 1995 (BCC)	Mean occupational sun exposure per year over lifetime, expressed in WBE	≥ 105 WBE/yr/lifetime 60–104 WBE/yr/lifetime 15–59 WBE/yr/lifetime <15 WBE/yr/lifetime	1.4 (0.8–2.4) 1.3 (0.8–2.3) 1.1 (0.6–1.8) 1.0 (–)	NS
Gallagher et al., 1995 *(113)*	Gallagher 1995 (SCC)	Mean occupational sun exposure per year over lifetime, expressed in WBE	≥105 WBE/yr/lifetime 60–104 WBE/yr/lifetime 15–59 WBE/yr/lifetime <15 WBE/yr/lifetime	1.4 (0.4–4.3) 1.5 (0.6–4.2) 0.8 (0.3–2.0) 1.0 (–)	NS
Gallagher et al., 1995 *(113)*	Gallagher 1995 (SCC)	Mean occupational sun exposure per year over lifetime, in last 10 yr	≥ 100 WBE/yr 30–99 WBE /yr 1–29 WBE/yr 0 WBE /yr	4.0 (1.2–13.1) 2.2 (0.8–6.4) 1.9 (0.6–5.6) 1.0 (–)	< 0.05 (Increase in risk with higher level of cumulative exposure)
Kricker et al., 1995 *(116)*	Kricker 1995	Cumulative no. hours of sun exposure per week on working days from age 15 yr	≥ 49 400 h 49 300–27 800 h 27 700–14 800 h 14 800–0 h	0.86 (0.50–1.51) 1.17 (0.72–1.90) 1.25 (0.79–1.97) 1.0 (–)	0.46 (No evidence of a trend)
Rosso et al., 1996 *(120)*, 1998 *(104)*	Rosso 1996 (BCC)	Lifetime hours of sun exposure during outdoor work	≥ 54 720 h/lifetime 12 481–54 720 h/lifetime 7200–12 480 h/lifetime < 7200 h/lifetime	0.84 (0.65–1.10) 1.01 (0.81–1.25) 0.95 (0.77–1.19) 1.0 (–)	0.186 (No evidence of a trend)
Rosso et al., 1996 *(120)*, 1998 *(104)*	Rosso 1996 (SCC)	Lifetime hours of sun exposure during outdoor work	≥ 54 720 h/lifetime 12 481–54 720 h/lifetime 7200–12 480 h/lifetime < 7200 h/lifetime	1.60 (0.93–2.75) 1.28 (0.77–2.14) 1.04 (0.62–1.75) 1.0 (–)	0.029 (Increase in risk with higher level of cumulative exposure)
Suárez-Varela et al., 1996 *(121)*	Suárez-Varela 1996 (NMSC, F)	Daily no. hours of sun exposure during occupational activity outdoor	> 4.8 h/day 3.6–4.8 h/day 1.7–3.6 h/day < 1.7 h/day	0.8 (0.1–8.2) 0.8 (0.2–4.2) 2.1 (0.8–5.6) 1.0 (–)	NR
Suárez-Varela et al., 1996 *(121)*	Suárez-Varela 1996 (NMSC, M)	Daily no. hours of sun exposure during occupational activity outdoor	> 4.8 h/day 3.6–4.8 h/day 1.7–3.6 h/day < 1.7 h/day	5.3 (3.1–9.2) 2.5 (1.5–4.3) 1.2 (0.6–2.2) 1.0 (–)	NR

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Author, year	Study ID	Exposure definition	Level of exposure	Adjusted OR (95% CI)	*P* value for trend (as reported)
Zanetti et al., 2006 *(63)*	Zanetti 2006 (BCC)	No. weighted hours of outdoor work in a lifetime	> 3878 h/lifetime 1128–3878 h/lifetime 320–1128 h/lifetime 1–320 h/lifetime Never	1.2 (0.70–2.13) 1.4 (0.80–2.40) 0.7 (0.41–1.35) 1.4 (0.83–2.51) 1.0 (–)	0.046 (Increase in risk with higher level of cumulative exposure)
Zanetti et al., 2006 *(63)*	Zanetti 2006 (SCC)	No. weighted hours of outdoor work in a lifetime	> 3878 h/lifetime 1128–3878 h/lifetime 320–1128 h/lifetime 1–320 h/lifetime Never	2.2 (1.13–4.08) 1.8 (0.92–3.54) 1.2 (0.57–2.31) 1.3 (0.62–2.77) 1.0 (–)	0.007 (Increase in risk with higher level of cumulative exposure)
Pelucchi et al., 2007 *(135)*	Pelucchi 2007 (BCC nodular)	Lifetime occupational sun exposure	Long duration/lifetime Short duration/lifetime None/lifetime	1.35 (0.85–2.14) 1.66 (1.08–2.55) 1.0 (–)	NR
Pelucchi et al., 2007 *(135)*	Pelucchi 2007 (BCC superficial)	Lifetime occupational sun exposure	Long duration/lifetime Short duration/lifetime None/lifetime	0.50 (0.25–1.00) 0.92 (0.52–1.62) 1.0 (–)	NR
Kenborg et al., 2010 *(139)*	Kenborg 2010	Lifetime no. years of outdoor occupation from pension plan records	> 10 yr/lifetime 5–10 yr/lifetime 1–5 yr/lifetime No outdoor work or < 1 yr/lifetime	0.83 (0.77–0.88) 0.85 (0.79–0.91) 0.78 (0.74–0.83) 1.0 (–)	<0.001 (Decrease in risk with higher level of cumulative exposure)
Iannacone et al., 2012 *(142)*	Iannacone 2012 (BCC)	No. years with a job in the sunlight for ≥ 3 months	> 10 yr ≤ 10 yr None	2.12 (1.05–4.27) 1.07 (0.61–1.86) 1.0 (–)	0.06 (No evidence of a trend)
Iannacone et al., 2012 *(142)*	Iannacone 2012 (SCC)	No. years with a job in the sunlight for ≥ 3 months	> 10 yr ≤ 10 yr None	2.36 (1.07–5.20) 1.64 (0.88–3.07) 1.0 (–)	0.02 (Increase in risk with higher level of cumulative exposure)
Surdu et al., 2013 *(144)*	Surdu 2013 (NMSC)	Cumulative lifetime exposure of occupational natural UVR, in hours	> 5075 h/lifetime 5075–1255 h/lifetime > 1225 h/lifetime Never outdoor	0.66 (0.32–1.34) 0.34 (0.15–0.73) 0.43 (0.19–0.94) 1.0 (–)	NR
Trakatelli et al., 2016 *(64)*	Trakatelli 2016 (BCC)	Self-reported duration of outdoor work	> 5 yr 1–5 yr > 1 yr Never outdoor	3.32 (2.55–4.33) 0.89 (0.48–1.65) 1.39 (0.60–3.21) 1.0 (–)	NR

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Author, year	Study ID	Exposure definition	Level of exposure	Adjusted OR (95% CI)	*P* value for trend (as reported)
Trakatelli et al., 2016 *(64)*	Trakatelli 2016 (SCC)	Self-reported duration of outdoor work	> 5 yr 1–5 yr > 1 yr Never outdoor	3.67 (2.63–5.11) 1.32 (0.64–2.70) 1.13 (0.35–3.72) 1.0 (–)	NR
Schmitt et al., 2018 *(41, 42)*	Schmitt 2018 (BCC)	Occupational exposure to UVR by SED level	≥ 5870.4 SED 532.2–5870.4 SED > 0.0–532.1 SED 0.0 SED	1.84 (1.19–2.83) 0.87 (0.65–1.15) 0.93 (0.66–1.32) 1.0 (–)	Non-linear trend assessed

BCC, basal cell carcinoma; CI, confidence interval; F, females; h, hour(s); M, males; NR, not reported; NMSC, non-melanoma skin cancer; NS, not significant; OR, odds ratio; SCC, squamous cell carcinoma; SED, standard erythema dose; UVR, ultraviolet radiation; WBE, whole-body equivalent; yr, year(s).

ship by one level (+1), the quality of evidence of an association between occupational exposure to solar UVR and NMSC incidence was assigned a final rating of "moderate".

3.7.4 NMSC mortality

For the single study reporting on the association between occupational exposure to solar UVR and NMSC mortality (Freedman et al. *(122, 123)*), there were some concerns regarding risk of exposure misclassification bias as exposure was assigned based on information extracted from death certificates; however, these concerns were judged to be of minor consequence and the quality of evidence was not downgraded for this consideration. There were also no serious concerns regarding inconsistency, and therefore the quality of evidence was not downgraded for this consideration. However, because evidence came from only one study from one country, which is unlikely to capture the global target population of the systematic review, there were very serious concerns for indirectness and therefore the quality of evidence was downgraded by two levels (–2). There were no serious concerns for imprecision, and the quality of evidence was not downgraded for this consideration. The 95% CI indicated what was judged to be a moderate increased risk. There were no serious concerns for reporting bias and quality of evidence was not upgraded for a large effect estimate, evidence of a dose–response relationship, or residual confounding or bias.

In conclusion, from a "moderate" grading for quality of evidence from observational studies, and downgrading by two levels (–2) for indirectness, the quality of evidence of an association between occupational exposure to solar UVR and NMSC mortality was assigned a final rating of "low".

3.8 Strength of evidence

According to the protocol *(5)*, the strength of evidence (Table 6) was rated for the association between occupational exposure to solar UVR and melanoma incidence and mortality and NMSC incidence and mortality using a combination of four criteria outlined in the Navigation Guide: (i) quality of the entire body of evidence (Table 6); (ii) direction of the effect estimate; (iii) confidence in the effect estimate; and (iv) other compelling attributes. The ratings and rationale are summarized in Table 24.

3.8.1 Melanoma incidence

(a) Quality of the entire body of evidence

In terms of the number, size and quality of individual studies, the body of evidence assessing the association between occupational exposure to solar UVR and melanoma incidence is sufficient to assess the harmfulness of the exposure. From the main meta-analysis based on 14 case–control studies (Fig. 7), conducted within two different WHO regions, including a very large number of participants and taking into account relevant confounders, a moderately increased risk of melanoma incidence in people with any (or high) occupational exposure to solar UVR (RR: 1.45; 95% CI: 1.08–1.94; Fig. 7) was obtained. The evidence from the 10 case–control studies that could not be included in the main meta-analysis (Table 11) provided negligible support to the findings from the main meta-analysis, but provided non-prioritized evidence (e.g. crude effect estimates with a high risk of confounding) that would not reasonably be expected to be similar to the results from the main meta-analysis. Evidence from three case–case studies and a cohort study (Table 15) offered some support, reporting a low to high increased risk of mel-

Table 24. **Summary of systematic review and meta-analysis of studies reporting on association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma and non-melanoma skin cancer prevalence, incidence and mortality, in all workers (aged ≥ 15 years), in any country or work setting, compared with no occupational exposure to solar ultraviolet radiation**

Health outcome	Assumed risk (unexposed workers)	Corresponding risk (95% CI) (exposed workers)	Relative effect(95% CI)	No. participants	Navigation Guide quality of evidence rating[a]	Navigation Guide strength of evidence rating[a]	Comments
Melanoma prevalence	–	–	–	–	–	–	No evidence was found on this outcome
Melanoma incidence	–	–	–[b]	268 603 (33 studies)	⊖⊖ Low	Limited evidence of harmfulness	The pooled effect estimate (main meta-analysis) indicated that any occupational exposure to solar UVR led to a moderate, clinically meaningful increase in risk of melanoma incidence; the 10 case–control studies that were excluded from the main meta-analysis provided crude risk estimates marginally supportive of the pooled estimate; one cohort study and three case–case studies provided additional support
Melanoma mortality	–	–	–[c]	20 231 (2 studies)	⊖⊖ Low	Inadequate evidence of harmfulness	The effect of occupational exposure to solar UVR on melanoma mortality is very uncertain
NMSC prevalence	–	–	–	–	–	–	No evidence was found on this outcome
NMSC incidence[d]	5.8 cases per 100 000 person-years[e]	9.3 per 100 000 person-years (7.0–12.0)	RR: 1.60 (1.21–2.11)[f]	286 131 (25 studies)	⊕⊖ Moderate	Sufficient evidence of harmfulness	In the main meta-analysis of case–control studies, any (or high) occupational exposure to solar UVR led to a moderate, clinically meaningful increase in risk of NMSC incidence; the two case–control studies that could not be included in the main meta-analysis provided crude risk estimates generally supportive of the pooled estimate, but imprecise; the two cohort studies and the case–case study provided supportive evidence
NMSC mortality	–	–	–[c]	80 987 (1 study)	⊖⊖ Low	Inadequate evidence of harmfulness	The effect of occupational exposure to solar UVR on NMSC mortality is very uncertain

CI: confidence interval; ICD, International Statistical Classification of Diseases and Related Health Problems; NMSC: non-melanoma skin cancer; RR: relative risk; UVR: ultraviolet radiation.

[a] See Table 6 for definitions of quality of evidence and strength of evidence ratings.

[b] Relative effect estimate from meta-analysis not displayed because of low quality of evidence.

[c] Prioritized relative effect estimate not displayed because of low quality of evidence.

[d] Measured from administrative records with a follow-up of an unclear number of years.

[e] For the outcome, the baseline risk (given by the incidence rate of cancer (ICD-7) in the low exposed or unexposed group) was extracted from the Håkansson et al. cohort study *(68)*, based on 323 860 men employed in the construction industry in Sweden and first examined between 1971 and 1993 (accruing a total of 4 542 911 person-years).

[f] Pooled effect estimate from the main meta-analysis of case–control studies.

anoma incidence in people occupationally exposed to solar UVR, compared with those occupationally unexposed to the risk factor, but effect estimates were imprecise (including the null value in the CI in three out of four risk estimates).

The quality of the entire body of evidence was judged to be "low" because of serious concerns of indirectness. Although it is recognized that the evidence points towards a positive association between the occupational risk factor and health outcome pair being investigated, it is not known if this association holds in geographical areas not covered by the meta–analysis (e.g. in the African Region, South-East Asia Region and Western Pacific Region). Further research is very likely to have an important impact on the confidence in the effect estimate and is likely to change this effect estimate.

(b) Direction of the effect estimate

From the main meta-analysis (RR: 1.45; 95% CI: 1.08–1.94; 14 studies; I^2 = 81%), the body of evidence clearly suggests an increased risk of melanoma incidence among those occupationally exposed to solar UVR, compared with those not occupationally exposed to solar UVR. Further, the leave-one-out analysis showed that leaving any one study out changed the lower limit of the 95% CI to 1.02–1.16, with the point estimate remaining relatively comparable (1.35–1.56; Table 14). The direction of the effect is unambiguously an increase.

(c) Confidence in the effect estimate

The evidence clearly indicates a positive association; however, it is not possible to be entirely confident about the exact size of this effect estimate. The pooled RR from the main meta–analysis indicated an increased risk of melanoma incidence associated with occupational exposure to solar UVR ranging in value from (a low) 8% to 94%.

(d) Other compelling attributes

Working Groups of experts convened by WHO IARC have classified exposure to solar UVR as a Group 1 carcinogen; solar UVR causes BCC of the skin, SCC of the skin and cutaneous melanoma *(2, 3)*. Exposure to solar UVR in general is such an established cause of melanoma and NMSC that there is no reason to believe that exposure during working time, likely to be more constant or chronic than exposure outside of work, would be less harmful or even not harmful simply because the association has not been consistently measured in studies assessing occupational exposure only. Further, melanoma subtypes may differ in the underlying aetiological pathways whereby chronic sun exposure might be less or more relevant to specific histologic types *(150)*. The recognized carcinogenicity of solar UVR on the skin and the diverse patterns of sun exposure linked to specific subtypes of melanoma should therefore be taken into account when assessing the harmfulness of occupational exposure to solar UVR in this systematic review. Given the Group 1 carcinogenicity rating assigned by IARC, the existing body of evidence, although of low quality (mainly due to concerns of indirectness), is therefore judged as indicative of the contribution of occupational exposure to solar UVR to the cause of melanoma incidence.

(e) Final rating

The strength of evidence for this outcome is rated as "limited evidence of harmfulness". See Table 6 for the full definitions of the various strength of evidence ratings.

3.8.2 Melanoma mortality

(a) Quality of the entire body of evidence

In terms of the number, size and quality of individual studies, the body of evidence (two studies only) on the association between occupational exposure to solar UVR and melanoma mortality is insufficient to assess the harmfulness of the exposure. The quality of the entire body of evidence is judged to be "low" as a result of serious concerns of indirectness and imprecision; the effect of occupational exposure to solar UVR on melanoma mortality is therefore very uncertain.

(b) Direction of the effect estimate

The study results are insufficient to assess the direction of the effect estimate with confidence. The prioritized effect estimate suggested no difference in risk (OR: 0.99; 95% CI: 0.87–1.12), but it is not possible to be confident of the direction of the effect estimate.

(c) Confidence in the effect estimate

There is a lack of confidence in the effect estimate and no conclusions can be drawn from it.

(d) Other compelling attributes

The classification of general exposure to solar UVR as a Group 1 carcinogen by IARC *(2, 3)* is a compelling attribute, even if the current body of evidence on the association between occupational exposure to solar UVR and melanoma mortality is very uncertain.

(e) Final rating

The strength of evidence for this outcome is rated as "inadequate evidence of harmfulness".

3.8.3 NMSC incidence

(a) Quality of the entire body of evidence

In terms of the number, size and quality of individual studies, the body of evidence on the association between occupational exposure to solar UVR and NMSC incidence is sufficient to assess the harmfulness of the exposure. The meta-analysis, based on 20 case–control studies, conducted within three different regions, including a very large number of participants from 21 countries and taking into account relevant confounders, indicated a moderately increased risk of NMSC incidence with any (or high) occupational exposure to solar UVR (RR: 1.60; 95% CI: 1.21–2.11; Fig. 8), compared with no (or low) occupational exposure to solar UVR. The quality of the individual included studies is adequate. Although there were some concerns regarding risk of bias, the body of evidence was judged to be of "moderate quality". Further research is likely to have an important impact on the confidence in the effect estimate, and may change this effect estimate.

(b) Direction of the effect estimate

The study results are sufficient to assess the direction of the effect estimate for NMSC incidence. In the main meta-analysis, a moderate, statistically significant increase was found in the risk of NMSC incidence with occupational exposure to solar UVR, compared with no (or low) occupational exposure to solar UVR.

(c) Confidence in the effect estimate

There is confidence in the effect estimate. The moderately increased risk is noted, with the lower limit of the 95% CI indicating a moderate increase (by 21%). The 95% CI of the RR ranged from 1.21 to 2.11, and this relatively wide range may reflect the two subtypes having increased risks of differing magnitude (Table 20).

(d) Other compelling attributes

As described in Section 3.8.1 (*d*), WHO IARC has classified exposure to solar UVR as a Group 1 carcinogen; solar UVR causes BCC of the skin, SCC of the skin and cutaneous melanoma *(2, 3)*. Given the Group 1 carcinogenicity rating assigned by WHO IARC, and the fact that the existing body of evidence has already been judged as being of "moderate" quality, the existing body of evidence is judged as indicative of the contribution of occupational exposure to solar UVR to the cause of NMSC incidence.

(e) Final rating

The strength of evidence for this outcome is rated as "sufficient evidence of harmfulness".

3.8.4 NMSC mortality

(a) Quality of the entire body of evidence

The entire body of evidence consists of a single study, which is judged to have some limitations in terms of quality. This evidence is insufficient to assess the harmfulness of occupational exposure to solar UVR. The quality of the entire body of evidence has already been judged as "low" as a result of very serious concerns for indirectness; therefore the association between occupational exposure to solar UVR and NMSC is very uncertain.

(b) Direction of the effect estimate

The study results are insufficient to assess the direction of the effect estimate with confidence. The single effect estimate suggested an increased risk (RR: 1.30; 95% CI: 1.14–1.47), but it is not possible to be confident of the direction of the effect estimate as only one study could be included in the systematic review.

(c) Confidence in the effect estimate

There is a lack of confidence in the effect estimate and no conclusions can be drawn from it, at least not for the global population.

(d) Other compelling attributes

The IARC classification of solar UVR as a Group 1 carcinogen *(2, 3)* is a compelling attribute, even if the current body of evidence on the association between occupational exposure to UVR and NMSC mortality is very uncertain.

(e) Final rating

The strength of evidence for this outcome is rated as "inadequate evidence of harmfulness".

CHAPTER 4
Discussion

4.1 Summary of evidence

This systematic review found no eligible study on the health outcomes of melanoma or NMSC prevalence in association with occupational exposure to solar UVR (Table 24). Very few studies reporting on the association between occupational exposure to solar UVR and mortality from melanoma (two studies) and NMSC (one study) were identified, which was inadequate for quantitatively summarizing and assessing the harmfulness of occupational exposure to solar UVR for these outcomes.

However, the systematic review and meta–analysis found that outdoor workers are at an increased risk of the incidence of melanoma and NMSC. These findings are based on low- and moderate-quality ratings of the body of evidence, for associations between occupational exposure to solar UVR and melanoma and NMSC incidence, respectively, of moderate effect size. Based on the other considerations for evaluating the strength of evidence, it was concluded that there was "limited evidence of harmfulness" and "sufficient evidence of harmfulness" of occupational exposure to solar UVR in terms of melanoma incidence and NMSC incidence, respectively. The findings were based on 47 incident case–control studies, 36 of which were included in meta-analyses, and supported by three case–case studies and two prospective cohort studies documenting moderate, but not always consistent, effects of occupational exposure to solar UVR on melanoma and NMSC incidence in a large sample with heterogeneous characteristics (e.g. geographical location and occupation). The pooled effect estimates displayed large statistical heterogeneity, which may reflect clinical heterogeneity of the existing body of evidence, especially with regards to the exposure and how it was assessed.

4.2 Comparison with previous systematic review evidence

4.2.1 Melanoma

Findings from previous systematic reviews and meta-analyses on the association between occupational exposure to solar UVR and melanoma risk are varied (Table 1; Section 1.1.1). Three of the four previously published reviews actually found a reduced risk *(32–34)*, and two of these three reported reductions in risk were statistically significant *(32, 33)*. In the 2006 WHO review of 49 studies reporting on solar UVR exposure and melanoma *(36)*, only eight of the studies reported on occupational exposure to solar UVR, and only one of these eight reported a positive association. In contrast, the findings of this systematic review (Fig. 7) are more in line with the most recently published review of 10 studies *(35)*, which found a statistically significant increased risk of melanoma incidence with occupational exposure to solar UVR in six out of 10 studies.

Although solar UVR was reassessed and classified as a Group 1 carcinogen most recently in the IARC *Monograph* volume 100D *(2, 3)* and results confirmed the aetiological role of intermittent solar UVR exposure, chronic exposure (usually associated with occupational exposure) "generally showed weak, null, or negative associations" with the occurrence of melanomas. It was suggested that individuals who tan easily (and therefore have a skin pigmentation that confers a lower risk of skin malignancies) may self-select to pursue outdoor occupations, possibly accounting for the weak association between occupational exposure to solar UVR and melanoma reported in some studies *(2)*.

4.2.2 NMSC

Findings from previous systematic reviews and meta-analyses on the association between occupational exposure to solar UVR and NMSC have been more harmonized, both with each other and with the results of this systematic review; positive associations were reported in all four previously published reviews (Table 2; Section 1.1.2) *(37–40)*. In the reviews on the association between occupational exposure to solar UVR and BCC *(37)* and SCC *(39)* individually, the authors concluded that outdoor workers are at significantly increased risk. Meta-regression analyses revealed an increasing size of the association between occupational exposure to solar UVR and SCC risk with decreasing latitude *(39)*. The review of 19 studies by Loney et al. *(40)* concluded that: "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 [United Nations] subregions, latitude or skin types". It did not present meta-analyses. The statistically significant increased risk in this systematic review (Fig. 8) was obtained from a meta–analysis of a larger number of studies (i.e. 25 studies included in systematic review, of which 20 studies were included in the main meta-analysis) spanning three WHO regions (Region of the Americas, European Region and Western Pacific Region).

4.3 Limitations of this review

There are several limitations of this systematic review.

First, even though the search strategy included a large number of academic and grey literature databases, potentially eligible studies may have been missed (e.g. those published in languages other than the 18 languages we covered). However, consultation of additional experts did not lead to the identification of any additional eligible studies. It is also considered that, given the large number of included studies and associated large numbers of study participants and disease events, the overall findings would not have been affected by the search not finding a small number of potentially eligible studies.

Second, all studies included in the meta-analysis used a subjective measure of occupational exposure to solar UVR assessment (e.g. questionnaires and lifetime occupational history, or by proxy of job task and/or occupation), which will have increased the risk of bias from exposure misclassification. Objective assessments of occupational exposure to solar UVR using personal dosimetry would have provided more accurate, valid and reliable estimates from which to disentangle the relationship between occupational exposure to solar UVR and melanoma and NMSC, but these were not available in any of the included studies. However, objective assessments are only feasible in prospective cohort and intervention studies; subjective measurements (e.g. self-reported years of outdoor work) are the most appropriate assessment method in case–control study designs assessing retrospective lifetime occupational exposure history. Nevertheless, the risk of bias assessment recognized this limitation and was considered in the final evaluations of the quality and strength of the evidence.

Third, no published studies were found on the association between occupational exposure to solar UVR and melanoma and NMSC prevalence. Very few studies were identified for the two outcomes of mortality from melanoma (two studies) and NMSC (one study), imposing limitations on the comprehensiveness of the available evidence. However, evidence was available for the other included health outcomes of melanoma and NMSC incidence. The judgement of "sufficient evidence for harmfulness" for NMSC incidence enables WHO and the ILO, in principle, to produce estimates of the burden of NMSC attributable to occupational exposure to solar UVR; however, the current body of evidence for melanoma incidence associated with occupational exposure to solar UVR was assessed to be of limited strength, leading to a final judgement of "limited evidence of harmfulness". According to pre-specified standard estimation criteria *(30)*, WHO and the ILO are not in a position to produce an estimate of the melanoma burden attributable to occupational exposure to solar UVR from the evidence presented in this systematic review alone.

Fourth, it is possible that the meta-analysis underestimated the true effect of occupational exposure to solar UVR on melanoma and NMSC. Previous work in Australia *(118)* has reported that men and women with olive skin colour (Fitzpatrick skin type IV) and with a low susceptibility to sunburn were significantly more likely to report lifetime outdoor work than those with fair or medium skin colour (Fitzpatrick skin types II and III). This suggests that outdoor workers, at least in low-latitude regions such as Australia, tend to be a self-selected group with intrinsically fewer of the established phenotypic risk factors for skin cancer than those in indoor occupations *(118)*. It is not clear to what extent self-selection of lower-risk people into outdoor work may occur in other countries or regions, such as northern Europe and North America; however, this selection bias cannot be ruled out in those working outdoors at relatively low latitudes and, if present, may weaken the observed association between occupational exposure to solar UVR and melanoma and NMSC (at least from a hazard identification perspective). Effect estimates may have been further underestimated as a result of health outcome definitions excluding particular cancer subtypes from enrolment or analysis. The sensitivity analyses revealed that studies excluding lentigo maligna melanoma consistently reported inverse associations and studies not applying such definitionally problematic exclusions consistently reported positive associations between occupational exposure to solar UVR and melanoma. This melanoma histological subgroup has previously been associated with chronic sun exposure and increases in prevalence in older individuals with invasive melanoma *(150)*.

Fifth, several studies were included that used the lowest level of occupational exposure to solar UVR as a comparator in their calculation of disease risk (for example, < 3.5 hours per week of outdoor work). The inclusion of such a reference group, as opposed to non-exposed workers, may have introduced a bias towards the null, diluting genuine associations. However, several of the studies that define their comparator in this way do report elevated effect estimates when comparing the group with the highest exposure level with the comparator.

Sixth, very few studies reported effect estimates for specific occupations or industrial sectors, using non-occupationally exposed groups as a comparator. This precluded the possibility of generating pooled risk estimates by occupation or industrial sector categories in subgroup analyses.

Seventh, the pooled effect estimates generated in the melanoma and NMSC incidence meta–analyses were characterized by high statistical heterogeneity. Although sensitivity analyses were performed to identify sources of heterogeneity and considered possibly more homogeneous subgroups with greater consistency in effect estimates, the level of statistical heterogeneity observed in subgroups was not meaningfully reduced in most cases. The exceptions to this were for the subgroups of SCC for NMSC (I^2 = 47%), the Region of the Americas for NMSC

(I^2 = 0%) and females for NMSC (I^2 = 0%), but noting that the latter pooled two studies only (Table 20). For NMSC, subgroup analyses may therefore have explained some of the observed overall heterogeneity.

Eighth, the systematic review was not designed to comprehensively establish a causal relationship or dose–response relationship between occupational exposure to solar UVR and melanoma and/or NMSC. International health risk assessments have already been conducted that conclude that exposure to solar UVR has a role in the development of melanoma and NMSC, and solar UVR has been classified as a Group 1 carcinogen *(2, 3)*. Instead, there was evaluation of criteria such as the temporal association between exposure and outcome, strength of association, control of relevant confounding factors, consistency of findings and biological plausibility along the Bradford–Hill considerations *(153)*. Dose–response data were extracted from those studies defining exposure based on cumulative lifetime hours or years of outdoor work (Tables 22 and 23) and used to inform the assessment of the quality of the evidence.

Ninth, and finally, the high degree of statistical heterogeneity detected raises the question of why an increased risk is not more clearly apparent in many studies. There are several possible reasons for this, including the fact that "outdoor work" is possibly not a universally good proxy for "occupational exposure to solar UVR". "Outdoor worker" is a heterogeneous category, with the number of hours, time of day, clothing worn (e.g. hat, long sleeves) and body parts exposed while in the sun likely to vary considerably, both between and within occupations (as well as geographical location and other factors). These different scenarios can modify the extent of occupational exposure to solar UVR during outdoor work without necessarily being captured by the exposure assessment approaches used or analyses conducted within studies. Self-selection into the job may also play a role in clinical heterogeneity, as individuals who easily sunburn may not choose to work in an outdoor job or, if they do, they may adopt sun protection measures according to skin type and tanning experience. Most outdoor jobs require that suitably protective clothing be worn, meaning that the main occupational exposure to solar UVR is likely restricted to face, head, neck and arms (and perhaps legs). Exposure will be less than that experienced during sun–seeking behaviour. Additionally, there may be differences by sex in exposure at work (e.g. less hair protection for males, and some male workers not wearing tops). Further, baseline risk from leisure-time solar UVR exposure is another consideration that is not easily controlled for; such exposure may be more intense, more intermittent, more often lead to sunburn or correlated in different ways with occupational UVR (e.g. positively for outdoor workers, negatively if working hours spent indoors are compensated for by outdoor leisure time). This may be more relevant for melanoma, for which there is some evidence that exposure during childhood and adolescence may influence the risk of such disease later in life *(154, 155)*, further differentiating baseline risk. All these potential sources of heterogeneity make a lack of association in some studies plausible.

4.4 Use of evidence for burden of disease estimation

This systematic review and meta-analysis was conducted by WHO and the ILO, supported by a large number of individual experts, for the development of the WHO/ILO Joint Estimates of the Work-related Burden of Disease and Injury *(156)*. More specifically, it provides the crucial evidence base from which the organizations can consider producing estimates of the burden of disease from melanoma and/or NMSC attributable to occupational exposure to solar UVR. The systematic review found large bodies of evidence, mainly from incident case–control studies (as well as a very few case–case and cohort studies), for comparison of the exposure category "Any (or high) occupational exposure to solar UVR" (often via proxy) with "No (or low) occupational exposure to solar UVR" (often via proxy) for the outcomes of melanoma and NMSC incidence.

These bodies of evidence were judged to be of low and moderate quality, and to provide "limited evidence of harmfulness" and "sufficient evidence for harmfulness", for the health outcomes of melanoma and NMSC incidence, respectively.

As per the pre-specified standard estimation criteria for the WHO/ILO Joint Estimates *(30)*, producing estimates of the burden of melanoma attributable to occupational exposure to solar UVR appears not evidence-based and is therefore not warranted at this point. Based on application of the criteria *(30)*, production of estimates of the burden of NMSC attributable to occupational exposure to solar UVR appears both evidence–based and warranted (with limitations acknowledged for the body of evidence), and the parameters reviewed (including the pooled RRs from the main meta–analysis for this outcome) appear suitable as input data for WHO/ILO modelling of work-related burden of disease and injury. Future estimates of NMSC fractions attributable to occupational exposure to solar UVR (if any) should acknowledge the limitations and the strengths of the input data (as for all estimates produced according to GATHER guidelines *(4)*).

CHAPTER 5
Conclusions

The body of evidence was judged as "inadequate" to assess the association between occupational exposure to solar UVR and the prevalence of, and mortality from, melanoma and NMSC. The strength of the evidence for the associations between occupational exposure to solar UVR and melanoma incidence and NMSC incidence was rated "limited evidence for harmfulness" and "sufficient evidence for harmfulness", respectively. Further, the IARC classification of solar UVR as a Group 1 carcinogen *(2, 3)* that causes melanoma and NMSC is a compelling attribute for the strength of evidence on occupational exposure to solar UVR and skin cancer, and the pooled effect estimates produced in this systematic review for the health outcome of NMSC incidence can be used as input data for the WHO/ILO Joint Estimates.

Several recommendations are made to improve the quality of evidence in both future research studies and the compilation of future systematic reviews and meta-analyses. (i) Ideally, the definition of a health outcome including cancer in a systematic review should specify eligible histology subgroups, or otherwise defined subgroups, and rules should be agreed upon in which to deal with studies that a priori exclude any of the eligible subgroups. In addition, and if applicable, the exclusion of subtypes that may carry no relevance to the exposure being investigated should be specified. (ii) To allow studies to be compared by health outcome, conventions for standardizing the reporting of health outcomes including cancer could include specification of the ICD system in defining and reporting the outcome. The majority of the studies in the systematic review did not specify whether the ICD system was used or, if it was, which version or which disease codes were applicable to the investigated outcome. (iii) Heat tables displaying the results of risk of bias assessments could present studies by design, and distinguish between studies included and not included in meta-analyses. Such reformatted tables would assist in the identification of possible patterns in risk of bias assessments. (iv) To ensure consistency in the weight attributed to the same limitation between studies relevant to any given risk of bias domain, the risk of bias assessment for each study could be conducted by the same two or more researchers who assessed other aspects of the body of studies, following available guidelines, and differences of rating discussed and agreed by consensus. (v) When cumulative exposure measures are available, conduct of a dose–response meta-analysis could improve future systematic reviews, and hence the burden of disease estimate, by identifying biological, clinical or health-relevant levels of exposure and defining the exposed population. (vi) Finally, this systematic review has revealed that there exist opportunities for studies to improve the quality of their assessments of occupational exposure to solar UVR. Future efforts could perhaps identify cohorts of assumed higher risk and, using within-cohort comparisons, reduce differences between the higher-risk and comparison populations; the development of an agreed solar UVR job–exposure matrix by occupation (and/or other proxies) is recommended.

CHAPTER 6
Differences between protocol and systematic review

Because of the nature and design of the studies included within this systematic review, it was not always possible to adhere strictly to the methods described in the pre-published protocol *(5)*. Explanations regarding the deviations from the protocol, and the reasons for these deviations, are provided in the following.

In the protocol, the risk factor, risk factor level and minimum risk exposure level were defined primarily with reference to quantitative limit values (measured in SED), but it was noted that "If quantitative estimates of solar UVR are unavailable, then workers will be categorized into dichotomous variables 'no occupational exposure to solar UVR' (i.e. unexposed) and 'exposed to any occupational solar UVR' (i.e. exposed)" (Paulo et al. *(5)*, p. 806). Because quantitative exposure measures of solar UVR were not used in included studies, these definitions were updated and broadened (as planned in the protocol) to also include exposure measures via established proxies, such as occupation, occupational group, job title, job task or other variables, and combinations of these including job–exposure matrices, as the risk of bias due to exposure measurement by these proxies was considered to be acceptable. The theoretical minimum risk exposure level definition was also updated to be: "No (or low) occupational exposure to solar UVR (e.g. as defined by exposure to < 0.33 SED/day or through proxy of occupation, occupational group, job task or other variable)", a standard definition of a binary exposure variable in burden of disease estimations.

Compared with the logic model presented in the protocol, the logic model presented in Fig. 1 was updated by removing "tobacco use" from the list of confounders. Tumours of the skin are not included among the cancer sites unequivocally associated with tobacco use based on studies published up to 2009, the last time the body of evidence was assessed for carcinogenicity by IARC *(2)*. A small number of studies reported an inverse association between tobacco smoking and melanoma, no association between tobacco smoking and BCC, and a positive association between tobacco smoking and SCC. IARC therefore concluded that the evidence for a causal association between tobacco smoking and skin cancer was sparse and inconsistent. To be a confounder, tobacco use would also need to be associated with the main exposure under investigation, that is, occupational exposure to solar UVR, an association that is not obvious or well documented. There is limited evidence of an association between cigarette smoking, or any other form of tobacco use, and skin cancer *(2)*, so smoking was excluded from the list of confounders in the logic model. Nevertheless, several studies included in this systematic review took this variable into account in their calculation of adjusted effect estimates.

Regarding the description of the health outcome, in the systematic review the specification was added that the standard WHO burden of disease categories exclude in situ melanoma but include all histologic melanoma subtypes (i.e. superficial spreading, nodular and lentigo

maligna melanoma). Regarding the eligibility criteria for the outcome of malignant skin melanoma, it was not specified in the protocol if melanoma of the lips and ocular melanoma were included or excluded, but their exclusion was specified during the conduct of the systematic review. These amendments to the protocol improved the comprehensiveness of the health outcome definition and its alignment with standard terms and classifications of disease.

The use of cumulative exposure measurements was not anticipated, but it was noted in the protocol that "If sufficient data are available, then additional risk factor levels will be constructed as multiples of the theoretical minimum risk exposure level" (p. 806). In the systematic review, eligibility criteria and methods were added for dealing with cumulative exposure measurements. As stated in the protocol, these cumulative exposure measurements are in principle the most relevant for burden of disease estimation, and the search unexpectedly identified a considerable number of studies with such measurements. It was felt that excluding these would have limited the comprehensiveness and robustness of the evidence synthesis.

It was stated in the protocol (Paulo et al. *(5)*, table 1) that the plan was to only include studies that used participants exposed to the theoretical minimum risk exposure level as the comparator. However, several studies were included where the comparator included some (low) level of occupational exposure to solar UVR because the comparator (as originally defined based on theory) was not implemented in any included studies in practice. Using a group with some exposure as the reference may have introduced a bias towards the null.

The planned Ovid MEDLINE search strategy was presented in the protocol, but this strategy (Annex 1) was revised in the systematic review for improved efficiency. As described in the protocol, searches of CISDOC and TOXNET databases were also planned but, after testing, the scope of these databases was judged as not sufficiently covering the scope of the systematic review and they were therefore excluded. The reference list of the IARC *Monograph* volume 100D was also hand-searched *(2)*.

In terms of data extraction, where no financial disclosure/conflict of interest statement was provided, it was planned (as described in the protocol) to search declarations of interest in other records from the particular study published in the previous 36 months and in other publicly available repositories *(73, 74)*; however, when conducting the systematic review, searches were made for the names of all authors of all study records associated with a particular study published in the previous 36 months and in other publicly available repositories and declarations of interest *(73, 74)*.

In addition to the sensitivity analyses pre-specified in the protocol, the following were added: between studies judged to have a "high" or "probably high" and a "low" or "probably low" risk of exposure assessment misclassification bias; between studies judged to have a "high" or "probably high" and a "low" or "probably low" risk of confounding; between studies with documented or approximated ICD-10 diagnostic codes (e.g. as recorded in administrative health records) and those without (e.g. self-reports); between studies with the exposed group definition being based on cumulative exposure and studies where it was not; for melanoma, between studies including and studies excluding the lentigo maligna melanoma subtype; for melanoma, between studies with in situ cases comprising up to 5% of cases and studies with no in situ cases; and for NMSC, between studies defining the outcome as "any NMSC" and studies defining the outcome as SCC or BCC subtype only. These additional analyses led to an improved understanding of the included studies in terms of their potential risk of bias or confounding, and of their outcome definition, allowing better assessment of heterogeneity in the bodies of evidence.

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Annex 1. Search strategies

Table A1.1. Search strategies for all databases and results

Database and search date	Search string
WHO International Clinical Trials Register Platform 05/10/2020	Ultraviolet radiation
Ovid MEDLINE, 08/08/2018	1 Radiation, Nonionizing/ 2 Light/ 3 ((solar or sun or UV or ultraviolet) adj3 (radiation or radiations or ray or rays or light or lights or lighting or source$)).ab. or ((solar or sun or UV or ultraviolet) adj3 (radiation or radiations or ray or rays or light or lights or lighting or source$)).kw. or ((solar or sun or UV or ultraviolet) adj3 (radiation or radiations or ray or rays or light or lights or lighting or source$)).tw. or ((solar or sun or UV or ultraviolet) adj3 (radiation or radiations or ray or rays or light or lights or lighting or source$)).ti. 4 exp Sunlight/ 5 exp Ultraviolet Rays/ 6 1 or 2 or 3 or 4 or 5 7 exp Workplace/ 8 Work/ 9 Occupational Exposure/ 10 (worker$ or occupation$ or job).ab. or (worker$ or occupation$ or job).kw. or (worker$ or occupation$ or job).tw. or (worker$ or occupation$ or job).ti. 11 ((((((worker$ adj3 expos$).ab. or worker$.mp.) adj3 expos$.kw.) or worker$.mp.) adj3 expos$.tw.) or worker$.mp.) adj3 expos$.ti. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 12 ((((((occupation$ adj3 expos$).ab. or occupation$.mp.) adj3 expos$.kw.) or occupation$.mp.) adj3 expos$.tw.) or occupation$.mp.) adj3 expos$.ti. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 13 (outdoor adj3 (work or job or occupation)).ab. or (outdoor adj3 (work or job or occupation)).kw. or (outdoor adj3 (work or job or occupation)).tw. or (outdoor adj3 (work or job or occupation)).ti. 14 (outside adj3 (work or job or occupation)).ab. or (outside adj3 (work or job or occupation)).kw. or (outside adj3 (work or job or occupation)).tw. or (outside adj3 (work or job or occupation)).ti. 15 Employment/ 16 employee.ab. or employee.kw. or employee.tw. 17 ((((((outdoor adj3 employee).ab. or outdoor.mp.) adj3 employee.kw.) or outdoor.mp.) adj3 employee.tw.) or outdoor.mp.) adj3 employee.ti. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

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Database and search date	Search string
	18 (outdoor or agricultural or breeder* or farmer* or labo$rer* or salt worker or construction or maritime or waterman or watermen or lifeguard* or gardener* or bricklayer* or mason* or traffic controller* or roofer* or rigger* or carpenter* or concreter* or road worker or quarryman or quarrymen or fisher# or fishermen or fisherman or forester$ or firefighter$ or geologist# or environmentalist# or traffic police or hunter# or mountain guide$ or mountaineer# or sport instructor# or golf caddie or greenkeeper# or traffic warden# or tree surgeon# or physical education teacher# or farm vet# or street vendor# or ordnance survey engineer# or overhead line engineer# or military or tour guide# or window cleaner# or lumberjack# or jockey# or courier#).ab. or (outdoor or agricultural or breeder* or farmer* or labo$rer* or salt worker or construction or maritime or waterman or watermen or lifeguard* or gardener* or bricklayer* or mason* or traffic controller* or roofer* or rigger* or carpenter* or concreter* or road worker or quarryman or quarrymen or fisher# or fishermen or fisherman or forester$ or firefighter$ or geologist# or environmentalist# or traffic police or hunter# or mountain guide$ or mountaineer# or sport instructor# or golf caddie or greenkeeper# or traffic warden# or tree surgeon# or physical education teacher# or farm vet# or street vendor# or ordnance survey engineer# or overhead line engineer# or military or tour guide# or window cleaner# or lumberjack# or jockey# or courier#). kw. or (outdoor or agricultural or breeder* or farmer* or labo$rer* or salt worker or construction or maritime or waterman or watermen or lifeguard* or gardener* or bricklayer* or mason* or traffic controller* or roofer* or rigger* or carpenter* or concreter* or road worker or quarryman or quarrymen or fisher# or fishermen or fisherman or forester$ or firefighter$ or geologist# or environmentalist# or traffic police or hunter# or mountain guide$ or mountaineer# or sport instructor# or golf caddie or greenkeeper# or traffic warden# or tree surgeon# or physical education teacher# or farm vet# or street vendor# or ordnance survey engineer# or overhead line engineer# or military or tour guide# or window cleaner# or lumberjack# or jockey# or courier#).tw. or (outdoor or agricultural or breeder* or farmer* or labo$rer* or salt worker or construction or maritime or waterman or watermen or lifeguard* or gardener*or bricklayer* or mason* or traffic controller* or roofer* or rigger* or carpenter* or concreter* or road worker or quarryman or quarrymen or fisher# or fishermen or fisherman or forester$ or firefighter$ or geologist# or environmentalist# or traffic police or hunter# or mountain guide$ or mountaineer# or sport instructor# or golf caddie or greenkeeper# or traffic warden# or tree surgeon# or physical education teacher# or farm vet# or street vendor# or ordnance survey engineer# or overhead line engineer# or military or tour guide# or window cleaner# or lumberjack# or jockey# or courier#).ti. 19 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 20 6 and 19 21 Skin Neoplasms/ 22 MELANOMA/ 23 Carcinoma, Basal Cell/ 24 Carcinoma, Squamous Cell/ 25 Bowen's Disease/ 26 melanoma.ab. or melanoma.kw. or melanoma.tw. or melanoma.ti. 27 basal cell carcinoma.ab. or basal cell carcinoma.kw. or basal cell carcinoma.tw. or basal cell carcinoma.ti. 28 squamous cell carcinoma.ab. or squamous cell carcinoma.kw. or squamous cell carcinoma.tw. or squamous cell carcinoma.ti. 29 bowen's disease.ab. or bowen's disease.kw. or bowen's disease.tw. or bowen's disease.ti. 30 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 31 20 and 30 32 limit 31 to humans 33 limit 32 to yr="1960 -Current

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Database and search date	Search string
PubMed, 08/08/2018	((((((((“radiation, nonionizing”[MeSH Terms]) OR sunlight[MeSH Terms]) OR ultraviolet rays[MeSH Terms]) OR (((((“solar radiation”[Title/Abstract]) OR sunlight[Title/Abstract]) OR (“ultraviolet radiation”[Title/Abstract] OR “ultraviolet radiations”[Title/Abstract])) OR (“UV ray”[Title/Abstract] OR “UV rays”[Title/Abstract])) OR “ultraviolet source”[Title/Abstract])))) AND (((((workplace[MeSH Terms]) OR occupational exposure[MeSH Terms]) OR employment[MeSH Terms]) OR ((((((((((worker*[Title/Abstract]) OR occupation*[Title/Abstract]) OR job[Title/Abstract]) OR (“exposed worker”[Title/Abstract] OR “exposed workers”[Title/Abstract])) OR “occupational exposure”[Title/Abstract]) OR “outdoor worker”[Title/Abstract]) OR “outdoor job”[Title/Abstract]) OR “outdoor occupation”[Title/Abstract]) OR “outdoor employee”[Title/Abstract]) OR “outside work”[Title/Abstract]) OR “outside job”[Title/Abstract]) OR “outside occupation”[Title/Abstract])))) OR ((((((((((((((((((((((((((“salt-worker*”[Title/Abstract]) OR breeder*[Title/Abstract]) OR farmer*[Title/Abstract]) OR construction[Title/Abstract]) OR maritime[Title/Abstract]) OR waterman[Title/Abstract]) OR watermen[Title/Abstract]) OR lifeguard*[Title/Abstract]) OR bricklayer*[Title/Abstract]) OR mason*[Title/Abstract]) OR “traffic controller*”[Title/Abstract]) OR roofer*[Title/Abstract]) OR rigger*[Title/Abstract]) OR carpenter*[Title/Abstract]) OR concreter*[Title/Abstract]) OR “road worker*”[Title/Abstract]) OR quarryman[Title/Abstract]) AND quarrymen[Title/Abstract]) OR fisher*[Title/Abstract]) OR forester*[Title/Abstract]) OR firefighter*[Title/Abstract]) OR geologist*[Title/Abstract]) OR environmentalist*[Title/Abstract]) OR traffic-police* AND “[Title/Abstract]) OR hunter*[Title/Abstract]) OR “ AND mountain guide* AND “[Title/Abstract]) OR “ AND mountaineer* AND “[Title/Abstract]) OR “ AND gardener* AND “[Title/Abstract]) OR “ AND physical education teacher* AND “[Title/Abstract]) OR “ AND street vendor* AND “[Title/Abstract]) OR military[Title/Abstract]) OR “ AND tour guide* AND “[Title/Abstract]) OR “ AND window cleaner* AND Title/Abstract) OR lumberjack*[Title/Abstract]) OR jockey*[Title/Abstract]) OR courier*[Title/Abstract])))) AND (“1960/01/01”[PDat] : “3000/12/31”[PDat]) AND Humans[Mesh])) AND (((((((((Skin Neoplasms[MeSH Terms] AND (“1960/01/01”[PDat] : “3000/12/31”[PDat]) AND Humans[Mesh])) OR (malignant melanoma[MeSH Terms] AND (“1960/01/01”[PDat] : “3000/12/31”[PDat]) AND Humans[Mesh])) OR (carcinoma, squamous cell[MeSH Terms] AND (“1960/01/01”[PDat] : “3000/12/31”[PDat]) AND Humans[Mesh])) OR (carcinoma, basal cell[MeSH Terms] AND (“1960/01/01”[PDat] : “3000/12/31”[PDat]) AND Humans[Mesh])) OR (bowen's disease[MeSH Terms] AND (“1960/01/01”[PDat] : “3000/12/31”[PDat]) AND Humans[Mesh])) OR (((((((“skin cancer”[Title/Abstract]) OR “skin malignancies”[Title/Abstract]) OR melanoma[Title/Abstract]) OR “squamous cell carcinoma”[Title/Abstract]) OR “basal cell carcinoma”[Title/Abstract]) OR “bowen's disease”[Title/Abstract]) AND (“1960/01/01”[PDat] : “3000/12/31”[PDat]) AND Humans[Mesh])) AND (“1960/01/01”[PDat] : “3000/12/31”[PDat]) AND Humans[Mesh])
EMBASE, 08/08/2018	#24 #17 AND #23 #23 #18 OR #19 OR #20 OR #21 OR #22 #22 ‘melanoma skin cancer’/exp #21 ‘squamous cell skin carcinoma’/exp #20 ‘basal cell carcinoma’/exp #19 ‘non melanoma skin cancer’/exp #18 ‘skin cancer’/de #17 #5 AND #14 AND [humans]/lim AND [embase]/lim AND [1–1–1960]/sd NOT [1–8–2018]/sd #16 #5 AND #14 AND [humans]/lim #15 #5 AND #14 #14 #12 OR #13 #13 (‘salt-worker*’ OR breeder* OR farmer* OR construction OR maritime OR waterman OR watermen OR lifeguard* OR bricklayer* OR mason* OR ‘traffic controller*’ OR roofer* OR rigger* OR carpenter* OR concreter* OR ‘road worker*’ OR quarryman) AND quarrymen OR fisher* OR forester*OR firefighter* OR geologist* OR environmentalist* OR ‘traffic-police*’ OR hunter* OR ‘mountain guide*’ OR mountaineer* OR ‘gardener*’ OR ‘physical education teacher*’ OR ‘street vendor*’ OR military OR ‘tour guide*’ OR ‘window cleaner*’ OR lumberjack* OR jockey* OR courier* #12 #6 OR #7 OR #8 OR #9 OR #10 OR #11 #11 outside AND (work OR job OR occupation OR employment) #10 outdoor AND (worker OR job OR occupation OR employee) #9 worker* OR occupation* OR job #8 ‘occupational exposure’/exp #7 ‘work’/de #6 ‘workplace’/exp #5 #1 OR #2 OR #3 OR #4 #4 (solar OR sun OR uv OR ultraviolet) AND (radiation OR radiations OR ray OR rays OR light OR lights OR lighting OR source) #3 ‘ultraviolet radiation’/de #2 ‘sunlight’/de #1 ‘solar radiation’/exp

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Database and search date	Search string	
Web of Sciences, 08/08/2018	# 27	#26 AND #20 *Timespan=1960-2018* *Search language=Auto*
	# 26	#25 OR #24 OR #23 OR #22 OR #21 *Timespan=1960-2018* *Search language=Auto*
	# 25	TS=bowen's disease *Timespan=1960-2018* *Search language=Auto*
	# 24	TS=basal cell carcinoma *Timespan=1960-2018* *Search language=Auto*
	# 23	TS=squamous cell carcinoma *Timespan=1960-2018* *Search language=Auto*
	# 22	TS=melanoma *Timespan=1960-2018* *Search language=Auto*
	# 21	TS=skin cancer *Timespan=1960-2018* *Search language=Auto*
	# 20	#18 AND #17 Refined by: [excluding] Databases: (MEDLINE) *Timespan=1960-2018* *Search language=Auto*
	# 19	#18 AND #17 *Timespan=1960-2018* *Search language=Auto*
	# 18	#16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 *Timespan=1960-2018* *Search language=Auto*
	# 17	#3 OR #2 OR #1 *Timespan=1960-2018* *Search language=Auto*
	# 16	TS="outside occupation" *Timespan=1960-2018* *Search language=Auto*
	# 15	TS="outside job" *Timespan=1960-2018* *Search language=Auto*
	# 14	TS="outside work" *Timespan=1960-2018* *Search language=Auto*
	# 13	TS="outside employee" *Timespan=1960-2018* *Search language=Auto*
	# 12	TS="outdoor employee" *Timespan=1960-2018* *Search language=Auto*
	# 11	TS="outdoor occupation" *Timespan=1960-2018* *Search language=Auto*
	# 10	TS="outdoor job" *Timespan=1960-2018* *Search language=Auto*

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Database and search date	Search string	
	# 9	TS="outdoor work" *Timespan=1960-2018* *Search language=Auto*
	# 8	TS= "exposed worker" *Timespan=1960-2018* *Search language=Auto*
	# 7	TS=(worker* OR occupation OR job) *Timespan=1960-2018* *Search language=Auto*
	# 6	TS=employment *Timespan=1960-2018* *Search language=Auto*
	# 5	TS=occupational exposure *Timespan=1960-2018* *Search language=Auto*
	# 4	TS=workplace *Timespan=1960-2018* *Search language=Auto*
	# 3	TS=((solar OR sun OR UV OR ultraviolet) AND (radiation OR radiations OR ray OR rays OR light OR lights OR lighting OR source*)) *Timespan=1960-2018* *Search language=Auto*
	# 2	TS=ultraviolet rays *Timespan=1960-2018* *Search language=Auto*
	# 1	TS=sunlight *Timespan=1960-2018* *Search language=Auto*

Annex 2. Sample of excluded studies

Table A2.1 The 30 study records that most closely met eligibility criteria but were not included in our systematic review, and reason for exclusion

Author, year	Reason for exclusion from systematic review
Beral & Robinson, 1981 *(1)*	Ineligible comparator (compared groups of occupations with the general population)
Marks et al., 1988 *(2)*	Ineligible study design
Strickland et al., 1989 *(3)*	No data on the effect of exposure and outcome
Vitasa et al., 1990 *(4)*	Ineligible study design
Weiss et al., 1990 *(5)*	No data on the effect of exposure and outcome
Morales Suárez-Varela et al., 1992 *(6)*	Ineligible exposure definition
Autier et al., 1994 *(7)*	Ineligible exposure and comparator (compared selected outdoor occupations with all other occupations without prior exposure assignment)
Linet et al., 1995 *(8)*	No data on the effect of exposure and outcome
Maia et al., 1995 *(9)*	Ineligible exposure and comparator (compared selected outdoor occupations with all other occupations without prior exposure assignment)
Pukkala & Saarni 1996 *(10)*	Ineligible comparator (general population)
Perez-Gomez et al., 2004 *(11)*	Ineligible exposure and comparator (compared selected outdoor occupations with all other occupations without prior exposure assignment)
Marehbian et al., 2007 *(12)*	Ineligible exposure and comparator (compared selected outdoor occupations with all other occupations without prior exposure assignment)
Suárez et al., 2007 *(13)*	Ineligible exposure and comparator (compared selected outdoor occupations with all other occupations without prior exposure assignment)
Seidler et al., 2008 *(14)*	No data on the effect of exposure and outcome
Lichte et al., 2010 *(15)*	Ineligible outcome
Caccialanza et al., 2012 *(16)*	Ineligible study design
Dyer et al., 2012 *(17)*	Ineligible population
Lindelöf et al., 2012 *(18)*	Ineligible population
Surdu et al., 2013 *(19)*	Duplicate
Milon et al., 2014 *(20)*	Ineligible study design
Atis et al., 2015 *(21)*	Lack of a reported risk estimate with corresponding confidence interval, either crude or adjusted
Orkić et al., 2015 *(22)*	Ineligible study design
Apalla et al., 2016 *(23)*	No data on the effect of exposure and outcome
Salavastru et al., 2016 *(24)*	Ineligible study design
Szewczyk et al., 2016 *(25)*	Ineligible study design
Husein-Elahmed et al., 2017 *(26)*	Ineligible study design

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Author, year	Reason for exclusion from systematic review
Kachuri et al., 2017 *(27)*	Ineligible exposure and comparator (compared selected outdoor occupations with all other occupations without prior exposure assignment)
Lindelöf et al., 2017 *(28)*	Ineligible population
Rushton, 2017 *(29)*	Ineligible study design and outcome
Larese Filon et al., 2019 *(30)*	Ineligible exposure and comparator (compared selected outdoor occupations with all other occupations without prior exposure assignment)

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Annex 3. Histology

Table A3.1. Histology reported in studies on association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence and mortality included in the systematic review (all) and in the main meta-analysis (shaded)

Author, year	Study ID	All	Superficial spread	Nodular	Lentigo maligna mela-noma	Acral lentig-inous	Not classified or other	In situ or border-line	Comment
Case–control									
Klepp & Magnus, 1979 *(1)*	Klepp 1979	X							Histology information not provided
MacKie & Autchison,1982 (2)	MacKie 1982		X	X					Melanomas of superficial spreading or of nodular histology types were included exclusively without reporting of distribution
Elwood et al., 1985 *(3,4)*; Gallagher et al., 1987 *(5)*	Elwood 1985		X	X			X	X (4.9%)	56 (8%) lentigo malignant melanoma cases were excluded from the original group of patients
Graham et al., 1985 *(6)*	Graham 1985	X	X	X	X		X		Distribution of tumours by histology type not provided, while inclusion of different types is mentioned; reference is made to a non-negligible number of advanced cases in whom it was not possible to determine histology type
Bell et al., 1987 *(7)*	Bell 1987		X	X					Superficial spreading melanoma and nodular melanoma alone constituted 100%
Cristofolini et al., 1987 *(8)*	Cristofolini 1987		X	X	X	X	X (2–4%)		Superficial spreading melanoma and nodular melanoma alone constituted 85% in men and 79% in women; lentigo maligna melanoma accounted for 6% of cases in men and 13% in women
Østerlind et al., 1988 *(9)*	Østerlind 1988		X	X			X (8.2%)		Lentigo maligna melanoma excluded

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Author, year	Study ID	All	Superficial spread	Nodular	Lentigo maligna mela-noma	Acral lentig-inous	Not classified or other	In situ or border-line	Comment
Zanetti et al., 1988, 1999 *(10, 11)*; Rosso et al., 1998, 2008 *(12,13)*	Zanetti 1988		X	X	X		X (4.8%)	X (1.4%)	Superficial spreading melanoma and nodular melanoma alone constituted 58-63%; lentigo melanoma constituted 7% of male cases and 11% of female cases
Dubin et al., 1989, 1990 *(14,15)*	Dubin 1989		X	X	X	X	X		Over three-quarters (223/289) of melanomas were of superficial spreading; approximately 6% were lentigo maligna
Garbe et al., 1989 *(16)*	Garbe 1989		X	X	X	X	X (19.5%)		Superficial spreading melanoma and nodular melanoma alone constituted 54%; lentigo maligna melanoma constituted 22.5%
Beitner et al., 1990 *(17)*	Beitner 1990	X	X	X	X		X (17%)		1.5% of malignant melanoma cases were lentigo maligna melanoma
Weiss et al., 1991 *(18)*	Weiss 1991		X	X	X				Superficial spreading melanoma and nodular melanoma alone constituted 70%; 14% were lentigo maligna melanoma
Nelemans et al., 1993 *(19)*	Nelemans 1993		X	X					Excludes lentigo maligna melanoma or acrolentiginous melanoma
White et al., 1994 *(20)*	White 1994		X						Superficial spreading melanoma constituted 60%; MM not otherwise specified included; nodular excluded; lentigo maligna excluded, unclear if lentigo maligna melanoma also excluded (ICD-O 8743, 8720, 8740, 8771, 8772, 8774; excluded nodular 8721, 8742)
Holly et al., 1995 *(21)*	Holly 1995	X	X	X	X		X		Reference to a small proportion of cases being lentigo maligna melanoma is made without specifying percentage (79% were superficial spreading melanoma)
Chen et al., 1996 *(22)*	Chen 1996	X	X	X	X		X (12%)		15% of malignant melanoma cases were lentigo maligna melanoma
Ródenas et al., 1996 *(23)*	Ródenas 1996		X	X	X	X	X (1.9%)		Superficial spreading melanoma and nodular melanoma alone constituted 75% (ICD-9, code 172); lentigo maligna melanoma constituted 16%
Freedman et al., 1997, 2002 *(24, 25)*	Freedman 1997								Melanoma ICD-9 code 172
Espinosa Arranz et al., 1999 *(26)*	Espinosa Arranz 1999		X	X					Superficial spreading and nodular accounted for 88% of cases; no additional information
Walter et al., 1999 *(27)*	Walter 1999		X	X	X	X	X (8.6%)	X (% not reported)	Superficial spreading and in situ combined; 7% of cases were lentigo maligna

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Author, year	Study ID	All	Superficial spread	Nodular	Lentigo maligna mela-noma	Acral lentig-inous	Not classified or other	In situ or border-line	Comment
Loria & Matos, 2001 *(28)*	Loria 2001		X	X	X	X	X (9%)		Superficial spreading melanoma and nodular melanoma alone constituted 79%; lentigo maligna constituted 7%
Bataille et al., 2004 *(29)*	Bataille 2004	X	X	X	X			X	Around 7% of malignant melanoma cases were lentigo maligna melanoma
Fargnoli et al., 2004 *(30)*	Fargnoli 2004		X	X	X	X	X (2%)		5% of cases had lentigo maligna
Nijsten et al., 2005 *(31)*	Nijsten 2005		X	X					Excluded patients with in situ CMM, lentigo maligna melanoma, acral lentiginous melanoma, naevoid melanoma or desmoplastic and neurotropic variants of CMM
Zanetti et al., 2006 *(32)*	Zanetti 2006		X				X (11.7%)		Superficial spreading melanoma, 59% prevalent cases excluded
Nikolaou et al., 2008 *(33)*	Nikolaou 2008		X	X	X	X		X (2%)	Superficial spreading melanoma and nodular melanoma alone constituted 77%; 9% of male cases and 8% of female cases had lentigo maligna melanoma
Kenborg et al., 2010 *(34)*	Kenborg 2010								ICD-7 and ICD-10 classification used in Danish cancer registration, method of verification, topography and morphology recorded; melanoma subtypes not reported in study record
Kaskel et al., 2015 *(35)*	Kaskel 2015		X	X					Superficial spreading melanoma and nodular melanoma alone constituted 72%
Fortes et al., 2016 *(36)*	Fortes 2016		X	X	X	X	X (3.5%)	X in situ and LM (6.5%)	24% and 10% of cases and controls, respectively, had actinic keratosis/NMSC; 6.5% had in situ or lentigo maligna
Trakatelli et al., 2016 *(37)*	Trakatelli 2016							X (17.6%)	Only invasive or in situ reported
Cohort									
Håkansson et al.,, 2001 2001 *(38)*	Håkansson 2001								ICD-7 four-digit code skin melanoma (190), head, face, neck (190.1–190.4)
Case–case									
Goodman et al., 1995 *(39)*	Goodman 1995		X	X			X (49%)		Other types specified (Hutchinson melanotic freckle)
Whiteman et al., 2006 *(40)*	Whiteman 2006		X	X	X			X (elevated % by body part)	Results for invasive melanoma are available
Radespiel-Tröger et al., 2009 *(41)*	Radespiel-Tröger 2009				X				Results for melanoma including lentigo maligna melanoma

CMM, cutaneous malignant melanoma; ICD, International Classification of Diseases; LM, lentigo maligna; MM, malignant melanoma; NMSC, non-melanoma skin cancer; UVR, ultraviolet radiation.

Table A3.2. Histology reported in studies on association between occupational exposure to solar ultraviolet radiation and non-melanoma skin cancer incidence and mortality included in the systematic review (all) and in the main meta-analysis (shaded)

Author, year	Study ID	All	Superficial spread	Nodular	Other	Not classified	In situ	Solar keratosis	Comment
Case–control									
Aubry & MacGibbon, 1985 *(42)*	Aubry 1985								Pure squamous cell type (excluding mixed basal BCC and SCC) with invasion of the dermis (excluding carcinoma in situ and Bowen disease)
Ferreira et al., 1992 *(43)*	Ferreira 1992								NMSC (68% of tumours BCC, 32% SCC)
Gallagher et al., 1995 *(44, 45)*	Gallagher 1995								BCC, SCC, males
Kricker et al., 1995 *(46)*	Kricker 1995								BCC
Rosso et al., 1996 *(47)*, 1998 *(12)*	Rosso 1996								BCC, SCC
Suárez-Varela et al., 1996 *(48)*	Suárez-Varela 1996								NMSC
Freedman et al., 1997, 2002 *(24, 25)*	Freedman 1997								NMSC (ICD-9 codes 173, 154.3, 187.7)
Rosso et al., 1999 *(49)*	Rosso 1999 (54)								BCC, SCC
Vlajinac et al., 2000 *(50)*	Vlajinac 2000								BCC
Corona et al., 2001 *(51)*	Corona 2001								BCC
Milán et al., 2003 *(52)*	Milán 2003								BCC
Walther et al., 2004 *(53)*	Walther 2004	X	X	X	X	X			BCC, superficial 5%, nodular 33%, other 40.3%, not classified 22%
Zanetti et al., 2006 *(32)*	Zanetti 2006								BCC, SCC
Pelucchi et al., 2007 *(54)*	Pelucchi 2007		X	X	X				BCC, superficial spreading and nodular constituted 87% of cases
Janković et al., 2010 *(55)*	Janković 2010								BCC
Kenborg et al., 2010 *(34)*	Kenborg 2010								NMSC (BCC, SCC, other), ICD-7 and ICD-10
Dessinioti et al., 2011 *(56)*	Dessinioti 2011		X	X	X				BCC nodular subtype 62%
Iannacone et al., 2012 *(57)*	Iannacone 2012								BCC, SCC
Sanchez et al., 2012 *(58)*	Sanchez 2012		X	X	X				BCC nodular 74%; superficial 3%

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Author, year	Study ID	All	Superficial spread	Nodular	Other	Not classified	In situ	Solar keratosis	Comment
Surdu et al., 2013 *(59)*	Surdu 2013								BCC (515 of 618 NMSC) (ICD-10, code 44)
Kaskel et al., 2015 *(35)*	Kaskel 2015			X					BCC
Trakatelli et al., 2016 *(37)*	Trakatelli 2016								BCC, SCC, actinic keratosis without specifying grade (if grade III = in situ); results reported separately
Schmitt et al., 2018 *(60)*	Schmitt 2018 (BCC)								BCC
Schmitt et al., 2018 *(61)*	Schmitt 2018 (SCC)	X					X		224 in situ included in 632 SCC cases (35%)
Cohort									
Green et al., 1996 *(62)*	Green 1996								BCC, SCC
Håkansson et al., 2001 *(38)*	Håkansson 2001								ICD-7 four-digit code NMSC (191), NMSC head, face, neck (191.1–191.4)
Case–case									
Radespiel-Tröger et al., 2009 *(41)*	Radespiel-Tröger 2009								BCC, SCC

BCC, basal cell carcinoma; ICD, International Classification of Diseases; NMSC, non-melanoma skin cancer; SCC, squamous cell carcinoma.

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Annex 4. Description of missing data requested and received

Table A4.1. Missing data requested and received

Author, year	Description of missing data	Person(s) from whom missing data were requested	Date(s) of request(s)	Data received
Green et al., 1996 *(1)*	Clarification of the study design and original protocol paper, and availability of any additional data	Professor Adele Green	3 April 2019	3 April 2019

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Annex 5. Risk of bias by health outcome

Table A5.1. Risk of bias in studies reporting on association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence

Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
Klepp & Magnus, 1979 *(1)* Klepp 1979 Case–control	Selection bias	Probably high	Cases and controls were enrolled at a single centre (a hospital in Norway that admits patients from the entire country); controls were patients with cancers other than skin cancer; cases and controls identified and completing the study questionnaire represented an undisclosed fraction of the total number of cases with eligible cancers (response rate not reported); authors acknowledged cases and controls differed geographically and, since exposures studied could vary geographically, cases and controls selected for the analysis were restricted to the same, more reduced, geographic area, ensuring study participants came from the same catchment areas; did not match for age or sex, meaning that sex and age distributions differed between cases and controls
	Performance bias	Probably low	Staff identifying eligible study participants were not blinded; the same questionnaire was used to collect information from cases and controls (self-compiled); the outcome measures as well as the exposure measures were not likely to be influenced by a lack of blinding
	Exposure misclassification bias	Probably high	Outdoor work definition specified ≥ 3–4 hours of daily outdoor work while the comparator included subjects with less daily outdoor exposure, which could include from 0 to < 3 hours daily; comparator could therefore include subjects that had experienced some (albeit minor) exposure; this definition potentially introduced bias towards the null
	Detection bias	Probably low	Although this study did not mention pathology confirmation of cancer cases, and cases were identified at the hospital as opposed to through a cancer registry, Norway is a country with very good cancer ascertainment standards; cancers included in this study were malignant and treated and, prior to treatment, there was pathology confirmation (although this information is missing from the description of method); national cancer registry of Norway has been operational for many years before this study; cases probably had pathology confirmation and one of the co-authors worked at the registry; no exclusions on the grounds of histology were reported

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Confounding	High	Effect estimates not adjusted by confounders; cases and controls differed in sex and age distribution; although some results were presented after stratification by sex and age (which mitigates potential confounding from these variables), several other confounders were not taken into account
	Incomplete outcome data bias	Probably low	As well as not reporting histology type, the study did not present results with estimates of precision (e.g. no confidence intervals)
	Reporting bias	Probably low	Results document to a certain extent the aims of the study mentioned in the introduction
	Conflict of interest bias	Low	Funded by the Norwegian Cancer Society
	Other bias	Probably high	Due to the fact that this study enrolled participants at a tertiary-level hospital that receives patients for treatment referred from the entire nation, and despite an attempt to reduce the potential bias introduced by cases and controls coming from different geographical regions of the country, selection of a sub-group of eligible cases and controls from a more restricted part of the country might not have completely controlled for this potential source of bias; controls were also cancer cases, which could introduce additional sources of bias
MacKie & Aitchison, 1982 *(2)* MacKie 1982 Case–control	Selection bias	Probably high	Case and control selection was not described with enough detail; unknown if the incident primary cases included in the study ($n = 113$) identified in west Scotland between 1978 and 1980 represent the total or a fraction of all cases identified in the area in that period (and, if the latter, where these cases were identified and on which basis, apart from being diagnosed with a specific histology); controls matched to cases by sex and age were selected from patients attending accident and emergency departments and females admitted for minor gynaecological procedures, without specifying in which hospitals/centres and how they were selected from all potentially eligible controls; likely that cases and controls may not have come from the same catchment area
	Performance bias	Probably low	Blinding was not explicitly mentioned in the methods; information on exposures and confounders was collected through a detailed questionnaire delivered by a single interviewer to study participants
	Exposure misclassification bias	Probably high	Total no. hours of occupational sun exposure per week in winter and in summer were collected; occupational exposure to sun was used as a dichotomous variable (exposed versus unexposed), with a history of ≥ 16 (< 16) hours per week spent outdoors at work defined as "exposed" ("unexposed"); not clear if the information was collected throughout life or for a specific time interval
	Detection bias	High	Although all cases were histologically confirmed, the study was restricted to cases with one of two histology types a priori; cases of lentigo maligna melanoma were excluded, which could potentially introduce bias towards the null hypothesis as this subtype is known to be more commonly diagnosed in people with chronic sun exposure (i.e. occupational)
	Confounding	Probably high	Risk estimates are presented for male and female study participants separately; adjusted risk estimates do not control for age; although controls were matched to cases by sex and age, the sex-specific age distribution of cases and controls have some differences; conditional logistic regression was used in the analysis; occupational sun exposure risk estimates were adjusted by skin type, severe sunburns, social class and recreational sun exposure

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Incomplete outcome data bias	Low	Information is complete for study participants according to counts presented; since cases are identified based on their outcome, it is reasonable to assume that they did not have missing outcome data
	Reporting bias	Low	All variables and aims described in the abstract and methods are documented in results
	Conflict of interest bias	Probably low	Study was authored by researchers affiliated to an academic research centre; however, no funding or conflict of interest statements were included
	Other bias	Probably low	Study appears to be free of other sources of bias, but recall bias cannot be ruled out
Elwood et al., 1985 *(3, 4)*; Gallagher et al., 1987 *(5)* Elwood 1985 Case–control	Selection bias	Low	Descriptions of the source population, inclusion/exclusion criteria, recruitment and enrolment procedures, and participation rates were sufficiently detailed, and adequate data were supplied on the distribution of relevant study sample and population characteristics to support the assertion that risk of selection effects was minimal; 83% of eligible cases interviewed and the response rate in controls, randomly selected from Provincial insurance records, was 48–59%
	Performance bias	Probably low	Blinding not part of the recruitment of the case–control study, but no information on whether data analyst/biostatistician was blinded to the outcome
	Exposure misclassification bias	Probably low	In-person interview, self-reported; lifetime occupational history of each job held for ≥ 6 months; usual no. hours per week of outdoor work during the winter and summer seasons was obtained for each job
	Detection bias	High	Presence or absence of melanoma confirmed by histology; cases of lentigo maligna melanoma and acral lentiginous melanoma were excluded; exclusion of the former, a subtype believed to be associated with chronic exposure to solar UVR, could potentially introduce bias (attenuation of association)
	Confounding	Low	Variables adjusted for confounding (age and sex, ethnic origin and educational attainment as a measure of socioeconomic status, phenotype attributes)
	Incomplete outcome data bias	Probably low	Case–control study; no incomplete outcome; outcome predefined in introduction and the method
	Reporting bias	Probably low	No study protocol identified; all variables mentioned in the present study were reported
	Conflict of interest bias	Low	National funds plus Alberta Heritage Trust Funds
	Other bias	Probably low	Appears to be free of other problems that can introduce bias, but recall bias cannot be ruled out
Graham et al., 1985 *(6)* Graham 1985 Case–control	Selection bias	Probably high	Included controls that are cancer patients with diagnoses other than skin cancer; all cases and controls selected from a single cancer centre in New York state during the same recruitment period of several years and probably from the same catchment population; cases represent consecutive patients diagnosed during the study period who consented to participate, but no participation rate is provided; not much detail provided on selection of controls; oversample of breast cancer controls in women and of lung cancer controls in men was reported; no mentioning of matching; no detail on eligibility criteria provided (apart from pathology confirmation and consent to participate); all study participants interviewed by the same nurse interviewers

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Performance bias	Probably low	Interviewers were not blind to the case–control status of study participants, but it is unknown if they were aware of the study hypothesis; outcome measure and exposure measures not likely to be influenced by this lack of blinding
	Exposure misclassification bias	Probably low	Lifetime occupational history, including no. hours spent outdoors per week, in winter and in summer, was collected from which a lifetime cumulative occupational sun exposure in hours was calculated; risk estimates provided by four cumulative exposure categories contrasted to the unexposed reference group (< 1 hour); a test for trend was reported
	Detection bias	Low	All cases were confirmed by histopathology; from the description, it was deduced that cases were not excluded based on histology type
	Confounding	Probably high	Risk estimates for occupational sun exposure were adjusted for type of skin burn reaction to sun exposure exclusively in male study participants; no adjustment for age is mentioned, but the text clarifies that male cases and male controls did not differ in their age distribution (data not shown); no risk estimates are provided for females
	Incomplete outcome data bias	Probably low	For cancer cases diagnosed at an advanced stage it was not possible to ascertain histology type; proportion of cases with this condition was not given but, from the discussion, this was not a negligible number
	Reporting bias	Probably low	Histology type was not reported; risk estimates by occupational sun exposure not provided for women
	Conflict of interest bias	Low	The study was supported by a United States government cancer research funding agency; authors affiliated to academic research centres; no declaration of interest statement included
	Other bias	Probably high	Recall bias cannot be ruled out; study included cancer cases as controls, which may introduce a source of bias; for cancer cases diagnosed at an advanced stage it was not possible to ascertain histology type; proportion of cases with this condition was not given but, from the discussion, this was not a negligible number (hinting that the centre receives a cancer population that may not be representative of all invasive melanoma cases, and such cases may differ by socioeconomic status or etiologically)
Bell et al., 1987 *(7)* Bell 1987 Case–control	Selection bias	Probably high	Inclusion criteria specified; although most participants were noted to be from south-east England, it was not clear from the text if cases and controls were as equally distributed; no information provided on participation rate in cases or controls; controls were patients attending the same hospital as cases but with other skin conditions; period of diagnosis of cases and controls was very long (1961–1982) and matching revealed significant differences between cases and controls in age and year of diagnosis, which may indicate inconsistency in recruitment efforts
	Performance bias	Probably low	Blinding not employed in this study; however, professionals involved in data collection and clinical examination were adequately educated and trained on study aims
	Exposure misclassification bias	Probably high	Study protocol took measures to ascertain sun exposure in both cases and controls using structured questionnaire; sun exposure at work given by occupation type (indoor, outdoor, indoor/outdoor); however, recall bias cannot be completely ruled out
	Detection bias	Low	Cases diagnosed with nodular or superficial spreading melanoma (histologically confirmed using standard histological classification through the study period)

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Confounding	Probably high	Study accounted for sex, but not adequately for age or for socioeconomic status; odds ratio for occupational sun exposure was unadjusted and no confidence limits were provided
	Incomplete outcome data bias	Low	Outcome data were adequate; participants were followed long enough between interviews and missing data were adequately managed by the study secretary who contacted the participants
	Reporting bias	Low	Outcome (malignant melanoma) was not selectively reported in this study as this was the only outcome metric
	Conflict of interest bias	Low	Despite having no conflict of interest declaration, study was noted to have been funded by governmental sources (Emmandjay Trust and Health and Safety Executive funding to second author)
	Other bias	Probably low	Study population may not have been well representative of the UK population; study design, with a huge reliance on recall for exposure to solar UVR and other carcinogens from occupational sources, could have led to errors in exposure metrics as these are all surrogates to actual measures of exposure; however, study protocol applied to all participants (cases and controls alike); eligible skin conditions in controls included diagnoses associated with chronic sun exposure, which could potentially introduce bias
Cristofolini et al., 1987 *(8)* Cristofolini 1987 Case–control	Selection bias	Low	The description of the inclusion/exclusion criteria and recruitment procedures were very detailed and adequate (p. 150); no participation rate was provided for cases or controls
	Performance bias	Probably low	Insufficient information about blinding to permit a judgment of low risk of bias, but there was indirect evidence to suggest the study was adequately blinded
	Exposure misclassification bias	Probably high	Study participants were interviewed in the hospital, during which they completed a study questionnaire including occupational exposure to sunlight (if prevalently outdoor or indoor occupation); analysis of exposure assessment was very detailed and accurate (p. 151), but based on a single metric of exposure by proxy of occupation
	Detection bias	Low	Cancer cases with pathology confirmation; outcomes were assessed and defined consistently across all study participants, using valid and reliable measures (p. 151)
	Confounding	Low	Study appropriately assessed and accounted for (i.e. matched, stratified, excluded certain populations or statistically controlled for) all important confounders (Tier 1) using appropriate statistical techniques (table 2, p. 151)
	Incomplete outcome data bias	Probably low	No missing outcome data
	Reporting bias	Probably low	All pre-specified outcomes presented in the abstract were discussed and reported adequately in the article
	Conflict of interest bias	Probably low	Funding source was limited to government, non-profit organizations or academic grants funded by government, foundations and/or non-profit organizations; only one source mentioned; it is possible that there were other funding sources, but these were not specified (p. 153)
	Other bias	Probably low	Study appears to be free of other sources of bias, but differential recall can affect case–control studies
Østerlind et al., 1988 *(9)* Østerlind 1988 Case–control	Selection bias	Probably low	Participant selection process appeared adequate in this population-based case–control study, where a large proportion of eligible incident cases (92%) and eligible randomly selected controls (82%) agreed to participate and were interviewed

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Performance bias	Low	Part of study procedures were conducted while blinding study personnel to the case–control status of patients
	Exposure misclassification bias	Probably high	Study ascertained occupational sun exposure in both cases and controls using structured questionnaire; exposure defined as periods of outdoor summer employment lasting ≥ 6 months, which defined ever working outside; however, recall bias cannot be completely ruled out
	Detection bias	High	Melanoma cases histologically confirmed; exclusion of lentigo maligna melanoma, a subtype believed to be associated with chronic exposure to solar UVR, could potentially introduce bias (attenuation of association)
	Confounding	Low	Appropriate control of confounding in analysis by taking into account important constitutional and environmental independent risk factors using multivariate analysis
	Incomplete outcome data bias	Low	Distribution of histologically confirmed cases by melanoma subtypes was provided; 8% of cases were unclassifiable melanomas
	Reporting bias	Probably low	Results by occupational exposure were not presented in detail or even in tabular form; effects of duration of outdoor employment assessed but data not presented (just the results)
	Conflict of interest bias	Low	Source of funding of first author declared, including national agencies on medical and on cancer research; authors affiliated to government agencies or similar
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias
Zanetti et al., 1988, 1999 *(10, 11)*; Rosso et al. 1998, 2008 *(12, 13)* Zanetti 1988 Case–control	Selection bias	Probably low	No information about sample size selection; insufficient information about participant selection to permit a judgment of low risk of bias, but indirect evidence suggesting that inclusion/exclusion criteria, recruitment and enrolment procedures were consistent across groups
	Performance bias	Probably low	Blinding of study personnel not mentioned; nevertheless, personnel delivering the study questionnaire were trained for this aim
	Exposure misclassification bias	Probably high	Exposure not defined in methods other than mentioning occupational history captured by questionnaire; in results, exposure presented by years of outdoor work (never, 1–5, 6–16, 17–32, ≥ 32 years); "Total number of years of outdoor work [...]" (p. 313 (*10*))
	Detection bias	Low	Cancer cases with histology confirmation
	Confounding	Probably low	Study appropriately accounted for most but not all of the important confounders (Tier 1) as well as the other potentially important confounders relevant (Tier 2), using appropriate statistical techniques
	Incomplete outcome data bias	Probably low	No reporting of missing information on cancer outcome
	Reporting bias	Low	All of the study's pre-specified (primary and secondary) outcomes outlined in the pre-published protocol or the published manuscript's methods, abstract and/or introduction that are of interest in this review were reported in the pre-specified way
	Conflict of interest bias	Low	Funding by philanthropic organization (non-profit organization)
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
Dubin et al., 1989, 1990 *(14, 15)* Dubin 1989 Case–control	Selection bias	Low	Description of the source population, inclusion/exclusion criteria, recruitment and enrolment procedures, participation and follow-up rates were sufficiently detailed, and adequate data were supplied on the distribution of relevant study sample and population characteristics to support the assertion that risk of selection effects was minimal; cases and controls were interviewed by different personnel
	Performance bias	Probably low	Blinding was not part of the recruitment of the case–control study; no information provided on whether data analyst/ biostatistician was blinded to the outcome
	Exposure misclassification bias	Probably high	Self-reported; metrics: mostly outdoor, outdoor/indoor versus mostly indoor, recreational versus occupational; temporal: long-term exposures
	Detection bias	Low	Outcome histopathologically confirmed
	Confounding	Low	Potential confounders included age, sex, ability to tan, history of freckling, number of moles and hair colour, eye colour, parents' ethnicity, history of using photosensitizing drugs and history of previous skin diseases; simultaneous control of several confounding factors, in addition to age and sex, was accomplished by multiple logistic regression
	Incomplete outcome data bias	Probably low	Case–control study; outcome pre-defined in the introduction and method section
	Reporting bias	Probably low	No study protocol identified; all variables mentioned in the present study were reported
	Conflict of interest bias	Low	Governmental funding, but no conflict of interest statement included in the study record
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias, although differential recall can be present in case–control studies
Garbe et al., 1989 *(16)* Garbe 1989 Case–control	Selection bias	Probably low	Insufficient details on selection of participants or population from which they originate; nevertheless, cases and control were identified at the same dermatological clinic and examined by the same physicians; groups matched for sex and age; response rate of participation in cases and controls 90%; controls may have had dermatological disease other than melanoma, which may have introduced bias
	Performance bias	Probably low	Researchers not blinded in selecting cases from the database, although study does not appear to be biased
	Exposure misclassification bias	Probably high	Exposure assessed by interview, possibly introducing recall bias; occupational sun exposure defined as sun exposure to the upper part of the body and/or the extremities on the occasion of sunshine during work: none, sometimes, nearly every time
	Detection bias	Low	Histology shown in table for $n = 200$
	Confounding	Probably low	Matched for age and sex; adjusted for other confounders (no. melanocytic naevi, skin type, no. actinic lentigines)
	Incomplete outcome data bias	Probably low	No clear information provided, but there do not appear to be any issues
	Reporting bias	Probably low	No study protocol identified; all variables mentioned in the study were reported
	Conflict of interest bias	Probably low	No funding source or declaration of interest included, but the study authors are affiliated to a university department of dermatology and an institute for medical statistics
	Other bias	Probably low	Dermatology controls may not represent same referral base as the melanoma cases; recall bias cannot be ruled out

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
Beitner et al., 1990 *(17)* Beitner 1990 Case–control	Selection bias	Probably low	All cases and controls were residents of the same city in Stockholm County; sample of study cases represented 64% of all cases diagnosed in the population of Stockholm County in the corresponding period, likely describing a representative sample of all cases from the county over a calendar period; controls selected from the city county population registry to match the sex and age distributions of cases; no evidence to suggest that inclusion/exclusion criteria, recruitment and enrolment procedures may have differed between cases and controls
	Performance bias	Probably low	No blinding reported; the same questionnaire was used to collect information from cases and controls; the outcome measures as well as the exposure measures were not likely to be influenced by lack of blinding
	Exposure misclassification bias	Probably high	Information on outdoor work and other sources of sunlight exposure was collected; however, it was not specified if occupational exposure data were collected for lifetime or for a reduced time interval; indoor workers were used as the reference group, probably offering a contrast capable of distinguishing true differences of exposure
	Detection bias	Low	Final examination and classification of pathology slides from all cases was conducted by the same expert pathologist; all histology types were considered for inclusion
	Confounding	Probably low	Occupational sun exposure risk estimates were adjusted for age, sex and hair colour; although other independent risk factors were not taken into account (e.g. skin type), because all cases and controls were residents of Stockholm County, study participants may not have been dissimilar in terms of socioeconomic status, which could alter risk factor exposure profile, or ethnic composition, which could impact susceptibility to the damaging effects of solar UVR
	Incomplete outcome data bias	Probably low	All cases were confirmed by histopathology; however, 17% of cases were classified as "unknown histology", but this lack of information was unlikely to introduce a risk of bias
	Reporting bias	Probably low	Questionnaire completed by 99.6% of the cases and 96.2% of the controls
	Conflict of interest bias	Probably low	No statement included on the source of funding or a declaration of interest; study conducted by researchers associated with the Karolinska Research Institute and from the Karolinska Hospital
	Other bias	Probably low	Study appears to be free of other sources of bias, but recall bias cannot be ruled out
Weiss et al., 1991 *(18)* Weiss 1991 Case–control	Selection bias	Probably high	Insufficient information on participant selection, in particular on controls; inclusion/exclusion criteria are described; participation rate not reported
	Performance bias	Probably low	No blinding, but we judged that the outcome measures as well as the exposure measures were not likely to be influenced by a lack of blinding
	Exposure misclassification bias	High	"Occupational sun exposure was categorized in full-time most of the life, part-time or some years and insignificant." (p. 110) No clear mention of the exposure assessment methods or definitions; risk estimates provided for occupational sun exposure (assumed comparator is never)
	Detection bias	Low	Diagnosis was confirmed histologically
	Confounding	High	Study did not account for or evaluate multiple important confounders (Tier 1), but did account for or evaluate multiple other potentially important confounders relevant (Tier 2)

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Incomplete outcome data bias	Probably low	No missing outcome data
	Reporting bias	Probably low	All of the study's pre-specified (primary and secondary) outcomes outlined in the pre-published protocol or the published manuscript's methods, abstract and/or introduction section that are of interest in this review were reported in the pre-specified way
	Conflict of interest bias	Probably low	No declaration of interest statement was included and funding was not specified; authors affiliated to a medical school and an academic centre
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias
Nelemans et al., 1993 *(19)* Nelemans 1993 Case–control	Selection bias	Probably low	Melanoma cases and control patients were selected from a regional cancer registry; however, there was not enough information on whether all of those in the registry, or a subset of them who were diagnosed during 1988–1990, were invited to participate in the study; authors stated that selection bias cannot be definitely ruled out; participation rate in cases and controls was reported
	Performance bias	Probably low	No specification of blinding described
	Exposure misclassification bias	Probably high	Information on the exposure was collected by professional interviewers using a questionnaire designed by the Western Canada Melanoma Study; however, sun radiation occupational exposure was restricted to early adult life (age 15–25 years), indoor or outdoor work (yes/no) held for ≥ 6 months; average no. hours per week spent outdoors for each job was recorded, but risk estimate provided for ever outdoor work versus never
	Detection bias	High	Outcome assessment was based on histopathology; exclusion of lentigo maligna melanoma, a subtype believed to be associated with chronic exposure to solar UVR, could potentially introduce bias (attenuation of association)
	Confounding	Probably low	The potential confounding effects of age, sex, education level, tendency to burn, hair colour and freckling were addressed using multivariable analyses
	Incomplete outcome data bias	Probably low	Cases and controls selected from databases; no evidence of missing outcome data for cases and controls
	Reporting bias	Probably low	No published protocol for this study; however, the description of the outcome of interest was outlined in the published manuscript's methods
	Conflict of interest bias	Probably low	No obvious conflict of interest; no declaration or source of funding specified; authors affiliated to academic centres or hospitals
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias
White et al., 1994 *(20)* White 1994 Case–control	Selection bias	Probably low	Insufficient information about participant selection to permit a judgment of low risk of bias, but there was indirect evidence to suggest that inclusion/exclusion criteria, recruitment and enrolment procedures, and participation and follow-up rates were consistent across groups
	Performance bias	Probably low	No blinding, but we judged that the outcome measures as well as the exposure measures were not likely to be influenced by lack of blinding

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Exposure misclassification bias	Probably high	"A structured questionnaire was used to obtain information on known and suspected risk factors for malignant melanoma, including (…) sunlight exposure, and reproductive factors." (p. 860) Indirect evidence to suggest that methods were not robust; odds ratios presented the percentage of time in lifetime outdoor occupations according to the United States Labor Department (0, < 50, ≥ 50)
	Detection bias	High	Information from cancer registry; eligibility limited to specific histologic subtypes (histology confirmation); lentigo maligna melanoma excluded (code 8742; malignant Hutchinson's melanotic freckle)
	Confounding	Probably low	"Adjustment for age, sex, and education was accomplished by including in the model four age categories, sex, and three levels of education." (p. 860) Study appropriately accounted for most but not all of the important confounders (Tier 1) and some of the other relevant and potentially important confounders (Tier 2), using appropriate statistical techniques
	Incomplete outcome data bias	Probably low	No missing outcome data; not all cancer cases from the cancer registry could be included as they were diagnosed at non-participating hospitals
	Reporting bias	Low	All of the study's pre-specified (primary and secondary) outcomes outlined in the pre-published protocol or the published manuscript's methods, abstract and/or introduction section that are of interest in this review were reported in the pre-specified way
	Conflict of interest bias	Low	Funded by United States Public Health Service contract N01-CN-05230 from the National Cancer Institute; no conflict of interest declared
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias; recall bias cannot be ruled out
Goodman et al., 1995 (21) Goodman 1995 Case–case	Selection bias	Probably high	All-cancer comparison group may not necessarily have come from the same source populations as melanoma cases; only males considered
	Performance bias	Low	Researchers were blinded to case–comparison group at the time to classify occupation into sun exposure category
	Exposure misclassification bias	Probably high	Only current job title as stated in cancer registry used to classify work sun exposure; occupational exposure to sunlight expressed as outdoor versus indoor
	Detection bias	Probably low	All cancer cases had pathology confirmation; histologic subtype not specified in a significant proportion of cancer cases, particularly those diagnosed earlier
	Confounding	Probably high	No accurate way of adjusting for phototype, recreational sun exposure, etc.; odds ratio adjusted for age, education level and birth place; only males included
	Incomplete outcome data bias	Probably high	No histology data provided to confirm quality
	Reporting bias	Probably low	The study included all the variables discussed in methods section
	Conflict of interest bias	Low	Study funded by the California Health Department; authors affiliated to cancer prevention, health services and public health government or academic entities

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Other bias	Probably high	Non-Spanish names inaccurate and error more likely to affect melanoma outcome (i.e. Spanish with non-Spanish name may be more likely to have outdoor occupation but low melanoma risk) than other cancer outcome
Holly et al., 1995 *(22)* Holly 1995 Case–control	Selection bias	Probably low	Controls were randomly selected from the population residing in the same San Francisco counties as cases at the time of diagnosis; similar age and race eligibility criteria were applied in female cases and controls; response rate in cases (79%) and controls (77%) were relatively high; reasons for missing cases were: 45 cases (8%) refused to participate, 14 cases (2%) had physicians who felt that there were medical contraindications to subject contact, 2 cases (0.3%) were too ill to complete the interview, 20 cases (3%) were deceased, and 43 (8%) could not be located; we judged these reasons to suggest no risk of selection bias; how participants were selected was described in detail
	Performance bias	Probably low	Blinding is not explicitly mentioned in the methods; trained interviewers, unaware of the study hypotheses, were probably not blind to the case–control status of study participants; for the majority of participants, the interview occurred at home
	Exposure misclassification bias	Probably high	Information on occupational history within the 10 years prior to melanoma diagnosis was collected, but the work-related sun exposure variable is not well described; risk estimates provided by time spent outdoors on weekdays with arms and legs exposed to the sun (in past 10 years) are reported without explicitly specifying whether related to occupation; exposure categorized by amount of time spent outdoors on weekdays (none; < 1/4 of time; ≥ 1/4 to < 1/2 of time; ≥ 1/2 of time); exposure history restricted to the last 10 years prior to cancer diagnosis limits the study of associations between exposure and cancer to chronic sun exposure (i.e. occupational)
	Detection bias	Low	Patients with histologically confirmed melanoma were ascertained through the San Francisco Bay Area cancer registry; no exclusion of specific histology subtypes
	Confounding	High	Risk estimates reported for occupational sun exposure were unadjusted for potential confounders
	Incomplete outcome data bias	Probably low	Histology type was not available in all cancer cases; pathology slides were retrieved for 77% of included cases from primary care physicians and were reviewed by two dermato-pathologists to obtain a uniform classification by histologic type
	Reporting bias	Probably low	Study restricted to women
	Conflict of interest bias	Low	Study supported by a United States government cancer research funding agency; authors affiliated to academic research centres; no statement included on declaration of interest
	Other bias	Probably high	Study appears to be free of other sources of bias, but recall bias cannot be ruled out; study participants restricted to an age range of 25–59 years, excluding melanoma cases occurring in older patients that tend to occur with chronic sun exposure; an etiologically relevant age period was excluded when considering occupational sun exposure, possibly introducing bias towards the null

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
Chen et al., 1996 *(23)* Chen 1996 Case–control	Selection bias	Probably low	All cases and controls were residents of the state of Connecticut and identified during the same recruitment period; cancer cases were identified from an established cancer ascertainment system employed by the academic centre, and the original study sample represented 82% of eligible cancer cases detected (physician consent to approach case not granted (majority reason), previous melanoma, not Caucasian, not reachable for interview); this preliminary sample was further reduced after pathology examination given that a number of cases were in situ melanoma or had a non-malignant lesion; approximately 63% of the original sample of cases detected by the rapid system in the state constitute the analysis set; population-based controls were selected by random-digit dialling using state telephone number roster as sampling frame; control selection matched the sex and age distributions of cases and 70% of the sample was interviewed; application of eligibility criteria reduced the final set of controls to 61% of the original random sample (non-Caucasian major reason)
	Performance bias	Probably low	No blinding reported; nurse interviewers used a structured questionnaire and conducted a skin examination of all participants; outcome measures as well as exposure measures are not likely to be influenced by a lack of blinding
	Exposure misclassification bias	Probably high	Information on ever holding an outdoor job, and for how long, was collected through an occupational history; categories referred to included lifeguard, construction worker, farmer or other outdoor job; risk estimates are provided by time in outdoor job categorized in < 5 years or ≥ 5 years compared with never an outdoor job (zero time); however, these exposure duration levels may not represent sufficiently distinct exposed groups with differing biological effects to inform dose–response trends, although probably sufficient to assess risk when compared with the unexposed reference group
	Detection bias	Low	A single dermato-pathologist confirmed case eligibility as invasive melanoma in all cases; all histology types were considered for inclusion
	Confounding	Probably low	Adjustment for multiple confounders (sex, age, skin colour, no. naevi on arms, skin type and total recreational sun exposure index); analysis sample reduced by approximately 4% and 5% in cases and controls, respectively, due to missing information in confounders
	Incomplete outcome data bias	Low	All cases had a pathology report; in cases with metastasis, if original pathology report did not specify histology this information was not available for analysis (in nine cases histopathology was not specified)
	Reporting bias	Probably low	Unfortunately, a risk estimate for all invasive melanoma was not provided; melanoma cases reported by anatomical site
	Conflict of interest bias	Low	Study was supported by a United States government cancer research funding agency and by an academic centre; authors affiliated to academic research centres and associated hospitals; no statement on declaration of interest
	Other bias	Probably low	Study appears to be free of other sources of bias, but recall bias cannot be ruled out

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
Ródenas et al., 1996 *(24)* Ródenas 1996 Case–control	Selection bias	Probably low	Description of cases and controls sufficiently detailed, compiled from randomly selected visitors to hospital departments (other than dermatology), although not as representative of the source population as a selection from population register; controls frequency-matched to cases for sex and age (more women in controls); participation rates reported (80% and 69% in cases and controls, respectively)
	Performance bias	Probably low	Absence of blinding not likely to influence outcome assessment; cases and controls were interviewed by the same individual
	Exposure misclassification bias	Probably low	Study protocol included measures to ascertain sun exposure and also employed validated methods in structured questionnaire to aid recall; no. hours spent daily, weekly and monthly in occupational outdoor exposure in summer and in winter in adulthood recorded; any margin of error from inability to objectively measure the actual solar UVR exposures would be minimal
	Detection bias	Low	Outcome ascertainment was based on histological confirmation
	Confounding	Probably low	All Tier 1 confounding variables were adjusted for (age, skin colour, skin type); adjustment for sex not cited in table 3 of the study
	Incomplete outcome data bias	Low	Only 2 of 105 cases had unknown histology; study centre is the referral hospital for malignant melanoma cases in the region and participation rate (80.2%) was adequate (reasons for exclusion all ethically sound)
	Reporting bias	Probably low	No published protocol for this study; however, the description of the outcome of interest was outlined in the published manuscript's methods
	Conflict of interest bias	Probably low	No declaration of interests or source of funding included; authors affiliated to academic centres and medical centres associated with universities
	Other bias	Probably low	Appears to be a well designed case–control study; cases clearly defined and controls selected randomly
Espinosa Arranz et al., 1999 *(25)* Espinao Arranz 1999 Case–control	Selection bias	Probably low	Participant selection process appears adequate as cases and controls were selected from a health facility that served a defined population; no information provided on participation rates in cases or controls
	Performance bias	Probably low	Insufficient information about blinding of personnel who carried out questionnaire administration and clinical examination; since this is a hospital-based study, it is highly likely that personnel were already aware of cases and control participants
	Exposure misclassification bias	Probably high	Self-reported information used as surrogate for occupational exposure to solar UVR (occupational activity outdoor versus indoor); validated methods to aid recall not stated in text
	Detection bias	Low	Tissue histology was likely used in determination of cases of malignant melanoma as histologic subtypes of melanoma are reported in results
	Confounding	Low	Adequate measures were taken to control for the Tier 1 (important confounders) by selecting age- and sex-matched controls and ascertaining place of residence in questionnaire; skin type and naevi adjusted for
	Incomplete outcome data bias	Probably low	Histology reported in 89% of cases
	Reporting bias	Probably low	All 116 melanoma cases were adequately described and presented in the results section of this paper

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Conflict of interest bias	Probably low	Despite having no conflict of interest declaration or statement of funding in text, study authors were noted to be employed by government-funded hospitals
	Other bias	Probably low	Study questionnaire could have been designed with validated means to add recall incorporated; blinding of personnel involved in interviews and clinical examination also necessary; recall bias is a possibility in case–control studies
Walter et al., 1999 *(26)* Walter 1999 Case–control	Selection bias	Low	Inclusion/exclusion criteria, recruitment and enrolment procedures, and participation and follow-up rates were consistent across groups as described by the criteria for a judgment of low risk of bias; population controls randomly selected from tax assessment rolls
	Performance bias	Probably low	Blinding of investigators or study personnel was not described
	Exposure misclassification bias	High	Occupational exposure was selective, defined as no. hours of daylight spent outdoors, on average, during the summers, in job held within 5 years before interview (0 versus > 0)
	Detection bias	Low	Laboratories provided pathology reports
	Confounding	Probably low	Study appropriately accounted for most but not all of the important confounders (Tier 1) and some of the other potentially important confounders (Tier 2), using appropriate statistical techniques
	Incomplete outcome data bias	Low	No missing outcome data
	Reporting bias	Probably low	All of the study's pre-specified (primary and secondary) outcomes outlined in the pre-published protocol or the published manuscript's methods, abstract and/or introduction section that are of interest in this review were reported in the pre-specified way
	Conflict of interest bias	Low	Grants from the National Cancer Institute of Canada and National Health Research and Development Program, Canada
	Other bias	Probably low	Paper mostly about intermittent exposure; occupation was not fully explored
Håkansson et al., 2001[a] *(27)* Håkansson 2001 Cohort	Selection bias	Low	The large cohort of construction workers participating in an occupational health service programme of the Swedish construction industry showed adequate representation of the source population
	Performance bias	Probably low	Blinding not employed in this study; however, professionals involved in data collection and clinical examinations were adequately educated and trained on study aims
	Exposure misclassification bias	Probably low	Exposure to sunlight was based on current occupation from study records and classified by an industrial hygienist
	Detection bias	Low	Outcome metrics (cancers defined in study objectives) were histopathologically diagnosed
	Confounding	Probably high	Confounders were adequately addressed in study, both Tier 1 and other possible occupational carcinogens in the different groups, but no adjustment for skin type or constitutional risk factors included
	Incomplete outcome data bias	Probably low	Patients with incomplete data were excluded
	Reporting bias	Probably low	Selective outcome reporting seems unlikely in this study; however, women were excluded from this study
	Conflict of interest bias	Low	Study funded by national grant
	Other bias	Probably low	No other problems identified

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
Loria & Matos, 2001 *(28)* Loria 2001 Case–control	Selection bias	Probably low	Cases and controls enrolled at the same several hospitals and may therefore originate from similar catchment populations; study participants were matched by age, sex and hospital of diagnosis; large proportion of cases and controls agreed to participate; controls randomly selected from hospital patients lists (without dermatological disease)
	Performance bias	Probably low	Blinding was not an element of study design
	Exposure misclassification bias	High	Information from interviews, but the duration of exposure was estimated by summing the no. hours spent over a lifetime for each particular outdoor activity; sun exposure (intermittent or chronic) was weighted by type of clothing, asking whether participants' arms, legs and trunk were usually exposed, sometimes covered or usually covered while in the sun; however, cumulative exposure in hours was grouped into a single category (basically reducing the contrast to exposed: yes/no)
	Detection bias	Low	Distribution of melanoma cases by histology subtype was reported, so it can be assumed histopathology confirmation was used
	Confounding	Probably high	Odds ratio for conditional univariate logistic regression analysis was reported; study subjects were matched by sex, age (± 5 years) and hospital, but the distribution of participants by these variables, to assess success of matching, was not reported; other important confounders not taken into account
	Incomplete outcome data bias	Probably low	No clear information provided, but there do not appear to be any issues
	Reporting bias	Probably low	No study protocol identified; all variables mentioned in the present study were reported
	Conflict of interest bias	Low	Study funded by a national foundation promoting development of health sciences and the National Council of Science, Technology and Research of Argentina
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias, but recall bias cannot be ruled out
Bataille et al., 2004 *(29)* Bataille 2004 Case–control	Selection bias	Probably low	Indirect evidence to suggest that inclusion/exclusion criteria and recruitment and enrolment procedures were consistent across groups; no participation rate provided for cases or controls (published elsewhere)
	Performance bias	Probably low	No blinding, but we judged that the outcome measures as well as the exposure measures were not likely to be influenced by lack of blinding; questionnaire and interviewer used the same wording for cases and controls
	Exposure misclassification bias	High	Occupational exposure variable not described in sufficient detail; total no. hours worked outdoors in the summer as an adult was the exposure variable analysed (not clear if it referred to daily no. hours or overall total; categories were not discriminatory enough to distinguish true levels of exposure with a biological effect); work-related exposure assessment methods were not robust
	Detection bias	Low	"All cases and controls were examined by one of two dermatologists" (p. 430); indirect evidence to suggest that methods were robust; outcome included in situ and invasive melanoma, including all histologies (presumed histological confirmation)

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Confounding	Low	"To control for potential confounding factors, multiple regression models were fitted. The regression equations included, when appropriate, terms for age, sex, four categories of skin type and sun exposure variables."(p. 430) Appropriately assessed and accounted for (i.e. matched, stratified, excluded certain populations or statistically controlled for) all important confounders (Tier 1) using appropriate statistical techniques
	Incomplete outcome data bias	Probably low	Evidence that incomplete outcome data are not capable of introducing risk of bias in the study
	Reporting bias	Probably low	All of the study's pre-specified (primary and secondary) outcomes outlined in the pre-published protocol or the published manuscript's methods, abstract and/or introduction section that are of interest in this review were reported in the pre-specified way
	Conflict of interest bias	Low	"This work was funded by Cancer Research UK, formerly known as the Imperial Cancer Research Fund." (p. 434) Funding source was limited to government, non-profit organizations or academic grants funded by government, foundations and/or non-profit organizations
	Other bias	Probably low	Appears to be free of other sources of bias, but recall bias cannot be ruled out
Fargnoli et al., 2004 *(30)* Fargnoli 2004 Case–control	Selection bias	Low	Descriptions of the source population, inclusion/exclusion criteria, recruitment and enrollment procedures, participation and follow-up rates were sufficiently detailed, and adequate data were supplied on the distribution of relevant study sample and population characteristics to support the assertion that the risk of selection effects was minimal; no information provided on participation rates in cases or controls
	Performance bias	Probably low	Blinding not part of the recruitment of the case–control participants, but no information on whether data analyst/ biostatistician was blinded to the outcome
	Exposure misclassification bias	Probably high	In-person interview by trained physician using questionnaire; qualitative exposure (occupational sun exposure for a period of ≥ 6 months/year including spring and summer) self-reported as "yes" or "no"; quantitative exposures (recreational) also self-reported; lifetime exposure considered
	Detection bias	Low	Presence or absence confirmed by histology
	Confounding	Low	Analysis adjusted for confounding (age, sex, phototype and interaction in the first model); study participants matched for sex, age, ethnicity and residential area
	Incomplete outcome data bias	Low	Case–control study; no incomplete outcome; outcome pre-defined in the introduction and the method section
	Reporting bias	Probably low	No study protocol identified; all variables mentioned in the present study were reported
	Conflict of interest bias	Low	Governmental funding
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias, but recall bias cannot be ruled out
Nijsten et al., 2005 *(31)* Nijsten 2005 Case–control	Selection bias	Probably low	Authors gave a clear inclusion and exclusion criteria for both cases and controls; however, it was unclear whether all or a subset of the eligible cases or controls were selected from all of those during the study period July 1998–July 2001; rate of participation not reported; participants identified at the same institution but at different departments
	Performance bias	Probably low	Use of blinding is not described

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Exposure misclassification bias	Probably high	Self-reported exposure status could introduce the risk of measurement bias; occupational sun exposure was categorized as "none", "a little", "moderate" or "a lot"
	Detection bias	High	CMM was confirmed based on pathological report; exclusion of lentigo maligna melanoma, a subtype believed to be associated with chronic exposure to solar UVR, could potentially introduce bias (attenuation of association)
	Confounding	Probably low	Cases and controls were matched by age, sex and skin phototype; adjustment was made for the exact age, sex and skin phototype in the multivariate analysis
	Incomplete outcome data bias	Probably low	No evidence of missing outcome data for cases and controls
	Reporting bias	Probably low	No published protocol for this study; however, the description of the outcome of interest was outlined in the published manuscript's methods
	Conflict of interest bias	Low	Study was supported by the Fund for Scientific Research, Flanders, Belgium
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias, but recall bias cannot be ruled out
Whiteman et al., 2006 *(32)* Whiteman 2006 Case–case	Selection bias	Probably low	Insufficient information about participant selection to permit a judgment of low risk of bias, but indirect evidence to suggest that inclusion/exclusion criteria, recruitment and enrolment procedures, and participation and follow-up rates were consistent across groups
	Performance bias	Probably low	No blinding, but we judged that the outcome measures as well as the exposure measures were not likely to be influenced by lack of blinding
	Exposure misclassification bias	Probably low	Occupational exposure history (including periods of study and unemployment) obtained that recorded, for each job, the no. days worked per week; respondents were asked "how much time did you spend outdoors in the sun in summer" on work days and non-work days (1, 1–4 or ≥ 4 hours per day); different metrics of exposure available in table 3 of the study
	Detection bias	Low	Histopathology-confirmed cases; not all melanoma subtypes eligible
	Confounding	Probably low	Study appropriately accounted for most but not all of the important confounders (Tier 1) and some of the other potentially important confounders (Tier 2), using appropriate statistical techniques
	Incomplete outcome data bias	Low	No missing outcome data
	Reporting bias	Low	All of the study's pre-specified (primary and secondary) outcomes outlined in the pre-published protocol or the published manuscript's methods, abstract and/or introduction section that are of interest in this review have been reported in the pre-specified way
	Conflict of interest bias	Low	Supported by grants from the Queensland Cancer Fund and the National Cancer Institute (CA 88363-01A1) of Australia
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias
Zanetti et al., 2006[a] *(33)* Zanetti 2006 Case–control	Selection bias	Probably low	Selection criteria well described, including eligibility criteria, quota recruitment per participating centre (country) and enrolment procedures; cases and controls enrolled at the same hospitals in same period; controls age- and frequency-matched to cases; study limited to men

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Performance bias	Probably low	No reference to blinding was found; lack of blinding not expected to introduce bias
	Exposure misclassification bias	Probably low	Outdoor work defined by number of weighted hours in a lifetime, categorized as never, < 320, > 320–1128, > 1128–3878, > 3878; interviewers asked questions on sun exposure using a structured questionnaire arranged by periods of life (before first employment, during active life and after retirement), places of residence for ≥ 6 months and type of outdoor activity (work, holidays, sports or other outdoor recreational activities)
	Detection bias	Low	Microscopically confirmed diagnosis of primary CMM
	Confounding	Low	Logistic regression model adjusted by age, country of residence and significant independent host factors
	Incomplete outcome data bias	Probably low	No missing data on cancer outcome
	Reporting bias	Low	All the outcomes reported
	Conflict of interest bias	Low	Founding from European Union Europe Against Cancer (grant nos SI2 129340, 99CVF2-015), Spanish Fund for Health Research and a foundation from Argentina promoting science
	Other bias	Probably low	Study appears to be free of other sources of bias
Nikolaou et al., 2008 *(34)* Nikolaou 2008 Case–control	Selection bias	Probably low	Newly diagnosed cutaneous melanoma patients were selected consecutively; controls were selected following clear inclusion/exclusion criteria from same institution but at different department; no indication given on how potential controls were approached, as the sample was not randomly selected; cases and controls not compared by age, sex or socioeconomic status; participation rate of a sub-group of controls (consisting of relatives of outpatients) was cited was high
	Performance bias	Probably low	Use of blinding not described
	Exposure misclassification bias	High	Self-report occupational sun exposure (yes/no): whether occupation mainly indoors or outdoors for a period of < 5 or ≥ 5 years; comparator includes subjects with outdoor work for < 5 years
	Detection bias	Low	Cutaneous melanoma was histologically confirmed
	Confounding	Probably high	Cases and controls were matched by sex and age; results for occupational exposure to sun radiation not adjusted for independent risk factors such as skin phototype
	Incomplete outcome data bias	Probably low	No evidence on incomplete data
	Reporting bias	Probably low	No published protocol for this study; however, the description of the outcome of interest was outlined in the published manuscript's methods
	Conflict of interest bias	Low	Partially funded by the Kapodistrias programme of the Special Account for Research Grants of the National and Kapodistrian University of Athens (code number: 70/4/5910) and by the Oncology Program fund, Greek Ministry of Health (grant no. 72K/115-30/11/2005)
	Other bias	Probably low	Apart from self-reported exposure and confounding, the study appears to be free of potential biases; recall bias cannot be ruled out

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
Radespiel-Tröger et al., 2009[a] *(35)* Radespiel-Tröger 2009 Case–case	Selection bias	Probably low	Registry-based study in Bavaria with a well defined population and compulsory/voluntary registration of cancer cases backed by the law (full-scale registration commenced in the year 2002, 1 year after commencement of the study); however, only a few Bavarian districts could be included because of the inclusion/exclusion criteria of the study; histogram comparing study population and Bavarian population according to the municipalities was not available for viewing
	Performance bias	Probably low	Study utilized set methods with suitable reference to previous studies (for exposure classification) and the cancer registry (outcome measure); impact of assessor subjectivity therefore ruled out
	Exposure misclassification bias	Probably high	Exposure assessment was indirect with job titles classified into three broad categories (suitable reference made to three previous publications); proportion of missing values for work-type in the registered cases was also fairly high (72% for CMM)
	Detection bias	Low	Outcome ascertainment was based on notifications sent to respective cancer registration authorities; cancer registry notifications include patient-related data (sex, age, residence, occupation), tumour-related data (date of diagnosis, cancer site and histology, malignancy grade, tumour-node-metastasis category) and basic treatment-related data; cancer diagnoses coded according to ICD-10 and ICD-O-3
	Confounding	Probably high	Age-adjusted estimates of relative risk calculated
	Incomplete outcome data bias	Probably low	Bavarian cancer registry data was likely complete on cancer outcome, despite study data aggregation commencing 1 year after full-scale cancer registration
	Reporting bias	Probably low	No published protocol for this study; however, the description of the outcome of interest was outlined in the published manuscript's method
	Conflict of interest bias	Probably low	It seems that all study authors were affiliated to a government agency and prohibited from involvement in projects for which there was (or was an appearance of) a conflict of interest
	Other bias	Probably high	Study authors elaborated on four important limitations of this study; the potential for non-representation of the Bavarian population is noteworthy as well as high propensity for exposure misclassification and uncertain effect on precision as a result of a high proportion of missing values (job types)
Kenborg et al., 2010[a] *(36)* Kenborg 2010 Case–control	Selection bias	Probably low	All cases diagnosed during the study period and registered in the Danish cancer database; random selection of controls matched by sex and year of birth from the Danish Central Person Registry; similar eligibility criteria applied to cases and controls; cases and controls may not have come from same catchment population
	Performance bias	Probably low	No information on blinding; however, the study appears to be free of bias
	Exposure misclassification bias	Probably low	Job–exposure matrix for Denmark developed for the Nordic Occupational Cancer Study; however, there was no information on individual sun exposure; risk estimates provided for outdoor occupation overall and for specific occupations (i.e. forestry) by duration of employment obtained from records from pension plan; lifetime years of outdoor occupation calculated
	Detection bias	Low	Outcome confirmed histopathologically

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Confounding	Probably low	Analysis adjusted for confounders including social class and skin colour; only males included; study matched cases and controls by year of birth
	Incomplete outcome data bias	Probably low	Only cases containing information about occupation and cancer were included
	Reporting bias	Low	All outcomes were reported
	Conflict of interest bias	Low	Study was supported by grants from the Danish Working Environment Authority
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias
Kaskel et al., 2015[a] *(37)* Kaskel 2015 Case–control	Selection bias	Probably low	Source population not specified but controls recruited from same institution, including same and additional department as cases, implying the same catchment population; eligibility and exclusion criteria were described; participation rate not disclosed; cases recruited from dermatology clinic and controls from allergology and phlebology unit at the same time
	Performance bias	Probably low	Blinding not an element of study design; absence of it not expected to have introduced important risk of bias
	Exposure misclassification bias	Probably high	Only items summarizing UVR behaviour were used to describe exposure to UVR; unclear whether this method was also used for occupational exposure; occupation in farming as proxy of exposure (comparing "full-time farming" with "no farming") problematic, as "no farming" could include occupations with sun exposure; crude estimate provided for occupational sun exposure using the contrast often/sometimes versus few/no
	Detection bias	Low	Body inspection using a tool and histopathologically confirmed cases
	Confounding	Probably high	Confounding was not mentioned, but there are data on confounders collected and analysis adjusted for potential confounders; however, the comparison "farming" versus "no farming" has problems for the comparator; only an unadjusted risk estimate provided for occupational sun exposure using the contrast often/sometimes versus few/no
	Incomplete outcome data bias	Probably low	No clear information provided, but there do not appear to be any issues
	Reporting bias	Probably low	No study protocol identified; all the variables mentioned in the present study were reported
	Conflict of interest bias	Probably low	No conflict of interest declared; work performed at and funded by academic centres; one author joined industry after completion of the operational part of the project, and is currently employed at Outcomes Research, Mercke Sharp & Dohme (MSD) GMBH, Haar, Germany; disclaimer reports that data presented in publication are in no way connected with professional activities at MSD GMBH
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias
Fortes et al., 2016 *(38)* Fortes 2016 Case–control	Selection bias	Low	Descriptions of the source population, inclusion/exclusion criteria, recruitment and enrolment procedures, participation and follow-up rates were sufficiently detailed, and adequate data were supplied on the distribution of relevant study sample and population characteristics to support the assertion that risk of selection effects was minimal; participation rate among cases and controls was 96% and 94%, respectively; Italian and Brazilian study recruitment conducted in different calendar years

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Author, year Study ID Study type	Risk of bias domain	Rating	Justification for rating
	Performance bias	Probably low	No information about blinding; physicians performing interviews would have been aware of the status of participants, but not influenced the study
	Exposure misclassification bias	Probably high	Method: questionnaire, in–person interviews with trained dermatologists; qualitative exposure as indoor, outdoor/indoor or outdoor
	Detection bias	Low	Outcome histopathologically confirmed, including melanoma subtypes
	Confounding	Probably low	Analysis adjusted for age and sex; although information on constitutional variables known to be independent risk factors for melanoma was collected, the reported risk estimate for occupational sun exposure appears to be unadjusteded
	Incomplete outcome data bias	Probably low	Case–control study; no incomplete outcome; outcome predefined in introduction and the method section
	Reporting bias	Probably low	No study protocol identified; all variables mentioned in the present study were reported
	Conflict of interest bias	Low	Study funded by Ministries of Health of each country; authors declared no conflicts of interest
	Other bias	Probably low	No additional sources of bias identified, but recall bias cannot be ruled out
Trakatelli et al., 2016[a] *(39)* Trakatelli 2016 Case–control	Selection bias	Probably high	Sparse information on selection of study participants; data for this study came from the EPIDERM case–control study, a large multicentre hospital-based case–control study (conducted in Finland, Germany, Greece, Italy, Malta, Poland, Scotland and Spain), including 360 with CMM and 1550 controls; participation rate in cases and controls not reported
	Performance bias	Probably low	Exposure self-reported and by non-blinded clinicians
	Exposure misclassification bias	Probably high	Interview based on the simple question: "Have you ever had an outdoor occupation (yes/no)"; outdoor workers subdivided according to the self-reported total duration of outdoor work: < 1 year (n = 72), 1 to < 5 years (n = 155) and ≥ 5 years (n = 1185), the latter exposure group not being very informative
	Detection bias	Low	Histologically confirmed cases, although only verbal skin cancer history for controls
	Confounding	Probably low	Model A corrected for country, age, sex and phototype, and Model B for these as well as sunscreen use in own country, smoking and outdoor hobbies
	Incomplete outcome data bias	Low	Evidence that the incomplete outcome data were not capable of introducing risk of bias in the study
	Reporting bias	Low	All of the study's pre-specified (primary and secondary) outcomes outlined in the pre-published protocol or the published manuscript's methods, abstract and/or introduction section that are of interest in this review have been reported in the pre-specified way
	Conflict of interest bias	High	Publication is based on data from the EPIDERM project, funded by the European Commission's Executive Agency for Health and Consumers (PHEA2007–A/100994HI); first and fifth authors received grants from Leo Pharma specifically for their time dedicated to study the association between skin cancer and outdoor occupation; first author affiliated to a university hospital in Greece and a second hospital in Belgium, and is a speaker for Leo Pharma, Janssen-Cilag
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias

CMM, cutaneous malignant melanoma; ICD, International Classification of Diseases; UVR, ultraviolet radiation.

[a] Risk of bias ratings also apply to the health outcome of NMSC incidence (see Table A5.3).

Table A5.2. Risk of bias in studies reporting on association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma mortality

Author, year Study type	Risk of bias domain	Rating	Justification for rating
Zanetti et al., 1988, 1999 *(10, 11)*; Rosso et al. 1998, 2008 *(12, 13)* Zanetti 1988 Case–control (extended follow-up)	Selection bias	Low	Almost the same cancer case population (96%) used in initial population-based case–control study in Turin (Italy) included in this study, in which survival was the objective; study population representative and length of follow-up (median, 17 years) was adequate
	Performance bias	Probably low	Study objective was determinants of cancer survival; blinding was not part of the study design
	Exposure misclassification bias	Probably low	Study protocol ascertained occupational sun exposure and also employed validated methods in structured questionnaire to aid recall; any margin of error from inability to objectively measure the actual solar UVR exposure would be minimal
	Detection bias	Probably low	Survival ascertained by active follow-up of cancer cases (date, place, initial cause of death and co-morbidities were recorded); cause of death was not available in a fraction of cases that died; cancers were originally histopathologically diagnosed
	Confounding	Probably low	Hazard ratio adjusted for age, sex, education and follow-up period; risk of dying could also be affected by other potential confounders such as other chronic diseases (diabetes and hypertension, stroke), particularly among older people
	Incomplete outcome data	Probably low	Patients included in the study were followed up long enough (median, 17 years); cause of death was unknown for 17% of deaths; adequate steps were taken to determine that there was no statistically significant difference in age, sex and melanoma thickness between patients followed up and the nine patients (3.5% of study population) lost to follow-up
	Reporting bias	Probably low	Study was on melanoma survival; only one outcome metric (cutaneous melanoma), which was adequately reported using the Piedmont Cancer Registry as source/reference
	Conflict of interest bias	Low	Authors declared no conflict of interest, are government employees and funding source is from non-profit organization without any financial interest in the study
	Other bias	Probably low	Recall bias cannot be completely ruled out despite validated methods employed in questionnaire design; study did not attempt to assess increased skin surveillance tendencies that are a natural expectation in the participants after being diagnosed with a skin cancer; this would influence survival considering the long follow-up period
Freedman et al., 1997, 2002 *(40, 41)* Freedman 1997 Case–control (based on death certificates)	Selection bias	Low	The descriptions of the source population, inclusion/exclusion criteria, recruitment and enrolment procedures, and participation and follow-up rates were sufficiently detailed, and adequate data were supplied on the distribution of relevant study sample and population characteristics to support the assertion that risk of selection effects was minimal
	Performance bias	Probably low	It was not mentioned whether the industrial hygienist classifying occupational sun exposure according to occupation declared on death certificate was blinded on the case–control status of cases and controls that had died
	Exposure misclassification bias	Probably high	Exposure classified from administrative records; qualitative data based on residence and usual occupation were collected from death certificate, and exposure to solar radiation was deduced (outdoor occupations) by industrial hygienist based on usual or last occupation

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Author, year Study type	Risk of bias domain	Rating	Justification for rating
	Detection bias	Probably low	Outcomes were collected by death certificate from a 24-state United States National Institutes of Health–National Institute for Occupational Safety and Health mortality database operative since 1984; unclear whether it was confirmed by pathological report
	Confounding	Low	Variables adjusted for confounding included age, sex, race, socioeconomic status and physical activity; effect of skin pigmentation (deduced from race and national origin in certificate) was assessed
	Incomplete outcome data	Low	Case–control study based on death certificates; no incomplete outcome; outcome was pre-defined in introduction and the method section
	Reporting bias	Probably low	No study protocol identified; all variables mentioned in the present study were reported
	Conflict of interest bias	Low	No funding source specified, but the study was conducted by United States government agency on cancer research, which uses intramural funding; authors declared no conflict of interest
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias

UVR, ultraviolet radiation.

Table A5.3. Risk of bias in studies reporting on the association between occupational exposure to solar ultraviolet radiation and non–melanoma skin cancer incidence

Author, year Study type	Risk of bias domain	Rating	Justification for rating
Aubry & MacGibbon, 1985 *(42)* Aubry 1985 Case–control	Selection bias	Probably low	"In spite of the low participation rate in the study, the comparisons made within and between cases and controls and their participation groups for age, sex, and hospital suggest that these selection factors did not operate differently in cases and controls." (p. 910) The description of the inclusion/exclusion criteria and recruitment procedures were very detailed and adequate, although the low participation rate (30.4% of original eligible sample and 55.7% of those receiving questionnaire) was a concern; the representativeness of cases and non-cases of the source population from which they originated remains uncertain
	Performance bias	Low	Blinding of key study personnel was ensured: "Telephone interviews were done only by one clerk unaware of the case-control status of the study participants. An attempt was also made at detecting recall biases by introducing in the questionnaire questions on childhood infectious diseases." (p. 911)
	Exposure misclassification bias	Probably high	Study participants completed a questionnaire; a comprehensive occupational sun exposure index was constructed based on self-reported occupational history; analysis and methods of exposure assessment were detailed, but risk estimates by sun exposure index level lack measures of precision; the available estimate with a 95% confidence interval was based on a dichotomous variable (exposed: yes/no)
	Detection bias	Low	Outcomes were assessed and defined consistently across all study participants, using valid and reliable measures (p. 909); included cases were histologically confirmed
	Confounding	Probably low	Study appropriately accounted for most but not all of the important confounders (Tier 1) or used appropriate statistical techniques (see list of all variables on p. 908)
	Incomplete outcome data bias	Probably low	No clear information provided, but there do not appear to be any issues
	Reporting bias	Probably low	All the pre-specified outcomes presented in the abstract were discussed and reported adequately in the article
	Conflict of interest bias	Low	Funding sources reported are limited to Canadian government research funding agencies
	Other bias	Probably low	Study appears to be free of other sources of bias, but recall bias cannot be ruled out
Gallagher et al., 1995 *(43, 44)* Gallagher 1995 Case–control	Selection bias	Probably low	Population-based cancer registry study; 30% of eligible registered male cancer cases were selected for the study based on tumour location; 72% of selected cases were interviewed; controls were randomly selected from insurance plan, and 71 of those contacted were interviewed; male controls were frequency-matched by age to male cases
	Performance bias	Low	Interviewers were blinded on the disease status of study participants and study hypothesis
	Exposure misclassification bias	Probably low	Interview by a trained interviewer using a standard questionnaire; occupational sun exposure index derived including clothing from disclosed lifetime occupational history; reference group includes some sun radiation exposure (< 3.5 hours per week)
	Detection bias	Low	Outcome histopathologically diagnosed and available at the population-based cancer registry
	Confounding	Probably low	Odds ratios adjusted for the effects of age, mother's ethnic origin, skin colour and hair colour
	Incomplete outcome data bias	Probably low	Eligible cases and controls that did not answer the questionnaire were not included (29%)
	Reporting bias	Probably low	No study protocol identified; all the variables mentioned in the study were reported; study reports the same variables as other studies from the same series

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Author, year Study type	Risk of bias domain	Rating	Justification for rating
	Conflict of interest bias	Low	Study funded by national funding agency
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias
Kricker et al., 1995 *(45)* Kricker 1995 Case–control	Selection bias	Probably low	Identical procedures were used to contact cases and controls; participants of a population-based survey investigating NMSC; 89% of eligible cases and controls participated
	Performance bias	Low	Interviewers were not aware of the case or control status of the study participants
	Exposure misclassification bias	Probably low	Exposure assessed by interview using same procedure in cases and controls: how many hours per day at work outside during 09:00–17:00 for each period of life; cumulative no. hours of sun exposure per week on working days from age 15 years calculated
	Detection bias	Low	Skin cancers were diagnosed clinically at the survey by dermatologist and confirmed by histopathology
	Confounding	Probably low	Variables adjusted for included age, sex and ability to tan
	Incomplete outcome data bias	Probably low	No clear information provided, but there do not appear to be any issues
	Reporting bias	Probably low	No study protocol identified; all the variables mentioned in the study were reported
	Conflict of interest bias	Low	Study was funded by a national cancer foundation and National Health and Medical Research Council of Australia
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias, but recall bias cannot be ruled out.
Green et al., 1996 *(46)* Green 1996 Cohort (prospective)	Selection bias	Low	Random sampling from compulsory electoral list to select study sample; 70% attended dermatology examination and 84% of those were contacted 2 years later to assess incident cancer
	Performance bias	Probably low	Standard questionnaire used for all participants; no blinding of study personnel mentioned
	Exposure misclassification bias	Probably high	Self-reported as mainly outdoors, mixed indoors/outdoors or indoors on average over life; no further details
	Detection bias	Low	Outcome confirmed histopathologically
	Confounding	Probably low	Age, sex and skin colour adjusted for
	Incomplete outcome data bias	Probably low	High follow-up rate; only a little outcome data were missing
	Reporting bias	Low	All types reported separately
	Conflict of interest bias	Low	National government funding sources
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias
Rosso et al., 1996 *(47)*, 1998 *(12)* Rosso 1996 Case–control	Selection bias	Low	Incident cases and randomly selected controls were selected from the same population in seven south European regions (three countries) in this multi-centre case–control study; Rosso et al. *(47)* describes selection of participants and enrolment procedures at centres based on cancer registries and hospitals; response rates reported
	Performance bias	Low	Outcome (BCC and SCC) assessment and validation was carried out by a panel of pathologists with adequate blinding; adequate measures were taken to assess exposure in both cases and controls, taking into account clothing, seasonality, type and length of sun exposure, and objective solar irradiance for geographic regions where study population resided
	Exposure misclassification bias	Probably low	No dosimeter was used to measure the exposure; information on exposure was collected by structured questionnaire; researchers estimated amount of solar irradiation as no. hours of sun exposure to broad body sites during different activities in a lifetime; information collected on each job held for ≥ 6 months, providing information about type of work and industry

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Author, year Study type	Risk of bias domain	Rating	Justification for rating
	Detection bias	Low	Both BCC and SCC diagnoses were validated by a panel of pathologists; diagnosis of cases was documented with histopathology reports
	Confounding	Low	Study controlled for confounding by adjusting for sex, age at interview and centres; exposures were also adjusted for significant pigmentary traits and skin characteristics in line with independent risk factors identified (hair colour, eye colour and skin reaction to sun exposure) and outdoor activities
	Incomplete outcome data bias	Low	All cases were validated by panel of pathologists who reviewed histologic slides with blinding included
	Reporting bias	Probably low	No published protocol for this study; however, the description of the outcome of interest was outlined in the published manuscript's methods
	Conflict of interest bias	Low	The study was supported by a research grant from Europe Against Cancer in addition to several, apparently governmental, entities in France, Italy and Spain
	Other bias	Low	Appears to be a well designed case–control study; cases were clearly defined and controls were selected randomly
Suárez-Varela 1996 *(48)* Suárez-Varela 1996 Case–control	Selection bias	Probably high	Cases and controls matched by age, sex and area of residence; cases identified at a hospital referral centre and controls (randomly selected) chosen without diseases that predispose to skin cancer, some of them identified at the same hospital; source of controls or enrolment process not described
	Performance bias	Probably low	Controls randomly selected; no blinding
	Exposure misclassification bias	Probably high	No information given to assess this, which means it is probably not low; exposure defined as daily no. hours of sun exposure during occupational activity outdoor (low, < 1.7; medium, 1.7–3.6; high, 3.6–4.8; very high, > 4.8 hours per day) from information collected by questionnaire
	Detection bias	Low	Histopathologically confirmed cases; only information is "free of skin cancer" (free of prevalent or past) for controls
	Confounding	Probably high	Only age-adjusted risk estimates presented, stratified by sex
	Incomplete outcome data bias	Probably low	Loss of information by not reporting risk estimates by NMSC histologic subtypes
	Reporting bias	Probably high	Not clear why statistical analysis did not adjust for risk factors analysed in bivariate analysis, and consequently no reporting of adjusted risk estimates of NMSC; no reporting of subtype risk
	Conflict of interest bias	Probably low	No source of funding or declaration of conflicts of interest included; however, authors are affiliated to a Spanish University Public Health and Environmental Care Unit
	Other bias	Probably high	This is an early study; methods not refined, and bias likely to be present
Rosso et al., 1999 *(49)* Rosso 1999 Case–control	Selection bias	Probably low	Cases: all residents aged 20–75 years with a diagnosis of a new NMSC during 1994–1996 in a Swiss canton area of 250 000 population were considered eligible to take part in the study, and 73% participated; response rate in eligible controls from the same area was 81%; not clear if controls selected randomly from a population-based list compiled by cancer league; some concern regarding cases and controls being somewhat different in socioeconomic status (cases more prevalently in agriculture, while controls from a more affluent recruitment base; p. 440)
	Performance bias	Low	Statement of blinding introduced in the work of the trained interviewers is uncertain in text; however, for the outcome metric the panel of pathologists (blinded) was involved
	Exposure misclassification bias	Probably low	Study protocol included measures to ascertain sun exposure in both cases and controls using structured questionnaire; however, recall bias cannot be completely ruled out; information on cumulative hours of sun exposure during work activity outdoor was collected: never, < 12 000, < 47 900, < 77 200, > 77 200 hours
	Detection bias	Low	Outcome metrics (cancers defined in study objectives) were histopathologically diagnosed

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Author, year Study type	Risk of bias domain	Rating	Justification for rating
	Confounding	Probably high	Study accounted for age, sex and socioeconomic status, although authors commented on a likely important difference in social stratification of cases (lower) and controls (higher) in study participants; the independent contribution of occupational sun exposure to BCC or SCC risk could not be evaluated in the multivariate logistic regression models because of sparse data (results are not presented in table 5 of study record); only OR estimates for number of outdoor work hours from conditional logistic regression (matched by sex and age, ± 5 years), not including any other variable, was reported
	Incomplete outcome data bias	Low	Skin cancer registry seems to have provided a complete dataset for the outcome metric
	Reporting bias	Low	Study report focused on BCC and SCC using the Sion Cancer Registry as a source
	Conflict of interest bias	Low	Study was supported by a research grant from Europe Against Cancer, in addition to the Swiss League for the Fight Against Cancer
	Other bias	Probably low	Sampling methodology for both cases and controls is unclear; recall bias cannot be ruled out
Vlajinac et al., 2000 *(50)* Vlajinac 2000 Case–control	Selection bias	Probably high	Cases recruited consecutively from two skin disease clinics in different cities in Yugoslavia upon diagnoses, and controls enrolled as consecutive patients aged > 30 years with no diagnose of BCC at the same clinics; not much detail provided, including response rates or if controls were matched to cases
	Performance bias	Probably low	Clinicians in dermatological clinic were not blinded
	Exposure misclassification bias	High	Questionnaires for exposure assessment; exposure definition: outdoor work in summer period (yes/no); no time reference available for information collected on outdoor work during summer; no information provided on exposure assessment in methods
	Detection bias	Low	Outcome histopathologically confirmed
	Confounding	Probably high	Insufficient information is provided, but methods state multivariate logistic regression was used; results in table 3 of paper include several variables of occupational sun exposure, including a few constitutional attributes, occupational exposure to chemicals, skin reaction to sun and previous skin cancer, but sex and age are not listed
	Incomplete outcome data bias	Probably low	No reference in the study, but study appears to be free of bias
	Reporting bias	Probably low	No study protocol identified; all variables mentioned in the study were reported
	Conflict of interest bias	Low	Supported by Ministry of Science and Technology
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias, but recall bias cannot be ruled out
Corona et al., 2001 *(51)* Corona 2001 Case–control	Selection bias	Probably high	The sample was selected conveniently; controls were identified at the same dermatology centre as cancer cases with eligible dermatology complaints not associated with sun exposure
	Performance bias	Probably low	No description of blinding of interviewers on the study hypothesis or case–control status; however, the impact of this may not be important
	Exposure misclassification bias	High	Data collected using a questionnaire and interviews; reference group could include study participants with up to 8 years of outdoor occupation, therefore exhibiting some degree of solar UVR exposure; use of such an "unexposed" group potentially introduces bias towards the null; in addition, the exposed group was poorly defined as > 8 years of outdoor work, which represents a wide range of potential accrued exposure, including an exposure level not very different from the level allowed in the "comparison" group
	Detection bias	Low	Histologically confirmed BCC

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Author, year Study type	Risk of bias domain	Rating	Justification for rating
	Confounding	Low	Age- and sex-adjusted odds ratios and 95% confidence intervals were calculated for known host risk factors: light hair and eye colour, fair skin complexion, skin phototype, sunlight-related skin lesions and family history of skin cancer, occupational and recreational sun exposure, exposure to non-solar UVR, history of sunburn and lifestyle-related habits (smoking status and alcohol, coffee and tea consumption) using unconditional logistic regression models; logistic regression models were built to allow for multiple adjustments of confounding
	Incomplete outcome data bias	Probably low	No clear information provided, but there do not appear to be any issues
	Reporting bias	Low	All the pre-specified outcomes presented in the abstract were discussed and reported adequately in the article
	Conflict of interest bias	Low	Study funded by the Ministry of Health
	Other bias	Probably low	Study appears to be free of other sources of bias, but recall bias cannot be ruled out
Håkansson et al., 2001[a] *(27)* Håkansson 2001 Cohort	Selection bias	Low	The large cohort of construction workers participating in an occupational health service programme of the Swedish construction industry showed adequate representation of the source population
	Performance bias	Probably low	Blinding not employed in this study; however, professionals involved in data collection and clinical examinations were adequately educated and trained on study aims
	Exposure misclassification bias	Probably low	Exposure to sunlight was based on current occupation from study records and classified by an industrial hygienist
	Detection bias	Low	Outcome metrics (cancers defined in study objectives) were histopathologically diagnosed
	Confounding	Probably high	Confounders were adequately addressed in study, both Tier 1 and other possible occupational carcinogens in the different groups, but no adjustment for skin type or constitutional risk factors included
	Incomplete outcome data bias	Probably low	Patients with incomplete data were excluded; risk estimates not provided by NMSC subtypes
	Reporting bias	Probably low	Selective outcome reporting seems unlikely in this study; however, women were excluded from this study
	Conflict of interest bias	Low	Study funded by national grant
	Other bias	Probably low	No other problems identified
Milán et al., 2003 *(52)* Milán 2003 Case–control	Selection bias	Probably low	The Finnish Adult Twin Cohort was compiled from the Central Population Registry of Finland using selection procedures described in detail elsewhere; questionnaire response rate > 90%; case-control study of discordant twins was initiated from subjects in the cohort; cases identified through the Finnish Cancer Registry
	Performance bias	Probably low	Researchers do not seem to have been blinded to select cases from the database, but this information is not clear in the study; however, study does not appear to be biased
	Exposure misclassification bias	Probably high	Exposure estimated through occupation using broad categories: "mainly inside", "mainly outside", "both" and "never worked"
	Detection bias	Low	Information on all histologically confirmed cases of BCC among the twin cohort members was retrieved from the nationwide Finnish Cancer Registry by a register linkage using personal identification numbers
	Confounding	Probably high	Data stratified by sex; no adjustment for independent risk factors
	Incomplete outcome data bias	Low	Only cases containing information about occupation and cancer were included

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Author, year Study type	Risk of bias domain	Rating	Justification for rating
	Reporting bias	Probably low	No study protocol identified; all variables mentioned in the present study were reported
	Conflict of interest bias	Low	Study was funded by national science and medical foundations and national cancer non-for-profit organization
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias
Walther et al., 2004 *(53)* Walther 2004 Case–control	Selection bias	Probably low	Insufficient information about participant selection (recruited from the same institution) to permit a judgment of low risk of bias, but there is indirect evidence to suggest that inclusion/exclusion criteria, recruitment and enrolment procedures, and participation and follow-up rates were consistent across groups; response rate not reported
	Performance bias	Probably low	No blinding, but we judged that the outcome measures as well as the exposure measures were not likely to be influenced by lack of blinding
	Exposure misclassification bias	Probably high	Patients were interviewed using a standardized skin cancer questionnaire adapted for BCC, and examined in person at a dermatology department; frequency of occupational exposure to solar UVR recorded as frequently/sometimes versus never/rarely (reference group)
	Detection bias	Low	Body inspections of patients and controls conducted by the same carefully tutored and experienced dermatology trainees, applying identical predefined diagnostic criteria under the supervision of qualified dermatologists; histopathology confirmation
	Confounding	Probably low	Study appropriately accounted for most but not all of the important confounders (Tier 1) as well as some of the other potentially important and relevant confounders (Tier 2), using appropriate statistical techniques
	Incomplete outcome data bias	Low	No missing outcome data
	Reporting bias	Probably low	All types reported separately
	Conflict of interest bias	Probably high	Source of funding not included; declaration of interests not included; authors affiliated to departments of dermatology and academic and medical centres
	Other bias	Probably high	It is reported in the paper that the senior author "recently joined Corporate Outcomes Research at Schering AG, Berlin, Germany" (p170 (*53*))
Zanetti et al., 2006[a] *(33)* Zanetti 2006 Case–control	Selection bias	Probably low	Selection criteria well described, including eligibility criteria, quota recruitment per participating centre (country) and enrolment procedures; cases and controls enrolled at the same hospitals in same period; controls age- and frequency-matched to cases; study limited to men
	Performance bias	Probably low	No reference to blinding was found; lack of blinding not expected to introduce bias
	Exposure misclassification bias	Probably low	Outdoor work defined by number of weighted hours in a lifetime, categorized as never, < 320, > 320–1128, > 1128–3878, > 3878; interviewers asked questions on sun exposure using a structured questionnaire arranged by periods of life (before first employment, during active life and after retirement), places of residence for ≥ 6 months and type of outdoor activity (work, holidays, sports or other outdoor recreational activities)
	Detection bias	Low	Microscopically confirmed diagnosis of primary SCC or BCC
	Confounding	Low	Logistic regression model adjusted by age, country of residence and significant independent host factors
	Incomplete outcome data bias	Probably low	No missing data on cancer outcome
	Reporting bias	Low	All the outcomes are reported
	Conflict of interest bias	Low	Funding from European Union Europe Against Cancer (grant nos SI2 129340, 99CVF2-015), Spanish Fund for Health Research and a foundation from Argentina promoting science
	Other bias	Probably low	Study appears to be free of other sources of bias

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Author, year Study type	Risk of bias domain	Rating	Justification for rating
Pelucchi et al., 2007 *(54)* Pelucchi 2007 Case–control	Selection bias	Low	Cases identified through a collaborative network of hospital-based dermatology and oncology centres; cases selected consecutively from participating hospitals during the study period following specific inclusion/exclusion criteria, and only 3% of eligible cases and controls refused participation; controls were identified through the same centres when presenting with non-cancer conditions; a total of 528 eligible cases and 512 controls entered the study; no important differences between participants and non-participants in terms of geographic origin, diagnoses, and age and sex distribution
	Performance bias	Probably low	No blinding; omission not expected to introduced important effects
	Exposure misclassification bias	Probably high	Detailed interviews on outdoor work, using standardized questionnaires and trained interviewers, of cases and controls to extract lifetime occupational sun exposure; subjects classified as "no occupational sun exposure" or "short/long duration of exposure", but no further specification provided
	Detection bias	Low	Histologically confirmed BCC
	Confounding	Low	Adjustment for possible confounders (age, sex, study centre, education, eye, hair and skin colour)
	Incomplete outcome data bias	Low	No evidence about incomplete outcome data
	Reporting bias	Probably low	No published protocol for this study; however, the description of the outcome of interest was outlined in the published manuscript's methods
	Conflict of interest bias	Low	Study authors report no conflict of interest; work conducted with contributions from the Italian Association for Cancer Research
	Other bias	Probably low	Apart from self-reported exposure, the study appears to be free of potential biases to assess the association between sun exposure and skin melanoma
Radespiel-Tröger et al., 2009[a] *(35)* Radespiel-Tröger 2009 Case–case	Selection bias	Probably low	A registry-based study in Bavaria with a well defined population and compulsory/voluntary registration of cancer cases backed by the law (full-scale registration commenced in the year 2002, 1 year after commencement of the study); however, only a few Bavarian districts could be included because of the inclusion/exclusion criteria of the study; histogram comparing study population and Bavarian population according to the municipalities was not available for viewing
	Performance bias	Probably low	Study utilized set methods with suitable reference to previous studies (for exposure classification) and the cancer registry (outcome measure); impact of assessor subjectivity therefore ruled out
	Exposure misclassification bias	Probably high	Exposure assessment was indirect with job titles classified as one of three broad categories (suitable reference made to three previous publications); proportion of missing values for work type in the registered cases was also fairly high (62% and 74% for BCC and SCC, respectively)
	Detection bias	Low	Outcome ascertainment was based on notifications sent to respective cancer registration authorities; cancer registry notifications include patient-related data (sex, age, residence, occupation), tumour-related data (date of diagnosis, cancer site and histology, malignancy grade, tumour-node-metastasis category) and basic treatment-related data; cancer diagnoses coded according to ICD-10 and ICD-O-3
	Confounding	Probably high	Age-adjusted estimates of relative risk calculated
	Incomplete outcome data bias	Probably low	Bavarian cancer registry data was likely complete on cancer outcome, despite study data aggregation commencing 1 year after full-scale cancer registration
	Reporting bias	Probably low	No published protocol for this study; however, the description of the outcome of interest was outlined in the published manuscript's method
	Conflict of interest bias	Probably low	It seems that all study authors were affiliated to a government agency and prohibited from involvement in projects for which there was (or was an appearance of) a conflict of interest

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Author, year Study type	Risk of bias domain	Rating	Justification for rating
	Other bias	Probably high	Study authors elaborated on four important limitations of this study; the potential for non-representation of the Bavarian population is noteworthy as well as high propensity for exposure misclassification and uncertain effect on precision as a result of a high proportion of missing values (job types)
Janković et al., 2010 *(55)* Janković 2010 Case–control	Selection bias	Probably high	Very little information about inclusion/exclusion criteria and selection of study participants in this dermatology clinic-based case–control study, where cases and controls were enrolled at the same centre during the same calendar period; participation rate not reported
	Performance bias	Probably low	No information on blinding, but the study appears to be free of bias
	Exposure misclassification bias	High	Exposure measured by standardized skin cancer questionnaires recording information on outdoor work during summer period (poorly documented)
	Detection bias	Low	Outcome confirmed histopathologically
	Confounding	Probably low	Study participants individually matched by sex and age; multivariate logistic regression analysis conducted, including occupational sun exposure variables and constitutional independent risk factors, as well as environmental sun exposure
	Incomplete outcome data bias	Low	No clear information provided, but there do not appear to be any issues
	Reporting bias	Probably low	No study protocol identified; all variables mentioned in the present study were reported
	Conflict of interest bias	Low	Authors declared an absence of conflict of interest; study was funded by a national grant
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias, but recall bias cannot be ruled out
Kenborg et al., 2010[a] *(36)* Kenborg 2010 Case–control	Selection bias	Probably low	All cases diagnosed during the study period and registered in the Danish cancer database; random selection of controls matched by sex and year of birth from the Danish Central Person Registry; similar eligibility criteria applied to cases and controls; cases and controls may not have come from same catchment population
	Performance bias	Probably low	No information on blinding; however, the study appears to be free of bias
	Exposure misclassification bias	Probably low	Job–exposure matrix for Denmark developed for the Nordic Occupational Cancer Study; however, there was no information on individual sun exposure; risk estimates provided for outdoor occupation overall and for specific occupations (i.e. forestry) by duration of employment obtained from records from pension plan; lifetime years of outdoor occupation calculated
	Detection bias	Low	Outcome confirmed histopathologically; distribution of subtypes presented
	Confounding	Probably low	Analysis adjusted for confounders including social class and skin colour; only males included; study matched cases and controls by year of birth
	Incomplete outcome data bias	Probably low	Only cases containing information about occupation and cancer were included; no reporting of risk estimates by NMSC subtypes
	Reporting bias	Low	All outcomes were reported
	Conflict of interest bias	Low	Study was supported by grants from the Danish Working Environment Authority
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias
Dessinioti et al., 2011 *(56)* Dessinioti 2011 Case–control	Selection bias	Probably low	Indirect evidence to suggest that inclusion/exclusion criteria, recruitment and enrolment procedures were consistent across groups
	Performance bias	Probably low	No blinding, but we judged that the outcome measures as well as the exposure measures were not likely to be influenced by a lack of blinding
	Exposure misclassification bias	High	Questions concerned the personal and family history of skin cancer and the history of sun exposure for recreational and occupational reasons; reference group could include study participants with up to 5 years of outdoor occupation; use of a reference group with such exposure allowance potentially introduces bias towards the null; methods not robust

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Author, year Study type	Risk of bias domain	Rating	Justification for rating
	Detection bias	Low	"From 2006 to 2009, patients with a new diagnosis of histologically confirmed BCC were asked to participate in the study." (p. 622) There is indirect evidence to suggest that methods were robust
	Confounding	Probably low	The study appropriately accounted for most, but not all, of the important confounders: "logistic regression models were employed to obtain age- and sex- adjusted odd ratios (OR) of BCC as well as OR adjusted for constitutional risk factors and sun exposure patterns along with their corresponding 95% confidence intervals (95% CI)" (p. 623)
	Incomplete outcome data bias	Probably low	Evidence that incomplete outcome data not capable of introducing bias in the study
	Reporting bias	Low	All of the study's pre-specified (primary and secondary) outcomes outlined in the pre-published protocol or the published manuscript's methods, abstract and/or introduction section that are of interest in this review have been reported in the pre-specified way
	Conflict of interest bias	Low	Authors declared an absence of conflict of interest; no funding declared; authors affiliated with oncology and dermatology departments of hospitals linked to academic centres
	Other bias	Probably low	Recall bias cannot be ruled out; problem with sample size calculation
Ferreira et al., 2011 *(57)* Ferreira 2011 Case–control	Selection bias	Probably high	Descriptions of the source population, inclusion/exclusion criteria, recruitment and enrolment procedures presented in this hospital-based case–control study; group of controls selected is described as a convenience sample among all non-cancer dermatology patients attending same centre as cases; controls were somewhat younger than cases and sex distribution is not shown in cases and controls; participation rates not provided
	Performance bias	Probably low	Blinding not part of the recruitment of the case–control study; questionnaire delivered by study author
	Exposure misclassification bias	High	Quantitative and qualitative exposures were all self-reported; mode of collection is not clear; although several occupational exposure variables were available, the reference category included exposed subjects; the adjusted effect estimate extracted was generated using an "unexposed" or comparison group with some exposure allowance, potentially introducing bias towards the null
	Detection bias	Low	Outcome histopathologically confirmed
	Confounding	Probably low	Variables adjusted for confounding included age, sex, phototype and interaction in the first model
	Incomplete outcome data bias	Probably low	Case–control study; no incomplete outcome data; outcome pre-defined in introduction and methods section; however, information was lost by reporting risk estimates for overall NMSC and not by cancer subtype
	Reporting bias	Probably low	No study protocol identified; all the variables mentioned in the present study were reported
	Conflict of interest bias	Low	Authors declared no conflict of interest; no statement regarding funding source; authors are affiliated with an academic centre
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias, but recall bias cannot be ruled out
Iannacone et al., 2012 *(58)* Iannacone 2012 Case–control	Selection bias	Probably low	In this university- and clinic-based case–control study, cases were recruited from dermatology clinic and controls from family medicine clinic at the same centre and at a second medical centre at the same time (participation rates: 80%, 47%, and 65%, respectively); responders and refusals were comparable in terms of sex and age; eligibility criteria and recruitment procedures described; majority of recruited participants completed the self-compiled questionnaire; few demographic significant differences between enrolled cases and controls
	Performance bias	Probably low	No information about blinding; physicians performed interviews and should have been aware of the status of participants, however, this had no influence on the study

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Author, year Study type	Risk of bias domain	Rating	Justification for rating
	Exposure misclassification bias	Probably low	Patterns of sunlight exposure were measured using a self-completed questionnaire including ever outdoor work and duration: no. years with a job exposed to sunlight for ≥ 3 months per year (< 1, 1–5, 6–10 or > 10 years)
	Detection bias	Low	Patients with histologically confirmed BCC or SCC
	Confounding	Low	Variables adjusted for included age, sex, education level and smoking status; further adjustments in regression (ethnicity, eye and hair colour, cutaneous sensitivity and tanning ability)
	Incomplete outcome data bias	Low	Patients with incomplete data were excluded
	Reporting bias	Probably low	No study protocol identified; all variables mentioned in the present study were reported
	Conflict of interest bias	Low	National government funding sources
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias, but recall bias cannot be ruled out
Sanchez et al., 2012 *(59)* Sanchez 2012 Case–control	Selection bias	Probably low	Sample size calculated; all consecutive newly diagnosed cases in the dermatologic national centre were included; controls selected from the same centre among patients without neoplastic disease or patients without recommendations to avoid sun exposure; selection of controls not described; no response rate cited for controls invited to participate; as centre is a national referral centre for dermatology, cases and controls may not be from the same baseline population
	Performance bias	Probably low	No blinding, but we judged that the outcome measures and exposure measures were not likely to be influenced by this
	Exposure misclassification bias	Probably high	Exposure of interest was obtained from information collected in questionnaire: lifetime outdoor occupational activity by age at exposure (< 15, 15–30, > 30 years); exposure variable used in multivariate analysis was outdoor occupational activities when aged > 30 years
	Detection bias	Low	Newly diagnosed patients with histologically confirmed BCC in 2010 were enrolled
	Confounding	Probably low	Study appropriately accounted for most, but not all, of the important confounders (Tier 1) as well as some of the other potentially relevant and important confounders (Tier 2), using appropriate statistical techniques
	Incomplete outcome data bias	Probably high	It is not known whether controls had a history of skin cancer
	Reporting bias	Probably low	All of the study's pre-specified (primary and secondary) outcomes outlined in the pre-published protocol or the published manuscript's methods, abstract and/or introduction section that are of interest in this review were reported in the pre-specified way
	Conflict of interest bias	Low	Authors declared absence of a conflict of interest; study conducted and financed by National Dermatology Center of Colombia
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias, but recall bias cannot be ruled out
Surdu et al., 2013 *(60)* Surdu 2013 Case–control	Selection bias	Probably low	Description of participant recruitment was published previously; indirect evidence to suggest that inclusion/exclusion criteria, recruitment and enrolment procedures, and participation and follow-up rates were consistent across groups
	Performance bias	Low	Occupational exposures were ascertained by local experts in industrial hygiene or occupational health, who were blinded to the case status
	Exposure misclassification bias	Probably high	Participants were interviewed at hospital or at home within 3 months of enrolment using a questionnaire developed specifically for the Arsenic Health Risk Assessment and Molecular Epidemiology Study; self-reported occupational history collected; exposure metrics included ever exposed occupationally to natural solar UVR and cumulative life exposure by tertile: ≤ 1225, 1225.5–5075 and > 5075 hours; indirect evidence to suggest that methods were not robust

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Author, year Study type	Risk of bias domain	Rating	Justification for rating
	Detection bias	Probably low	NMSC histologically confirmed in 94% of cases; BCC and SCC with known heterogeneity were combined
	Confounding	Low	Skin complexion, family history of cancer and lifetime average exposure to arsenic in drinking water were identified as confounding factors (i.e. statistically significant association with both occupational exposure to UVR in controls and NMSC among unexposed participants) and included in the final multivariable regression models, along with the matching variables sex, age and county of residence
	Incomplete outcome data bias	Probably low	Incomplete outcome characterization, contributing to loss of information (BCC and SCC risks unknown)
	Reporting bias	Probably low	All of the study's pre-specified (primary and secondary) outcomes outlined in the pre-published protocol or the published manuscript's methods, abstract and/or introduction section that are of interest in this review were reported in the pre-specified way
	Conflict of interest bias	Low	Financial support provided by European Commission project QLK4-CT-2001-00264 (Arsenic Health Risk Assessment and Molecular Epidemiology Study)
	Other bias	Probably low	Recall bias cannot be ruled out
Kaskel et al., 2015[a] *(37)* Kaskel 2015 Case–control	Selection bias	Probably low	Source population not specified, but controls recruited from same institution, including same and additional department as cases, implying the same catchment population; eligibility and exclusion criteria were described; participation rate not disclosed; cases recruited from dermatology clinic and controls from allergology and phlebology unit at the same time
	Performance bias	Probably low	Blinding is not an element of study design in this study; absence of it is not expected to have introduced important risk of bias
	Exposure misclassification bias	Probably high	Only items summarizing UVR behaviour were used to describe exposure to UVR light; unclear whether this method was also used for occupational exposure; occupation in farming as proxy of exposure (comparing "full-time farming" with "no farming") problematic, as "no farming" could include occupations with sun exposure; crude estimate provided for occupational sun exposure using the contrast often/sometimes versus few/no
	Detection bias	Low	Body inspection using a tool and histopathologically confirmed cases
	Confounding	Probably high	Confounding was not mentioned, but there are data on confounders collected and analysis adjusted for potential confounders; however, the comparison "farming" versus "no farming" has problems for the comparator; only an unadjusted risk estimate provided for occupational sun exposure using the contrast often/sometimes versus few/no
	Incomplete outcome data bias	Probably low	No clear information provided, but there do not appear to be any issues
	Reporting bias	Probably low	No study protocol identified; all the variables mentioned in the present study were reported
	Conflict of interest bias	Probably low	No conflict of interest declared; work performed at and funded by academic centres; one author joined industry after completion of the operational part of the project, and is currently employed at Outcomes Research, Mercke Sharp & Dohme (MSD) GMBH, Haar, Germany; disclaimer reports that data presented in publication are in no way connected with professional activities at MSD GMBH
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias
Trakatelli et al., 2016[a] *(39)* Trakatelli 2016 Case–control	Selection bias	Probably high	Sparse information provided on selection of study participants; data for this study came from the EPIDERM case–control study, a large multicentre hospital-based case–control study (conducted in Finland, Germany, Greece, Italy, Malta, Poland, Scotland and Spain), including 409 patients with SCC and 602 with BCC and 1550 controls; participation rate in cases and controls not reported
	Performance bias	Probably low	Exposure self-reported and by non-blinded clinicians

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Author, year Study type	Risk of bias domain	Rating	Justification for rating
	Exposure misclassification bias	Probably high	Interview based on the simple question: "Have you ever had an outdoor occupation (yes/no)"; outdoor workers subdivided according to the self-reported total duration of outdoor work: < 1 year (n = 72), 1 to < 5 years (n = 155) and ≥ 5 years (n = 1185), the latter exposure group not being very informative
	Detection bias	Low	Histologically confirmed cases, although only verbal skin cancer history for controls
	Confounding	Probably low	Model A corrected for country, age, sex and phototype, and Model B for these as well as sunscreen use in own country, smoking and outdoor hobbies
	Incomplete outcome data bias	Low	Evidence that the incomplete outcome data were not capable of introducing risk of bias in the study
	Reporting bias	Low	All of the study's pre-specified (primary and secondary) outcomes outlined in the pre-published protocol or the published manuscript's methods, abstract and/or introduction section that are of interest in this review have been reported in the pre-specified way
	Conflict of interest bias	High	Publication is based on data from the EPIDERM project, funded by the European Commission's Executive Agency for Health and Consumers (PHEA2007–A/100994HI); first and fifth authors received grants from Leo Pharma specifically for their time dedicated to study the association between skin cancer and outdoor occupation; first author affiliated to a university hospital in Greece and a second hospital in Belgium, and is a speaker for Leo Pharma, Janssen-Cilag
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias
Schmitt et al., 2018 *(61, 62)* Schmitt 2018 Case–control	Selection bias	Probably low	"At each of the eight main study sites, sex and age-weighted population-based controls were recruited from local residents' registration offices by mail and offered physical examination and study participation" (p. 37 (*61*)) Cases and controls recruited at the same time, matched and from the same clinics belonging to a national dermatology network, allowing identification of consecutive incident cancers; participation rates provided
	Performance bias	Low	Researchers classifying sun exposure were blinded about the case or control status of the study participants
	Exposure misclassification bias	Low	Lifetime occupational UVR exposure measured by interview in cases and controls using a comprehensive and standardized tool and classified according to matrix; lifetime exposure calculated as the sum of all annual dosages throughout the different periods of working life: < 44th percentile (0 SED), 44th to < 60th percentile (> 0–532.1 SED), 60th to < 90th percentile (532.2–5870.4 SED) and 90th percentile (> 5870.5 SED)
	Detection bias	Low	Outcome histopathologically confirmed
	Confounding	Probably low	Analysis adjusted for several but not all important confounders (sex, age, phototype, non-occupational sun exposure)
	Incomplete outcome data bias	Probably low	No clear indication on how this was managed, but there does not appear to be a problem
	Reporting bias	Probably low	Study protocol reports the variables they intended to use in their study
	Conflict of interest bias	Low	Study funded by a grant from the German Social Accident Insurance (DGUV); authors declared absence of a conflict of interest
	Other bias	Probably low	Study appears to be free of other problems that can introduce bias

BCC, basal cell carcinoma; CI, confidence interval; ICD, International Classification of Diseases; OR, odds ratio; NMSC, non-melanoma skin cancer; SCC, squamous cell carcinoma; SED, standard erythema doses; UVR, ultraviolet radiation.

[a] Risk of bias ratings also apply to the health outcome of melanoma incidence (see Table A5.1).

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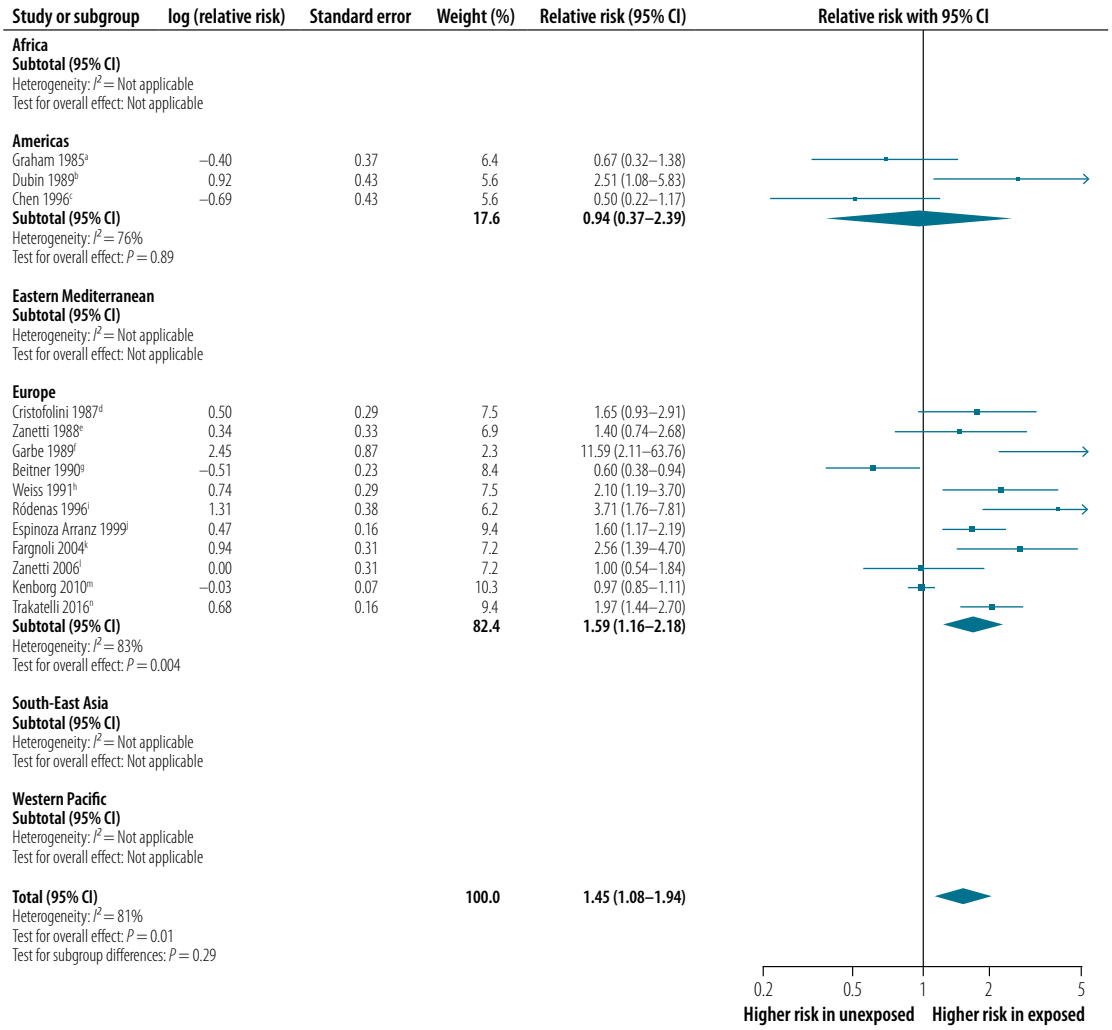
Annex 6. Subgroup analyses

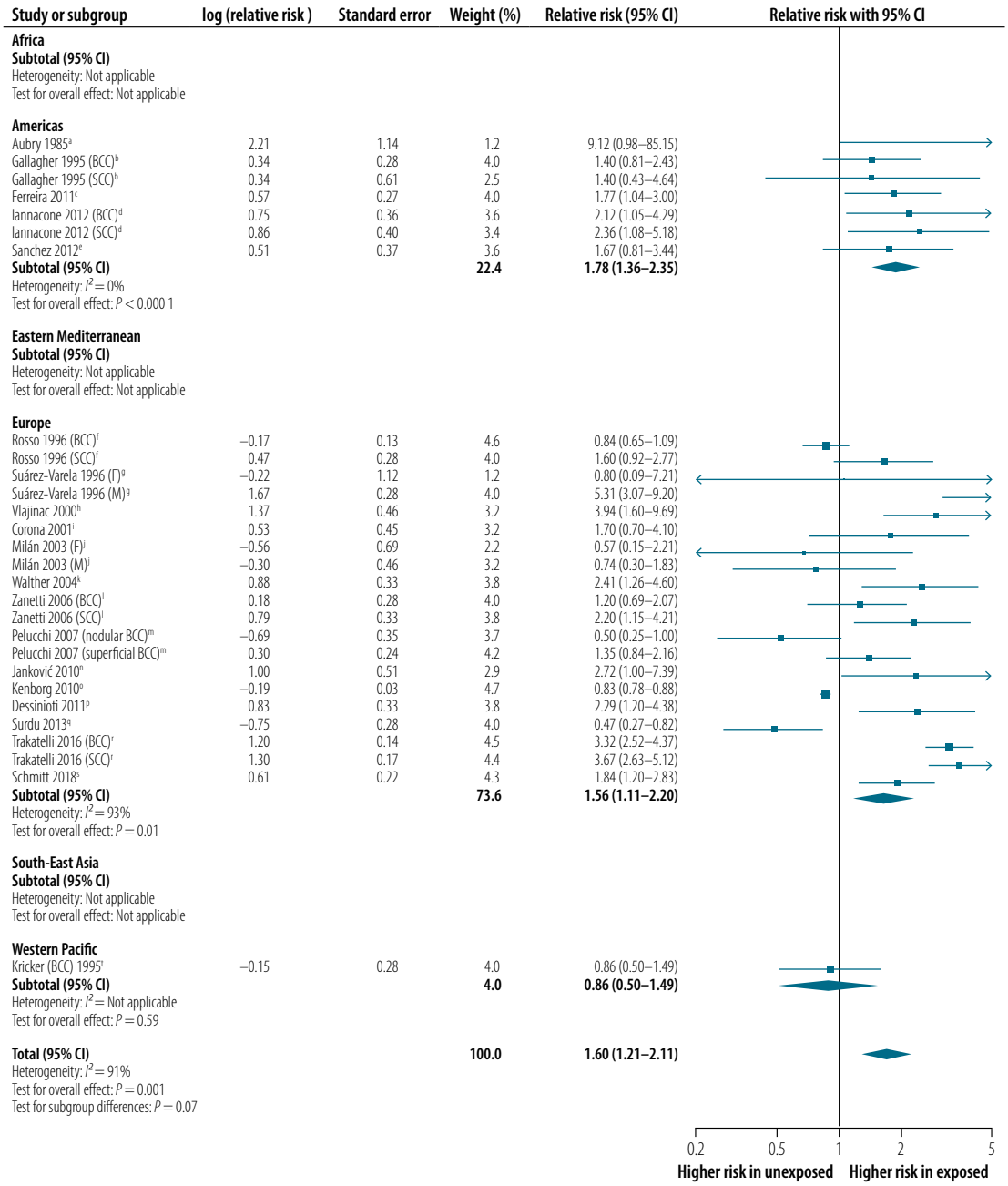
Fig. A6.1. Subgroup analysis of main meta-analysis of studies reporting on the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence, by WHO region



CI, confidence interval.

Notes: [a] Graham et al., 1985 ***(1)***; [b] Dubin et al., 1989, 1990 ***(2, 3)***; [c] Chen et al., 1996 ***(4)***; [d] Cristofolini et al., 1987 ***(5)***; [e] Zanetti et al., 1988, 1999 ***(6, 7)***, Rosso et al., 1998, 2008 ***(8, 9)***; [f] Garbe et al., 1989 ***(10)***; [g] Beitner et al., 1990 ***(11)***; [h] Weiss et al., 1991 ***(12)***; [i] Ródenas et al., 1996 ***(13)***; [j] Espinosa Arranz et al., 1999 ***(14)***; [k] Fargnoli et al., 2004 ***(15)***; [l] Zanetti et al., 2006 ***(16)***; [m] Kenborg et al., 2010 ***(17)***; [n] Trakatelli et al., 2016 ***(18)***.

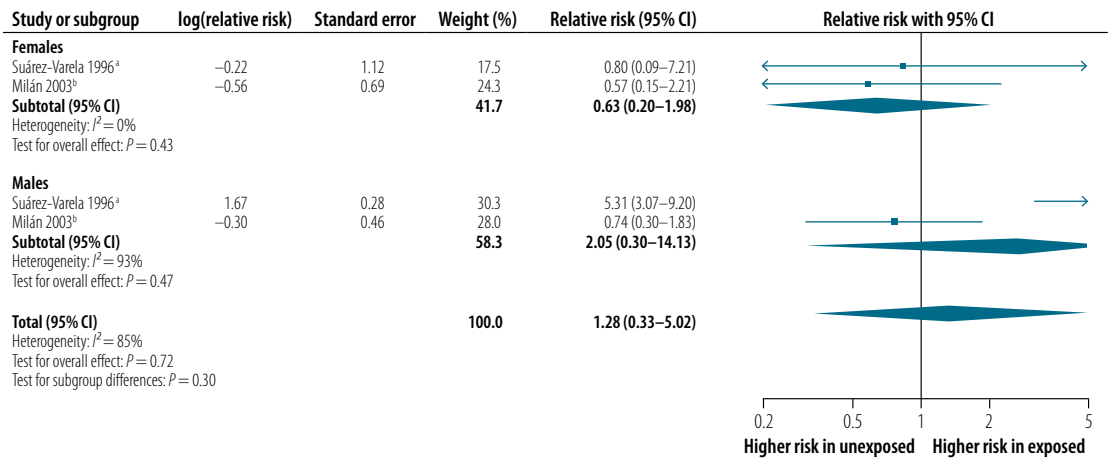
Fig. A6.2. Subgroup analysis of main meta-analysis of studies reporting on the association between occupational exposure to solar ultraviolet radiation and non–melanoma skin cancer incidence, by WHO region



BCC, basal cell carcinoma; CI, confidence interval; F, females; M, males; SCC, squamous cell carcinoma.

Notes: [a] Aubry & MacGibbon, 1985 ***(19)***; [b] Gallagher et al., 1995 ***(20, 21)***; [c] Ferreira et al., 2001 ***(22)***; [d] Iannacone et al., 2012 ***(23)***; [e] Sanchez et al. 2012 ***(24)***; [f] Rosso et al., 1996 ***(25)***, 1998 ***(8)***; [g] Suárez-Varela et al., 1996 ***(26)***; [h] Vlajinac et al., 2000 ***(27)***; [i] Corona et al., 2001 ***(28)***; [j] Milán et al., 2003 ***(29)***; [k] Walther et al., 2004 ***(30)***; [l] Zanetti et al., 2006 ***(31)***; [m] Pelucchi et al., 2007 ***(32)***; [n] Janković et al., 2010 ***(33)***; [o] Kenborg et al., 2010 ***(17)***; [p] Dessinioti et al., 2011 ***(34)***; [q] Surdu et al., 2013 ***(35)***; [r] Trakatelli et al., 2016 ***(18)***; [s] Schmitt et al., 2018 ***(36, 37)***; [t] Kricker et al. 1995 ***(38)***.

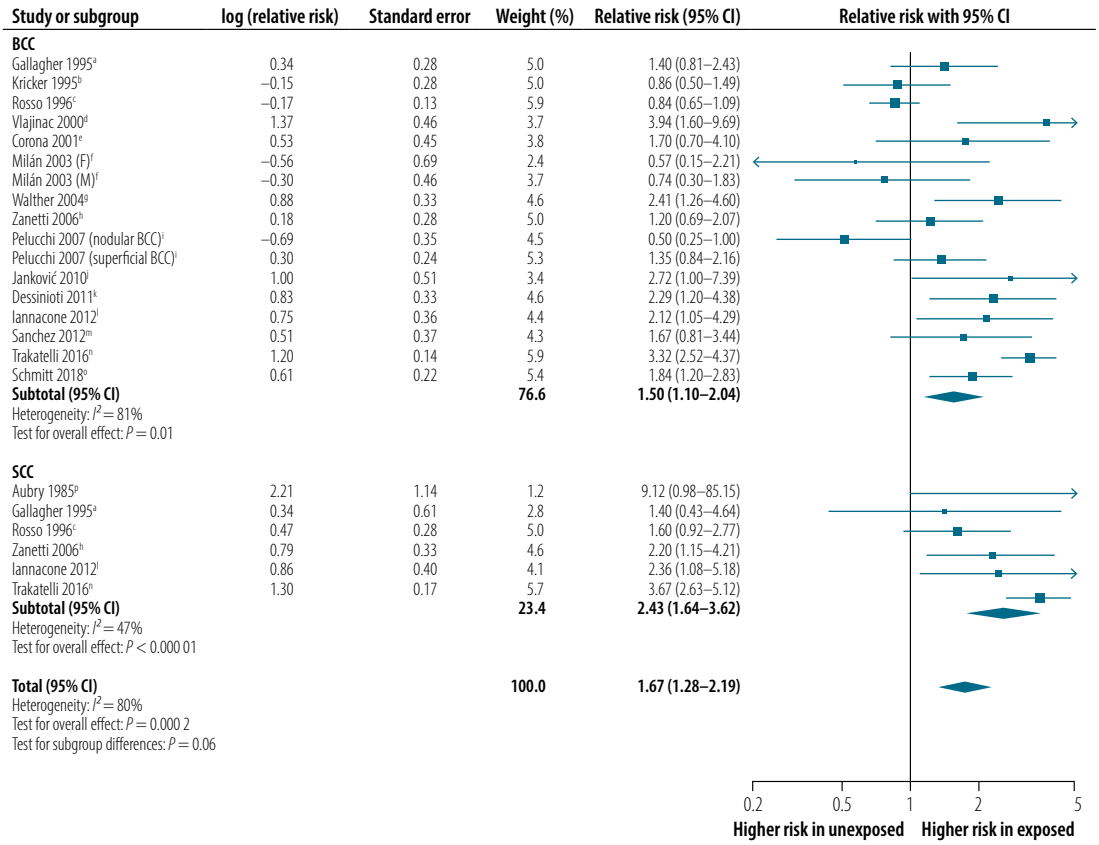
Fig. A6.3. Subgroup analysis of main meta-analysis of studies reporting on the association between occupational exposure to solar ultraviolet radiationand non–melanoma skin cancer incidence, by sex



CI, confidence interval.

Notes: [a] Suárez-Varela et al., 1996 *(26)*; [b] Milán et al., 2003 *(29)*.

Fig. A6.4. Subgroup analysis of main meta-analysis of studies reporting on the association between occupational exposure to solar ultraviolet radiation and non–melanoma skin cancer incidence, by subtype



BCC, basal cell carcinoma; CI, confidence interval; F, females; M, males.

Notes: [a] Gallagher et al., 1995 ***(20, 21)***; [b] Kricker et al., 1995 ***(38)***; [c] Rosso et al., 1996 ***(25)***, 1998 (8); [d] Vlajinac et al., 2000 ***(27)***; [e] Corona et al., 2001 ***(28)***; [f] Milán et al., 2003 ***(29)***; [g] Walther et al., 2004 ***(30)***; [h] Zanetti et al., 2006 ***(31)***; [i] Pelucchi et al., 2007 ***(32)***; [j] Janković et al., 2010 ***(33)***; [k] Dessinioti et al., 2011 ***(34)***; [l] Iannacone et al., 2012 ***(23)***; [m] Sanchez et al., 2012 ***(24)***; [n] Trakatelli et al., 2016 ***(18)***; [o] Schmitt et al., 2018 ***(37)***; [p] Aubry & MacGibbon, 1985 ***(19)***.

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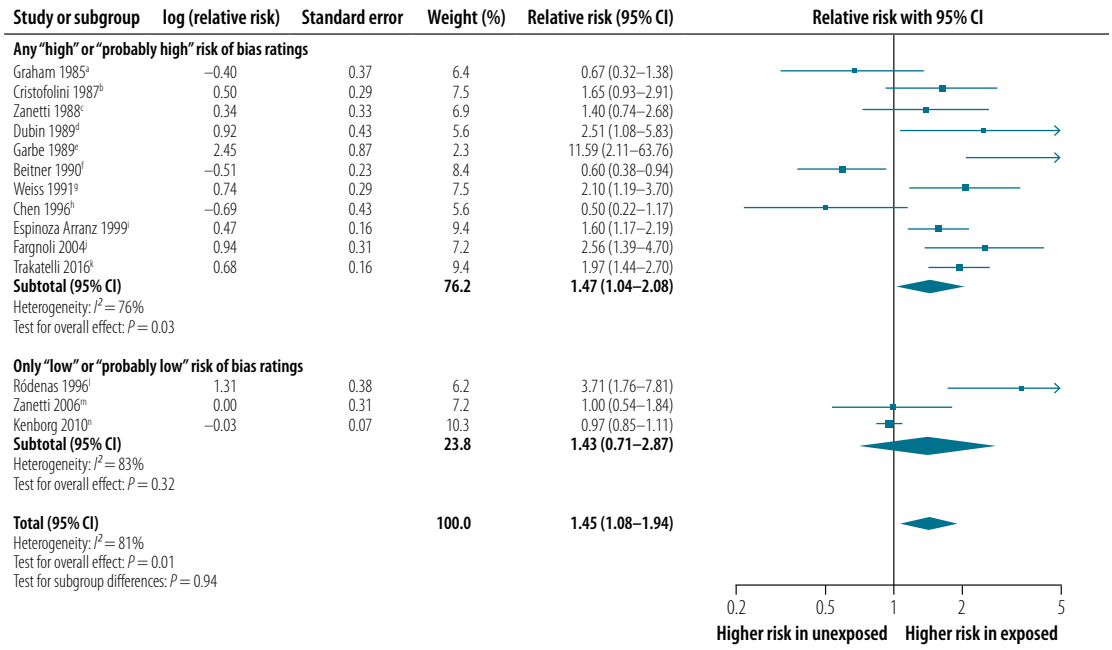
Annex 7. Sensitivity analyses

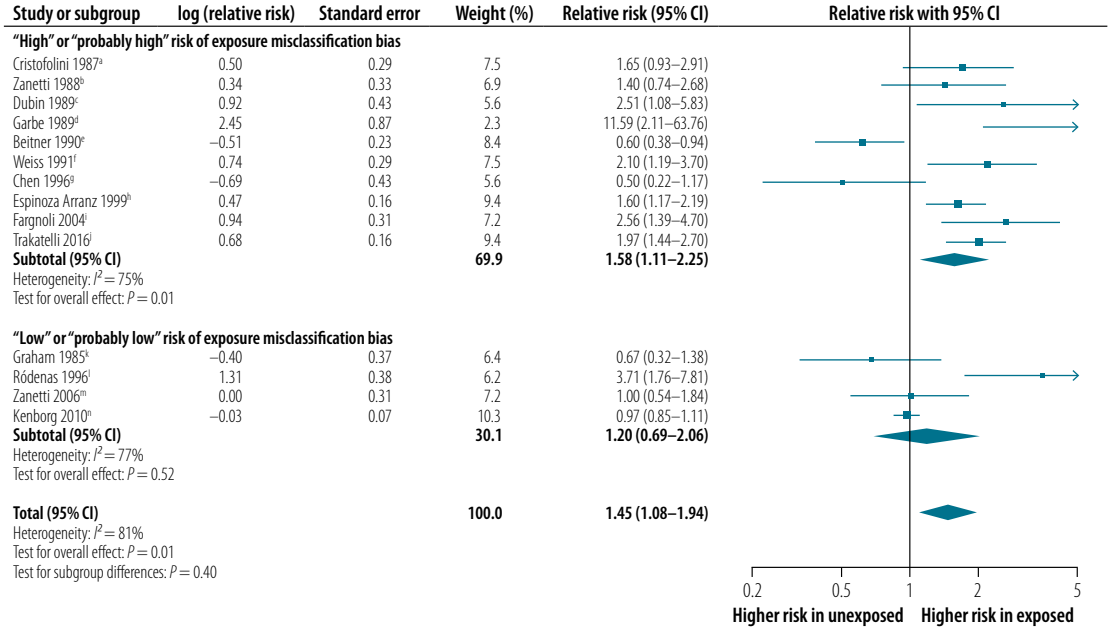
Fig. A7.1. Sensitivity analysis of studies judged to have a "high" or "probably high" risk of bias in any domain, compared with those with a "low" or "probably low" risk of bias in all domains, for the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence



CI, confidence interval.

Notes: [a] Graham et al., 1985 ***(1)***; [b] Cristofolini et al., 1987 ***(2)***; [c] Zanetti et al., 1988, 1999 ***(3, 4)***, Rosso et al., 1998, 2008 ***(5, 6)***; [d] Dubin et al., 1989, 1990 ***(7, 8)***; [e] Garbe et al., 1989 ***(9)***; [f] Beitner et al., 1990 ***(10)***; [g] Weiss et al., 1991 ***(11)***; [h] Chen et al., 1996 ***(12)***; [i] Espinosa Arranz et al., 1999 ***(13)***; [j] Fargnoli et al., 2004 ***(14)***; [k] Trakatelli et al., 2016 ***(15)***; [l] Ródenas et al., 1996 ***(16)***; [m] Zanetti et al., 2006 ***(17)***; [n] Kenborg et al., 2010 ***(18)***.

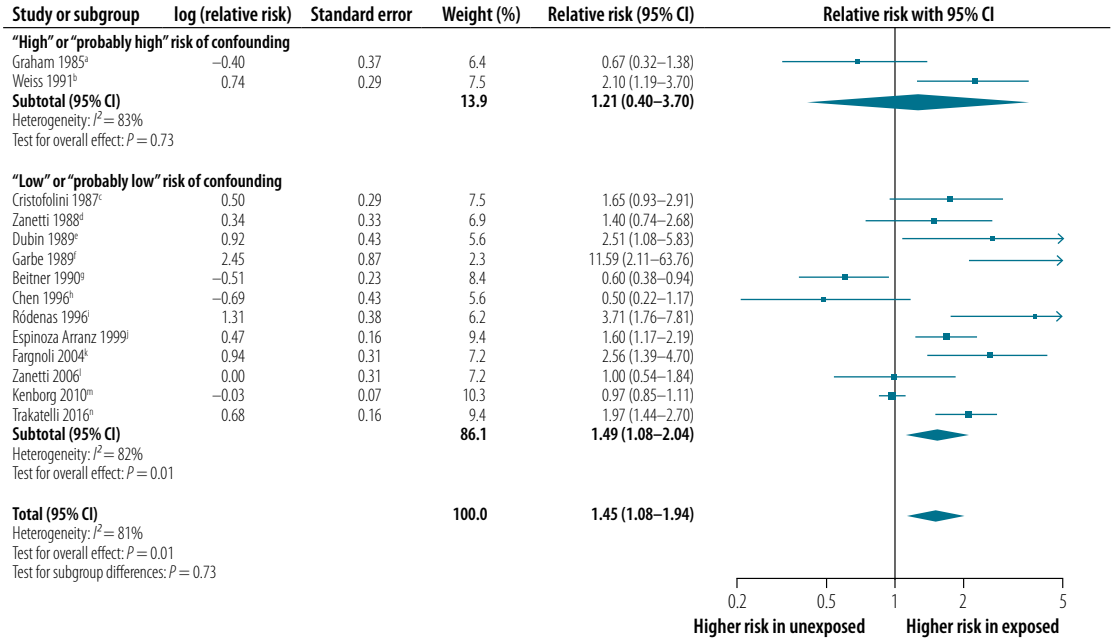
Fig. A7.2. Sensitivity analysis for studies judged to have a "low" or "probably low" risk of exposure misclassification bias, compared with studies judged to have a "high" or "probably high" risk of bias in this domain, for the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence



CI, confidence interval.

Notes: [a] Cristofolini et al., 1987 ***(2)***; [b] Zanetti et al., 1988, 1999 ***(3, 4)***, Rosso et al., 1998, 2008 ***(5, 6)***; [c] Dubin et al., 1989, 1990 ***(7, 8)***; [d] Garbe et al., 1989 ***(9)***; [e] Beitner et al., 1990 ***(10)***; [f] Weiss et al., 1991 ***(11)***; [g] Chen et al., 1996 ***(12)***; [h] Espinosa Arranz et al., 1999 ***(13)***; [i] Fargnoli 2004 ***(14)***; [j] Trakatelli et al., 2016 ***(15)***; [k] Graham et al., 1985 ***(1)***; [l] Ródenas et al., 1996 ***(16)***; [m] Zanetti 2006 ***(17)***; [n] Kenborg 2010 ***(18)***.

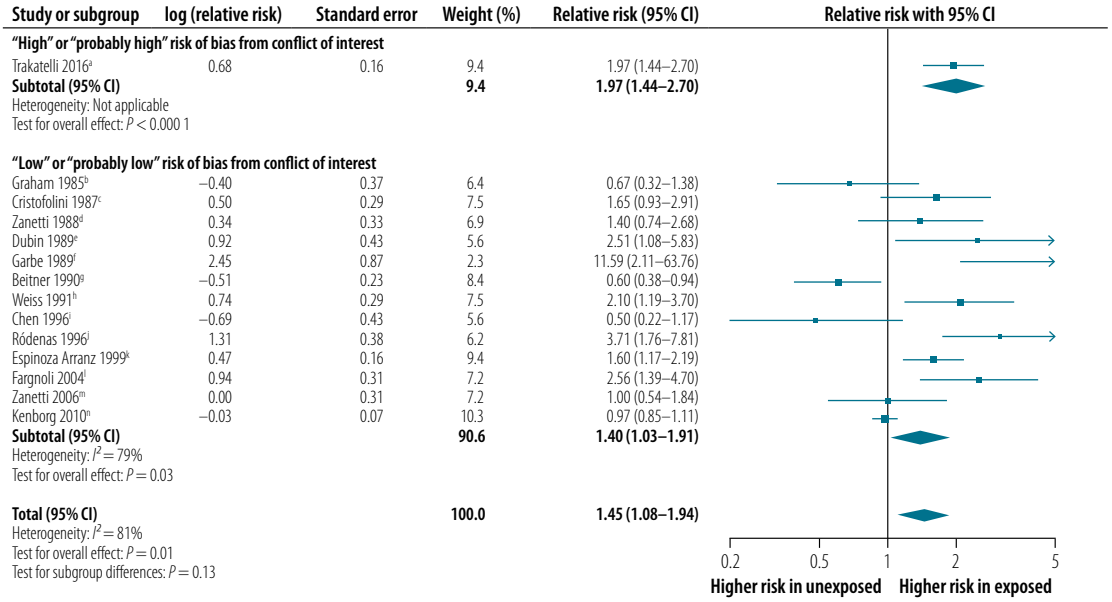
Fig. A7.3. Sensitivity analysis for studies judged to have a "low" or "probably low" risk of confounding, compared with studies judge to have a "high" or "probably high" risk of confounding, for the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence



CI, confidence interval.

Notes: [a] Graham et al., 1985 ***(1)***; [b] Weiss et al., 1991 ***(11)***; [c] Cristofolini et al., 1987 ***(2)***; [d] Zanetti et al., 1988, 1999 ***(3, 4)***, Rosso et al., 1998, 2008 ***(5, 6)***; [e] Dubin et al., 1989, 1990 ***(7, 8)***; [f] Garbe et al., 1989 ***(9)***; [g] Beitner et al., 1990 ***(10)***; [h] Chen et al., 1996 ***(12)***; [i] Ródenas et al., 1996 ***(16)***; [j] Espinosa Arranz et al., 1999 ***(13)***; [k] Fargnoli 2004 ***(14)***; [l] Zanetti 2006 ***(17)***; [m] Kenborg 2010 ***(18)***; [n] Trakatelli et al., 2016 ***(15)***.

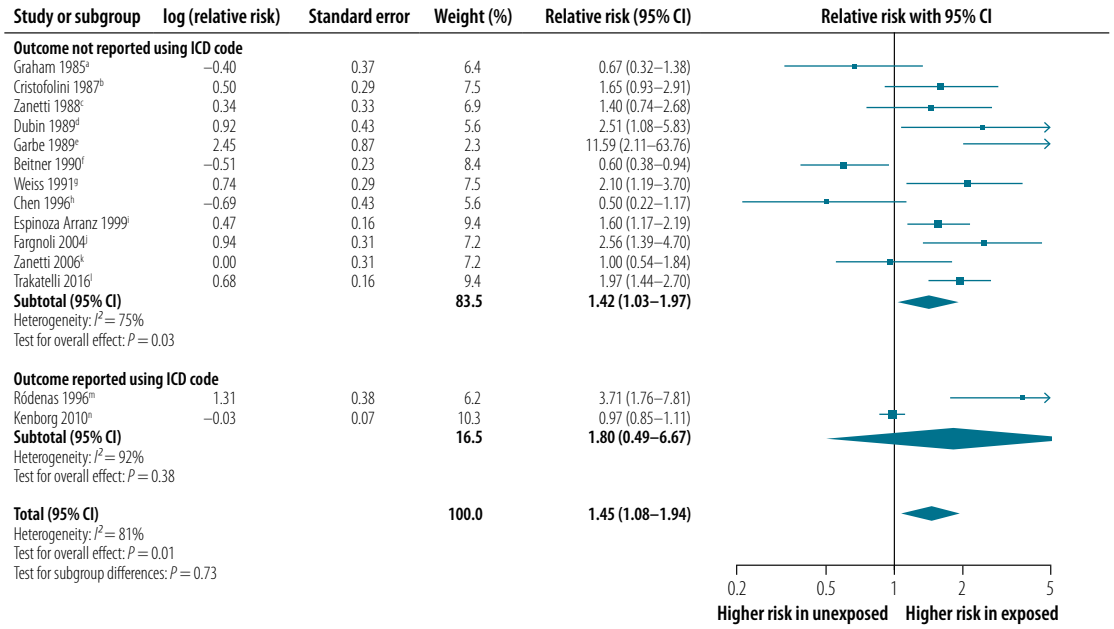
Fig. A7.4. Sensitivity analysis of studies judged to have a "low" or "probably low" risk of conflict of interest bias compared with studies judged to have a "high" or "probably high" risk of bias in this domain, for the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence



CI, confidence interval.

Notes: [a] Trakatelli et al., 2016 ***(15)***; [b] Graham et al., 1985 ***(1)***; [c] Cristofolini et al., 1987 ***(2)***; [d] Zanetti et al., 1988, 1999 ***(3, 4)***, Rosso et al., 1998, 2008 ***(5, 6)***; [e] Dubin et al., 1989, 1990 ***(7, 8)***; [f] Garbe et al., 1989 ***(9)***; [g] Beitner et al., 1990 ***(10)***; [h] Weiss et al., 1991 ***(11)***; [i] Chen et al., 1996 ***(12)***; [j] Ródenas et al., 1996 ***(16)***; [k] Espinosa Arranz et al., 1999 ***(13)***; [l] Fargnoli 2004 ***(14)***; [m] Zanetti 2006 ***(17)***; [n] Kenborg 2010 ***(18)***.

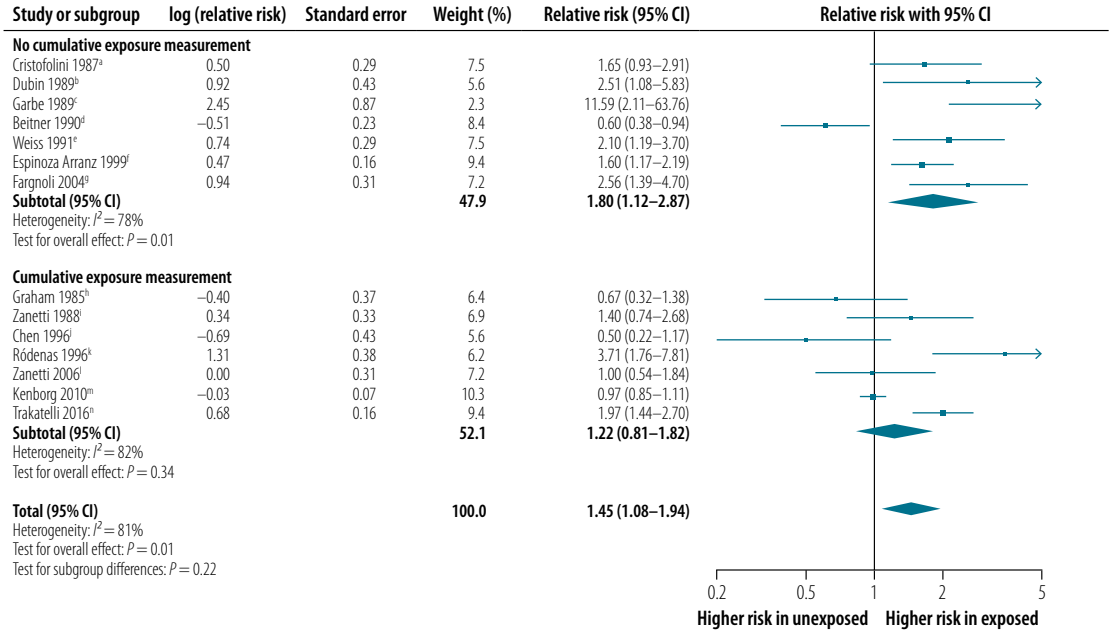
Fig. A7.5. Sensitivity analysis for studies with reported or approximated ICD-10 diagnostic codes, compared with studies without ICD-10 diagnostic codes, for the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence



CI, confidence interval; ICD, International Classification of Diseases.

Notes: [a] Graham et al., 1985 ***(1)***; [b] Cristofolini et al., 1987 ***(2)***; [c] Zanetti et al., 1988, 1999 ***(3, 4)***, Rosso et al., 1998, 2008 ***(5, 6)***; [d] Dubin et al., 1989, 1990 ***(7, 8)***; [e] Garbe et al., 1989 ***(9)***; [f] Beitner et al., 1990 ***(10)***; [g] Weiss et al., 1991 ***(11)***; [h] Chen et al., 1996 ***(12)***; [i] Espinosa Arranz et al., 1999 ***(13)***; [j] Fargnoli 2004 ***(14)***; [k] Zanetti 2006 ***(17)***; [l] Kenborg 2010 ***(18)***; [m] Ródenas et al., 1996 ***(16)***; [n] Trakatelli et al., 2016 ***(15)***.

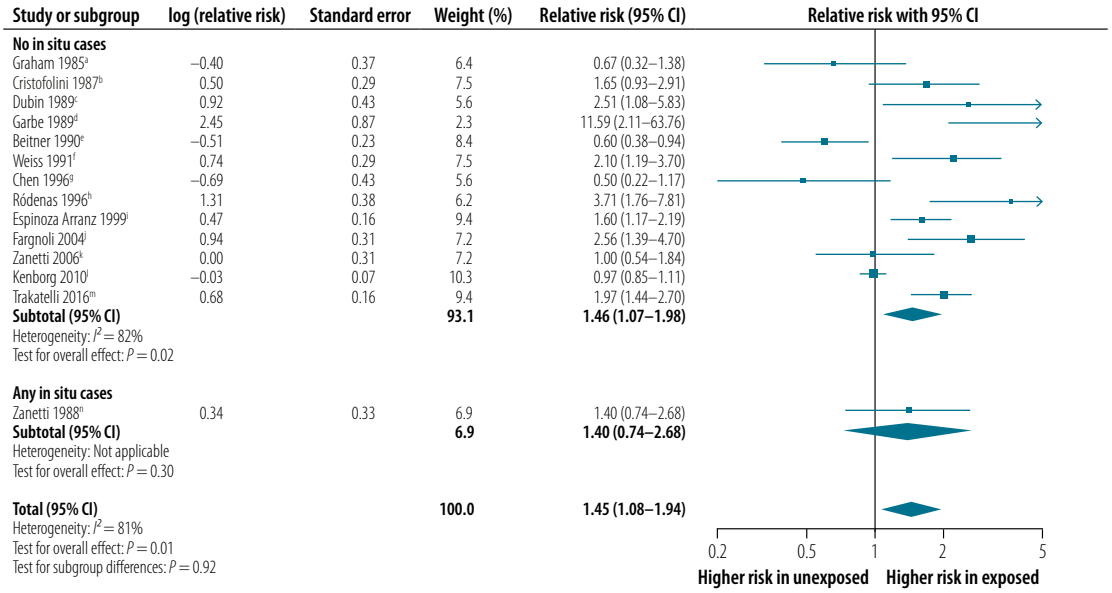
Fig. A7.6. Sensitivity analysis for studies that did not measure the exposure as a cumulative measure, compared with studies that measured the exposure as a cumulative measure, for the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence



CI, confidence interval.

Notes: [a] Cristofolini et al., 1987 ***(2)***; [b] Dubin et al., 1989, 1990 ***(7, 8)***; [c] Garbe et al., 1989 ***(9)***; [d] Beitner et al., 1990 ***(10)***; [e] Weiss et al., 1991 ***(11)***; [f] Espinosa Arranz et al., 1999 ***(13)***; [g] Fargnoli 2004 ***(14)***; [h] Graham et al., 1985 ***(1)***; [i] Zanetti et al., 1988, 1999 ***(3, 4)***, Rosso et al., 1998, 2008 ***(5, 6)***; [j] Chen et al., 1996 ***(12)***; [k] Ródenas et al., 1996 ***(16)***; [l] Zanetti 2006 ***(17)***; [m] Kenborg 2010 ***(18)***; [n] Trakatelli et al., 2016 ***(15)***.

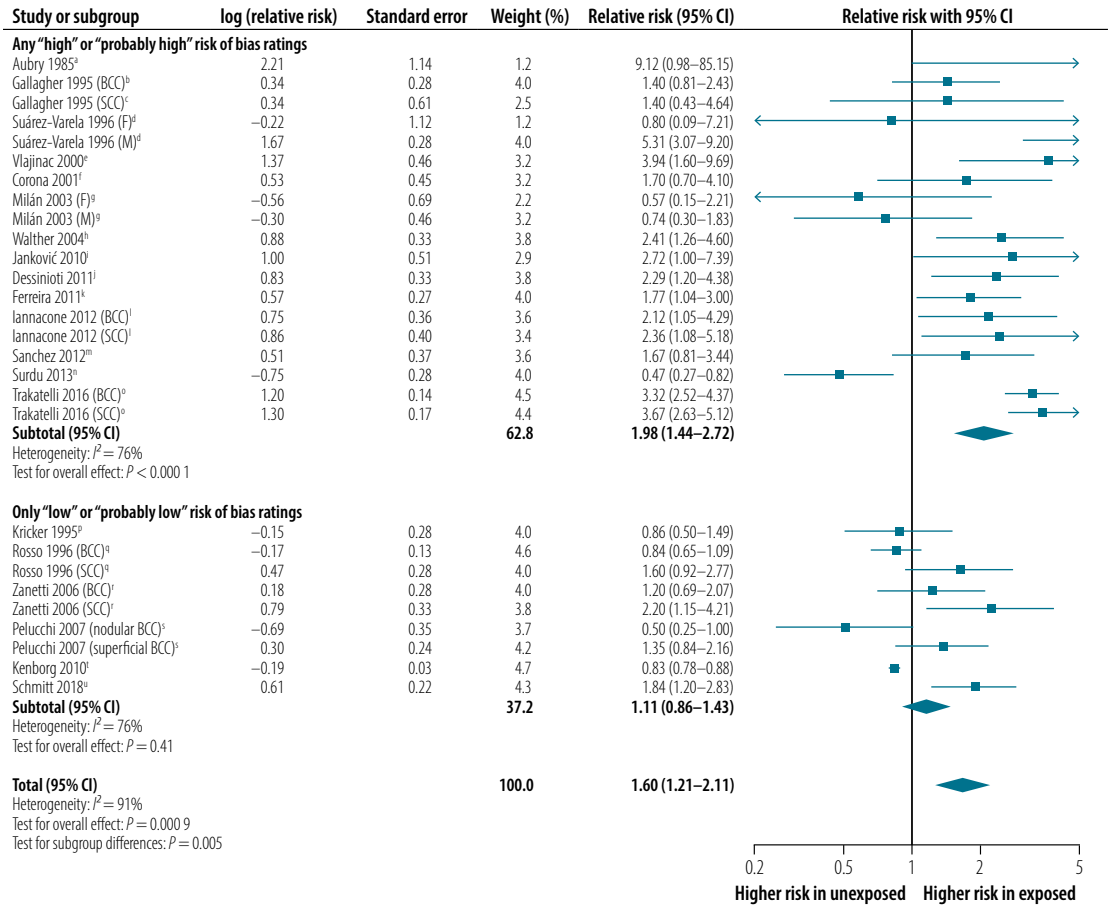
Fig. A7.7. Sensitivity analysis for studies that defined the outcome as including any in situ cases (≤ 5%), compared with studies with no in situ cases, for the association between occupational exposure to solar ultraviolet radiation and malignant skin melanoma incidence



CI, confidence interval.

Notes: [a] Graham et al., 1985 ***(1)***; [b] Cristofolini et al., 1987 ***(2)***; [c] Dubin et al., 1989, 1990 ***(7, 8)***; [d] Garbe et al., 1989 ***(9)***; [e] Beitner et al., 1990 ***(10)***; [f] Weiss et al., 1991 ***(11)***; [g] Chen et al., 1996 ***(12)***; [h] Ródenas et al., 1996 ***(16)***; [i] Espinosa Arranz et al., 1999 ***(13)***; [j] Fargnoli 2004 ***(14)***; [k] Zanetti 2006 ***(17)***; [l] Kenborg 2010 ***(18)***; [m] Trakatelli et al., 2016 ***(15)***; [n] Zanetti et al., 1988, 1999 ***(3, 4)***, Rosso et al., 1998, 2008 ***(5, 6)***.

Fig. A7.8. Sensitivity analysis for studies judged to have a "high" or "probably high" risk of bias in any domain, compared with "low" or "probably low" risk of bias in all domains, for the association between occupational exposure to solar ultraviolet radiation and non–melanoma skin cancer incidence

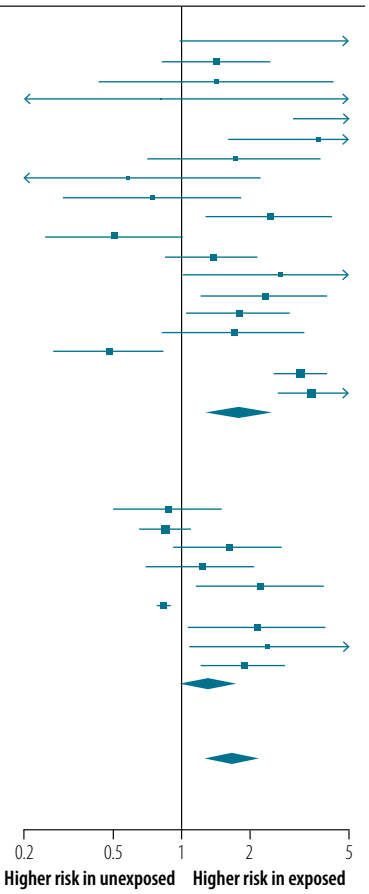


BCC, basal cell carcinoma; CI, confidence interval; F, females; M, males; SCC, squamous cell carcinoma.

Notes: [a] Aubry & MacGibbon, 1985 ***(19)***; [b] Gallagher et al., 1995 ***(20)***; [c] Gallagher et al., 1995 ***(21)***; [d] Suárez-Varela et al., 1996 ***(22)***; [e] Vlajinac et al., 2000 ***(23)***; [f] Corona et al., 2001 ***(24)***; [g] Milán et al., 2003 ***(25)***; [h] Walther et al., 2004 ***(26)***; [i] Janković et al., 2010 ***(27)***; [j] Dessinioti et al., 2011 ***(28)***; [k] Ferreira et al., 2011 ***(29)***; [l] Iannacone et al., 2012 ***(30)***; [m] Sanchez et al., 2012 ***(31)***; [n] Surdu et al., 2013 ***(32)***; [o] Trakatelli et al., 2016 ***(15)***; [p] Kricker et al., 1995 ***(33)***; [q] Ródenas et al., 1996 ***(16)***; [r] Zanetti et al., 2006 ***(17)***; [s] Pelucchi et al., 2007 ***(34)***; [t] Kenborg et al., 2010 ***(18)***; [u] Schmitt et al., 2018 ***(35, 36)***.

Fig. A7.9. Sensitivity analysis for studies judged to have a "high" or "probably high" risk of exposure misclassification bias, compared with studies judged to have a "low" or "probably low" risk of bias in this domain, for the association between occupational exposure to solar ultraviolet radiation and non–melanoma skin cancer incidence

Study or subgroup	log (relative risk)	Standard error	Weight (%)	Relative risk (95% CI)
"High" or "probably high" risk of exposure misclassification bias				
Aubry 1985[a]	2.21	1.14	1.2	9.12 (0.98–85.15)
Gallagher 1995 (BCC)[b]	0.34	0.28	4.0	1.40 (0.81–2.43)
Gallagher 1995 (SCC)[c]	0.34	0.61	2.5	1.40 (0.43–4.64)
Suárez-Varela 1996 (F)[d]	–0.22	1.12	1.2	0.80 (0.09–7.21)
Suárez-Varela 1996 (M)[d]	1.67	0.28	4.0	5.31 (3.07–9.20)
Vlajinac 2000[e]	1.37	0.46	3.2	3.94 (1.60–9.69)
Corona 2001[f]	0.53	0.45	3.2	1.70 (0.70–4.10)
Milán 2003 (F)[g]	–0.56	0.69	2.2	0.57 (0.15–2.21)
Milán 2003 (M)[g]	–0.30	0.46	3.2	0.74 (0.30–1.83)
Walther 2004[h]	0.88	0.33	3.8	2.41 (1.26–4.60)
Pelucchi 2007 (nodular BCC)[i]	–0.69	0.35	3.7	0.50 (0.25–1.00)
Pelucchi 2007 (superficial BCC)[i]	0.30	0.24	4.2	1.35 (0.84–2.16)
Janković 2010[j]	1.00	0.51	2.9	2.72 (1.00–7.39)
Dessinioti 2011[k]	0.83	0.33	3.8	2.29 (1.20–4.38)
Ferreira 2011[l]	0.57	0.27	4.0	1.77 (1.04–3.00)
Sanchez 2012[m]	0.51	0.37	3.6	1.67 (0.81–3.44)
Surdu 2013[n]	–0.75	0.28	4.0	0.47 (0.27–0.82)
Trakatelli 2016 (BCC)[o]	1.20	0.14	4.5	3.32 (2.52–4.37)
Trakatelli 2016 (SCC)[o]	1.30	0.17	4.4	3.67 (2.63–5.12)
Subtotal (95% CI)			**63.6**	**1.75 (1.23–2.47)**
Heterogeneity: $I^2 = 82\%$				
Test for overall effect: $P = 0.002$				
"Low" or "probably low" risk of exposure misclassification bias				
Kricker 1995[p]	–0.15	0.28	4.0	0.86 (0.50–1.49)
Rosso 1996 (BCC)[q]	–0.17	0.13	4.6	0.84 (0.65–1.09)
Rosso 1996 (SCC)[q]	0.47	0.28	4.0	1.60 (0.92–2.77)
Zanetti 2006 (BCC)[r]	0.18	0.28	4.0	1.20 (0.69–2.07)
Zanetti 2006 (SCC)[r]	0.79	0.33	3.8	2.20 (1.15–4.21)
Kenborg 2010[s]	–0.19	0.03	4.7	0.83 (0.78–0.88)
Iannacone 2012 (BCC)[t]	0.75	0.36	3.6	2.12 (1.05–4.29)
Iannacone 2012 (SCC)[t]	0.86	0.40	3.4	2.36 (1.08–5.18)
Schmitt 2018[u]	0.61	0.22	4.3	1.84 (1.20–2.83)
Subtotal (95% CI)			**36.4**	**1.31 (0.98–1.74)**
Heterogeneity: $I^2 = 80\%$				
Test for overall effect: $P = 0.07$				
Total (95% CI)			**100.0**	**1.60 (1.21–2.11)**
Heterogeneity: $I^2 = 91\%$				
Test for overall effect: $P = 0.000\,9$				
Test for subgroup differences: $P = 0.20$				

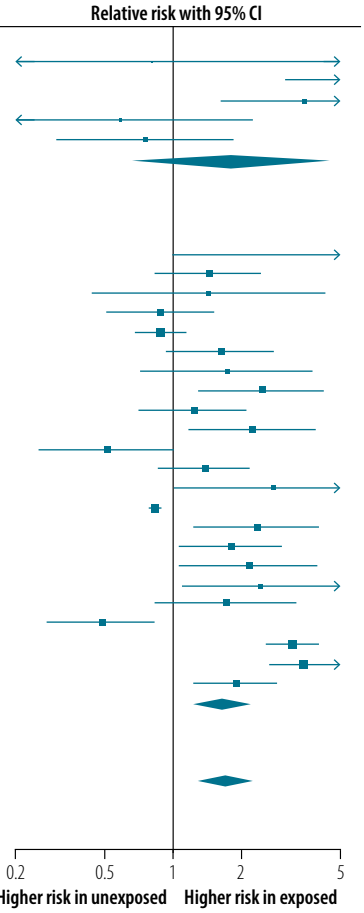


BCC, basal cell carcinoma; CI, confidence interval; F, females; M, males; SCC, squamous cell carcinoma.

Notes: [a] Aubry & MacGibbon, 1985 ***(19)***; [b] Gallagher et al., 1995 ***(20)***; [c] Gallagher et al., 1995 ***(21)***; [d] Suárez-Varela et al., 1996 ***(22)***; [e] Vlajinac et al., 2000 ***(23)***; [f] Corona et al., 2001 ***(24)***; [g] Milán et al., 2003 ***(25)***; [h] Walther et al., 2004 ***(26)***; [i] Pelucchi et al., 2007 ***(34)***; [j] Janković et al., 2010 ***(27)***; [k] Dessinioti et al., 2011 ***(28)***; [l] Ferreira et al., 2011 ***(29)***; [m] Sanchez et al., 2012 ***(31)***; [n] Surdu et al., 2013 ***(32)***; [o] Trakatelli et al., 2016 ***(15)***; [p] Kricker et al., 1995 ***(33)***; [q] Rosso et al. 1996, 1998 ***(5, 37)***; [r] Zanetti et al., 2006 ***(17)***; [s] Kenborg et al., 2010 ***(18)***; [t] Iannacone et al., 2012 ***(30)***; [u] Schmitt et al., 2018 ***(35, 36)***.

Fig. A7.10. Sensitivity analysis for studies judged to have a "high" or "probably high" risk of confounding, compared with studies judged to have a "low" or "probably low" risk of confounding, for the association between occupational exposure to solar ultraviolet radiation and non–melanoma skin cancer incidence

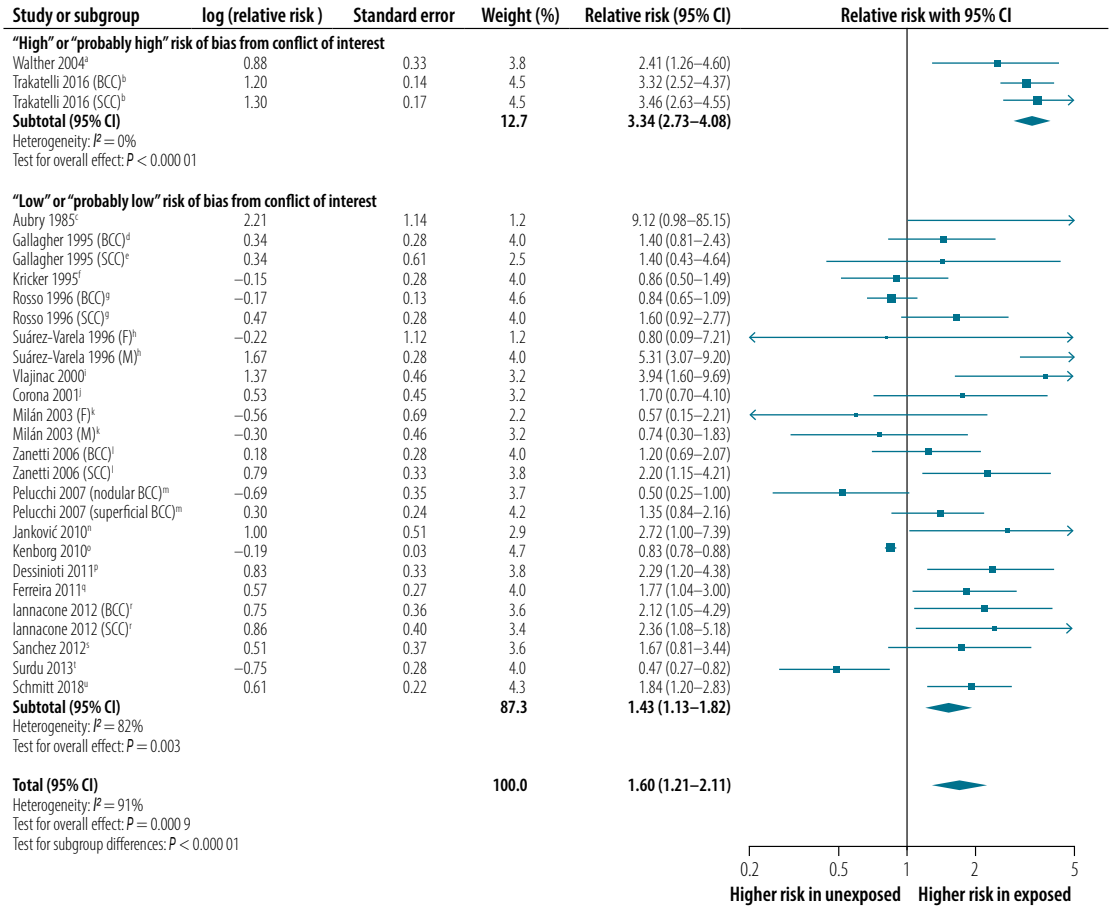
Study or subgroup	log (relative risk)	Standard error	Weight (%)	Relative risk (95% CI)
"High" or "probably high" risk of confounding				
Suárez-Varela 1996 (F)[a]	−0.22	1.12	1.2	0.80 (0.09–7.21)
Suárez-Varela 1996 (M)[a]	1.67	0.28	4.0	5.31 (3.07–9.20)
Vlajinac 2000[b]	1.37	0.46	3.2	3.94 (1.60–9.69)
Milán 2003 (F)[c]	−0.56	0.69	2.2	0.57 (0.15–2.21)
Milán 2003 (M)[c]	−0.30	0.46	3.2	0.74 (0.30–1.83)
Subtotal (95% CI)			**13.8**	**1.70 (0.61–4.70)**
Heterogeneity: $I^2 = 81\%$				
Test for overall effect: $P = 0.31$				
"Low" or "probably low" risk of confounding				
Aubry 1985[d]	2.21	1.14	1.2	9.12 (0.98–85.15)
Gallagher 1995 (BCC)[e]	0.34	0.28	4.0	1.40 (0.81–2.43)
Gallagher 1995 (SCC)[f]	0.34	0.61	2.5	1.40 (0.43–4.64)
Kricker 1995[g]	−0.15	0.28	4.0	0.86 (0.50–1.49)
Rosso 1996 (BCC)[h]	−0.17	0.13	4.6	0.84 (0.65–1.09)
Rosso 1996 (SCC)[h]	0.47	0.28	4.0	1.60 (0.92–2.77)
Corona 2001[i]	0.53	0.45	3.2	1.70 (0.70–4.10)
Walther 2004[j]	0.88	0.33	3.8	2.41 (1.26–4.60)
Zanetti 2006 (BCC)[k]	0.18	0.28	4.0	1.20 (0.69–2.07)
Zanetti 2006 (SCC)[k]	0.79	0.33	3.8	2.20 (1.15–4.21)
Pelucchi 2007 (nodular BCC)[l]	−0.69	0.35	3.7	0.50 (0.25–1.00)
Pelucchi 2007 (superficial BCC)[l]	0.30	0.24	4.2	1.35 (0.84–2.16)
Janković 2010[m]	1.00	0.51	2.9	2.72 (1.00–7.39)
Kenborg 2010[n]	−0.19	0.03	4.7	0.83 (0.78–0.88)
Dessinioti 2011[o]	0.83	0.33	3.8	2.29 (1.20–4.38)
Ferreira 2011[p]	0.57	0.27	4.0	1.77 (1.04–3.00)
Iannacone 2012 (BCC)[q]	0.75	0.36	3.6	2.12 (1.05–4.29)
Iannacone 2012 (SCC)[q]	0.86	0.40	3.4	2.36 (1.08–5.18)
Sanchez 2012[r]	0.51	0.37	3.6	1.67 (0.81–3.44)
Surdu 2013[s]	−0.75	0.28	4.0	0.47 (0.27–0.82)
Trakatelli 2016 (BCC)[t]	1.20	0.14	4.5	3.32 (2.52–4.37)
Trakatelli 2016 (SCC)[t]	1.30	0.17	4.4	3.67 (2.63–5.12)
Schmitt 2018[u]	0.61	0.22	4.3	1.84 (1.20–2.83)
Subtotal (95% CI)			**86.2**	**1.56 (1.17–2.08)**
Heterogeneity: $I^2 = 91\%$				
Test for overall effect: $P = 0.002$				
Total (95% CI)			**100.0**	**1.60 (1.21–2.11)**
Heterogeneity: $I^2 = 91\%$				
Test for overall effect: $P = 0.000\,9$				
Test for subgroup differences: $P = 0.88$				



BCC, basal cell carcinoma; CI, confidence interval; F, females; M, males; SCC, squamous cell carcinoma.

Notes: [a] Suárez-Varela et al., 1996 ***(22)***; [b] Vlajinac et al., 2000 ***(23)***; [c] Milán et al., 2003 ***(25)***; [d] Aubry & MacGibbon, 1985 ***(19)***; [e] Gallagher et al., 1995 ***(20)***; [f] Gallagher et al., 1995 ***(21)***; [g] Kricker et al., 1995 ***(33)***; [h] Rosso et al. 1996, 1998 ***(5, 37)***; [i] Corona et al., 2001 ***(24)***; [j] Walther et al., 2004 ***(26)***; [k] Zanetti et al., 2006 ***(17)***; [l] Pelucchi et al., 2007 ***(34)***; [m] Janković et al., 2010 ***(27)***; [n] Kenborg et al., 2010 ***(18)***; [o] Dessinioti et al., 2011 ***(28)***; [p] Ferreira et al., 2011 (***29***); [q] Iannacone et al., 2012 ***(30)***; [r] Sanchez et al., 2012 ***(31)***; [s] Surdu et al., 2013 ***(32)***; [t] Trakatelli et al., 2016 ***(15)***; [u] Schmitt et al., 2018 ***(35, 36)***.

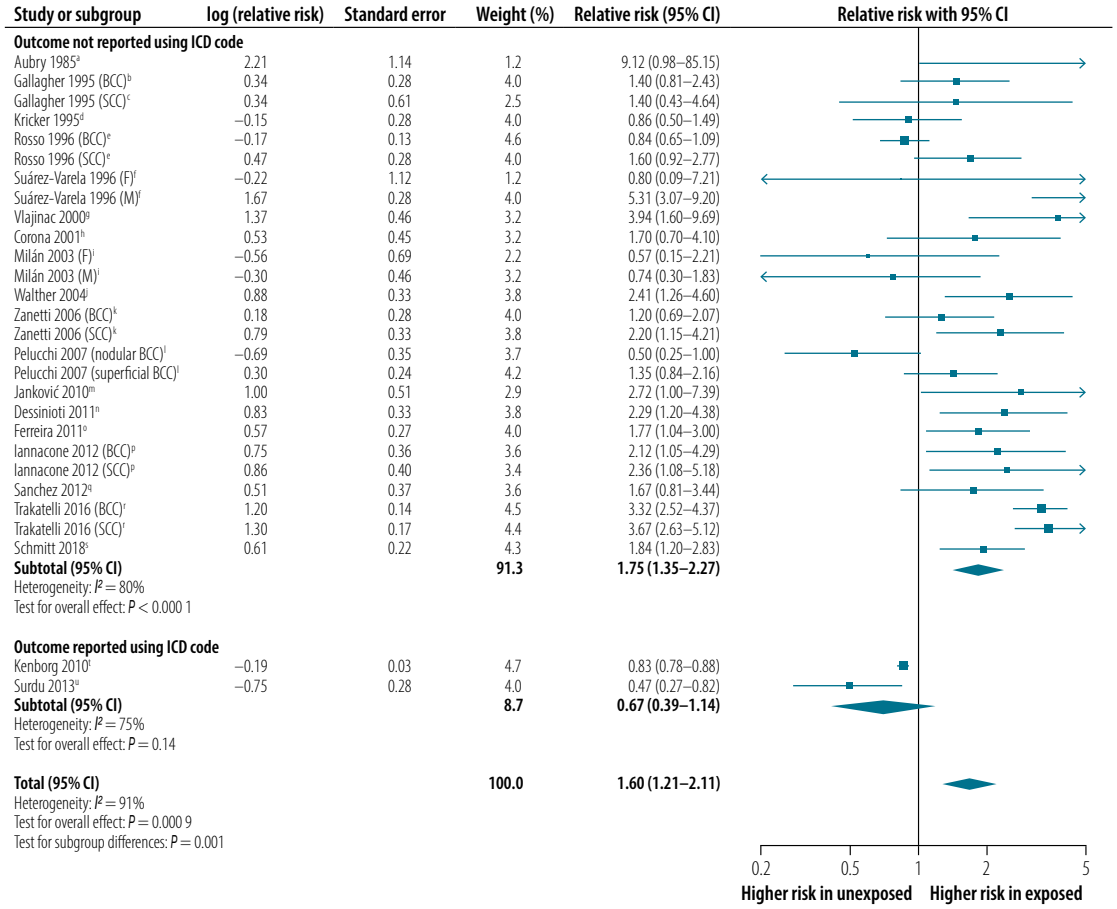
Fig. A7.11. Sensitivity analysis for studies judged to have a "low" or "probably low" risk of conflict of interest bias, compared with studies judged to have a "high" or "probably high" risk of bias in this domain, for the association between occupational exposure to solar ultraviolet radiation and non–melanoma skin cancer incidence



BCC, basal cell carcinoma; CI, confidence interval; F, females; M, males; SCC, squamous cell carcinoma.

Notes: [a] Walther et al., 2004 ***(26)***; [b] Trakatelli et al., 2016 ***(15)***; [c] Aubry & MacGibbon, 1985 ***(19)***; [d] Gallagher et al., 1995 ***(20)***; [e] Gallagher et al., 1995 ***(21)***; [f] Kricker et al., 1995 ***(33)***; [g] Rosso et al. 1996, 1998 ***(5, 37)***; [h] Suárez-Varela et al., 1996 ***(22)***; [i] Vlajinac et al., 2000 ***(23)***; [j] Corona et al., 2001 ***(24)***; [k] Milán et al., 2003 ***(25)***; [l] Zanetti et al., 2006 ***(17)***; [m] Pelucchi et al., 2007 ***(34)***; [n] Janković et al., 2010 ***(27)***; [o] Kenborg et al., 2010 ***(18)***; [p] Dessinioti et al., 2011 ***(28)***; [q] Ferreira et al., 2011 ***(29)***; [r] Iannacone et al., 2012 ***(30)***; [s] Sanchez et al., 2012 ***(31)***; [t] Surdu et al., 2013 ***(32)***; [u] Schmitt et al., 2018 ***(35, 36)***.

Fig. A7.12. Sensitivity analysis for studies with documented or approximated ICD-10 diagnostic codes, compared with studies without reported ICD-10 diagnostic codes, for the association between occupational exposure to solar ultraviolet radiation and non–melanoma skin cancer incidence

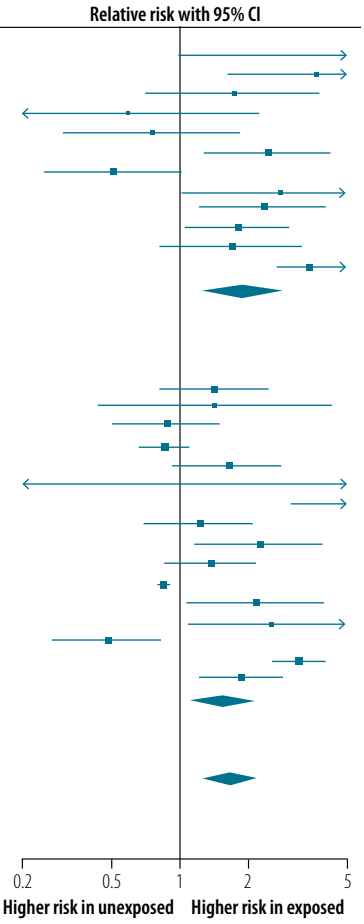


BCC, basal cell carcinoma; CI, confidence interval; F, females; ICD, International Classification of Disease; M, males; SCC, squamous cell carcinoma.

Notes: [a] Aubry & MacGibbon, 1985 ***(19)***; [b] Gallagher et al., 1995 ***(20)***; [c] Gallagher et al., 1995 ***(21)***; [d] Kricker et al., 1995 ***(33)***; [e] Rosso et al. 1996, 1998 ***(5, 37)***; [f] Suárez-Varela et al., 1996 ***(22)***; [g] Vlajinac et al., 2000 ***(23)***; [h] Corona et al., 2001 ***(24)***; [i] Milán et al., 2003 ***(25)***; [j] Walther et al., 2004 ***(26)***; [k] Zanetti et al., 2006 ***(17)***; [l] Pelucchi et al., 2007 ***(34)***; [m] Janković et al., 2010 ***(27)***; [n] Dessinioti et al., 2011 ***(28)***; [o] Ferreira et al., 2011 ***(29)***; [p] Iannacone et al., 2012 ***(30)***; [q] Sanchez et al., 2012 ***(31)***; [r] Trakatelli et al., 2016 ***(15)***; [s] Schmitt et al., 2018 ***(35, 36)***; [t] Kenborg et al., 2010 ***(18)***; [u] Surdu et al., 2013 ***(32)***.

Fig. A7.13. Sensitivity analysis for studies that did not measure the exposure as a cumulative measure, compared with studies that measured the exposure as a cumulative measure, for the association between occupational exposure to solar ultraviolet radiation and non–melanoma skin cancer incidence

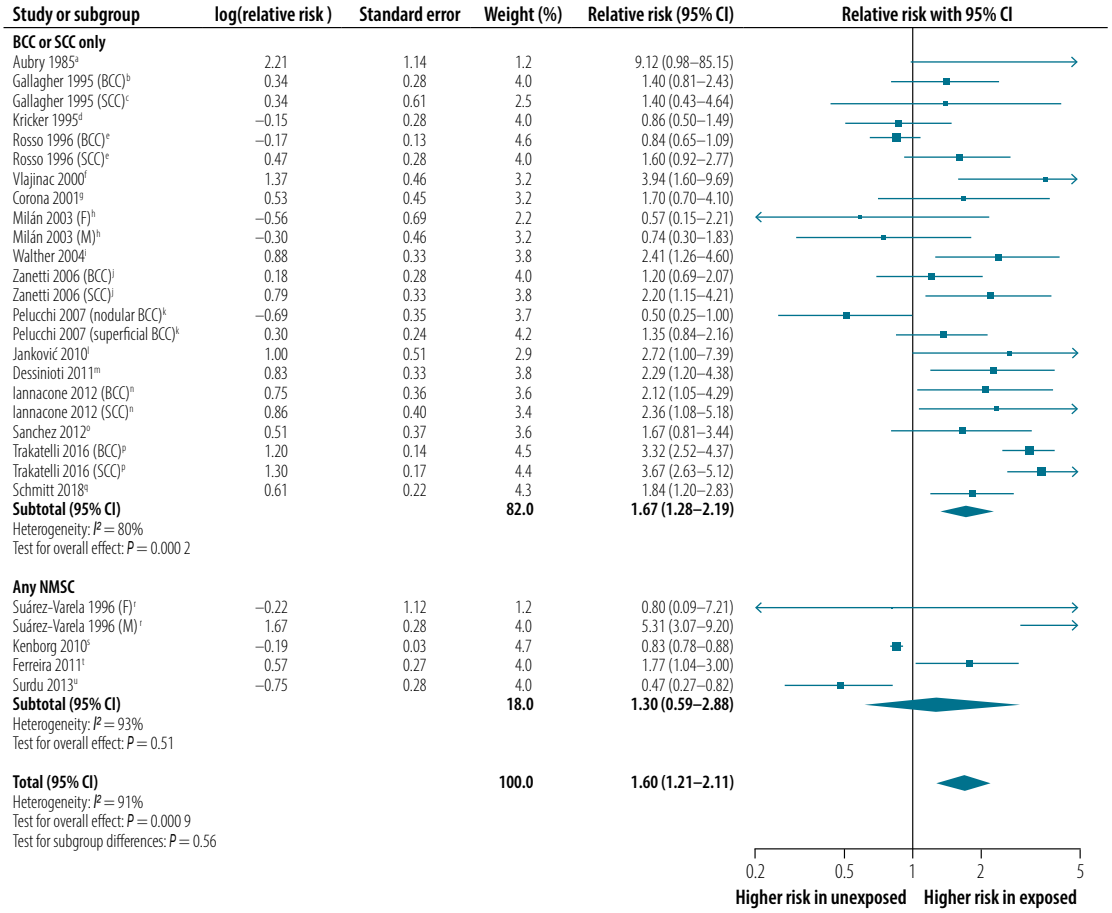
Study or subgroup	log (relative risk)	Standard error	Weight (%)	Relative risk (95% CI)
No cumulative exposure measurement				
Aubry 1985[a]	2.21	1.14	1.2	9.12 (0.98–85.15)
Vlajinac 2000[b]	1.37	0.46	3.2	3.94 (1.60–9.69)
Corona 2001[c]	0.53	0.45	3.2	1.70 (0.70–4.10)
Milán 2003 (F)[d]	−0.56	0.69	2.2	0.57 (0.15–2.21)
Milán 2003 (M)[d]	−0.30	0.46	3.2	0.74 (0.30–1.83)
Walther 2004[e]	0.88	0.33	3.8	2.41 (1.26–4.60)
Pelucchi 2007 (nodular BCC)[f]	−0.69	0.35	3.7	0.50 (0.25–1.00)
Janković 2010[g]	1.00	0.51	2.9	2.72 (1.00–7.39)
Dessinioti 2011[h]	0.83	0.33	3.8	2.29 (1.20–4.38)
Ferreira 2011[i]	0.57	0.27	4.0	1.77 (1.04–3.00)
Sanchez 2012[j]	0.51	0.37	3.6	1.67 (0.81–3.44)
Trakatelli 2016 (SCC)[k]	1.30	0.17	4.4	3.67 (2.63–5.12)
Subtotal (95% CI)			**39.2**	**1.81 (1.20–2.74)**
Heterogeneity: $I^2 = 73\%$				
Test for overall effect: $P = 0.005$				
Cumulative exposure measurement				
Gallagher 1995 (BCC)[l]	0.34	0.28	4.0	1.40 (0.81–2.43)
Gallagher 1995 (SCC)[m]	0.34	0.61	2.5	1.40 (0.43–4.64)
Kricker 1995[n]	−0.15	0.28	4.0	0.86 (0.50–1.49)
Rosso 1996 (BCC)[o]	−0.17	0.13	4.6	0.84 (0.65–1.09)
Rosso 1996 (SCC)[o]	0.47	0.28	4.0	1.60 (0.92–2.77)
Suárez-Varela 1996 (F)[p]	−0.22	1.12	1.2	0.80 (0.09–7.21)
Suárez-Varela 1996 (M)[p]	1.67	0.28	4.0	5.31 (3.07–9.20)
Zanetti 2006 (BCC)[q]	0.18	0.28	4.0	1.20 (0.69–2.07)
Zanetti 2006 (SCC)[q]	0.79	0.33	3.8	2.20 (1.15–4.21)
Pelucchi 2007 (superficial BCC)[f]	0.30	0.24	4.2	1.35 (0.84–2.16)
Kenborg 2010[r]	−0.19	0.03	4.7	0.83 (0.78–0.88)
Iannacone 2012 (BCC)[s]	0.75	0.36	3.6	2.12 (1.05–4.29)
Iannacone 2012 (SCC)[s]	0.86	0.40	3.4	2.36 (1.08–5.18)
Surdu 2013[t]	−0.75	0.28	4.0	0.47 (0.27–0.82)
Trakatelli 2016 (BCC)[k]	1.20	0.14	4.5	3.32 (2.52–4.37)
Schmitt 2018[u]	0.61	0.22	4.3	1.84 (1.20–2.83)
Subtotal (95% CI)			**60.8**	**1.48 (1.06–2.07)**
Heterogeneity: $I^2 = 92\%$				
Test for overall effect: $P = 0.02$				
Total (95% CI)			**100.0**	**1.60 (1.21–2.11)**
Heterogeneity: $I^2 = 91\%$				
Test for overall effect: $P = 0.000\,9$				
Test for subgroup differences: $P = 0.46$				



BCC, basal cell carcinoma; CI, confidence interval; F, females; M, males; SCC, squamous cell carcinoma.

Notes: [a] Aubry & MacGibbon, 1985 ***(19)***; [b] Vlajinac et al., 2000 ***(23)***; [c] Corona et al., 2001 ***(24)***; [d] Milán et al., 2003 ***(25)***; [e] Walther et al., 2004 ***(26)***; [f] Pelucchi et al., 2007 ***(34)***; [g] Janković et al., 2010 ***(27)***; [h] Dessinioti et al., 2011 ***(28)***; [i] Ferreira et al., 2011 ***(29)***; [j] Sanchez et al., 2012 ***(31)***; [k] Trakatelli et al., 2016 ***(15)***; [l] Gallagher et al., 1995 ***(21)***; [m] Gallagher et al., 1995 ***(20)***; [n] Kricker et al., 1995 ***(33)***; [o] Rosso et al. 1996, 1998 ***(5, 37)***; [p] Suárez-Varela et al., 1996 ***(22)***; [q] Zanetti et al., 2006 ***(17)***; [r] Kenborg et al., 2010 ***(18)***; [s] Iannacone et al., 2012 ***(30)***; [t] Surdu et al., 2013 ***(32)***; [u] Schmitt et al., 2018 ***(35, 36)***.

Fig. A7.14. Sensitivity analysis for studies that defined the outcome as any non–melanoma skin cancer, compared with studies that defined the outcome as squamous cell carcinoma or basal cell carcinoma subtype only, for the association between occupational exposure to solar ultraviolet radiation and non–melanoma skin cancer incidence



BCC, basal cell carcinoma; CI, confidence interval; F, females; M, males; SCC, squamous cell carcinoma.

Notes: [a] Aubry & MacGibbon, 1985 *(19)*; [b] Gallagher et al., 1995 *(20)*; [c] Gallagher et al., 1995 *(21)*; [d] Kricker et al., 1995 *(33)*; [e] Rosso et al. 1996, 1998 *(5, 37)*; [f] Vlajinac et al., 2000 *(23)*; [g] Corona et al., 2001 *(24)*; [h] Milán et al., 2003 *(25)*; [i] Walther et al., 2004 *(26)*; [j] Zanetti et al., 2006 *(17)*; [k] Pelucchi et al., 2007 *(34)*; [l] Janković et al., 2010 *(27)*; [m] Dessinioti et al., 2011 *(28)*; [n] Iannacone et al., 2012 *(30)*; [o] Sanchez et al., 2012 *(31)*; [p] Trakatelli et al., 2016 *(15)*; [q] Schmitt et al., 2018 *(35, 36)*; [r] Suárez-Varela et al., 1996 *(22)*; [s] Kenborg et al., 2010 *(18)*; [t] Ferreira et al., 2011 *(29)*; [u] Surdu et al., 2013 *(32)*.

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