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WHO/ILO work-related burden of disease and injury: Protocol for systematic reviews of occupational exposure to solar ultraviolet radiation and of the effect of occupational exposure to solar ultraviolet radiation on melanoma and non-melanoma skin cancer

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ABSTRACT

Background: The World Health Organization (WHO) and the International Labour Organization (ILO) are developing a joint methodology for estimating the national and global work-related burden of disease and injury (WHO/ILO joint methodology), with contributions from a large network of experts. In this paper, we present the protocol for two systematic reviews of parameters for estimating the number of deaths and disability-adjusted life years from melanoma and non-melanoma skin cancer (or keratinocyte carcinoma) from occupational exposure to solar ultraviolet radiation, to inform the development of the WHO/ILO joint methodology.
Objectives: We aim to systematically review studies on occupational exposure to solar ultraviolet radiation (Systematic Review 1) and systematically review and meta-analyse estimates of the effect of occupational exposure to solar ultraviolet radiation on melanoma and non-melanoma skin cancer (Systematic Review 2), applying the Navigation Guide systematic review methodology as an organizing framework and conducting both systematic reviews in tandem and in a harmonized way.
Data sources: Separately for Systematic Reviews 1 and 2, we will search electronic academic databases for potentially relevant records from published and unpublished studies, including Ovid Medline, PubMed, EMBASE, and Web of Science. We will also search electronic grey literature databases, Internet search engines

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and organizational websites; hand-search reference list of previous systematic reviews and included study records and consult additional experts.
Study eligibility and criteria: We will include working-age (≥15 years) workers in the formal and informal economy in any WHO and/or ILO Member State, but exclude children (< 15 years) and unpaid domestic workers. For Systematic Review 1, we will include quantitative studies on the prevalence of relevant levels of occupational exposure to solar ultraviolet radiation (i.e. < 0.33 SED/d and ≥0.33 SED/d) and of the total working time spent outdoors, stratified by country, sex, age and industrial sector or occupation, in the years 1960 to 2018. For Systematic Review 2, we will include randomized controlled trials, cohort studies, case-control studies and other non-randomized intervention studies with an estimate of the effect of any occupational exposure to solar ultraviolet radiation (i.e., ≥0.33 SED/d) on the prevalence of, incidence of or mortality due to melanoma and non-melanoma skin cancer, compared with the theoretical minimum risk exposure level (i.e. < 0.33 SED/d).
Study appraisal and synthesis methods: At least two review authors will independently screen titles and abstracts against the eligibility criteria at a first stage and full texts of potentially eligible records at a second stage, followed by extraction of data from qualifying studies. At least two review authors will assess the risk of bias and the quality of evidence, using the most suited tools currently available. For Systematic Review 2, if feasible, we will combine relative risks using meta-analysis. We will report results using the guidelines for accurate and transparent health estimates reporting (GATHER) for Systematic Review 1 and the preferred reporting items for systematic reviews and meta-analyses guidelines (PRISMA) for Systematic Review 2.
PROSPERO registration number: CRD42018094817.

1. Background

The World Health Organization (WHO) and the International Labour Organization (ILO) are developing a joint methodology for estimating the work-related burden of disease and injury (WHO/ILO joint methodology) (Ryder, 2017). The organizations plan to estimate the numbers of deaths and disability-adjusted life years (DALYs) that are attributable to selected occupational risk factors for the year 2015. The WHO/ILO joint methodology will be based on already existing WHO and ILO methodologies for estimating the burden of disease for selected occupational risk factors (International Labour Organization, 2014; Prüss-Üstün et al., 2017). It will expand existing methodologies with estimation of the burden of several prioritized additional pairs of occupational risk factors and health outcomes. For this purpose, population attributable fractions (Murray et al., 2004) – the proportional reduction in burden from the health outcome achieved by a reduction of exposure to the risk factor to zero – will be calculated for each additional risk factor-outcome pair, and these fractions will be applied to the total disease burden envelopes for the health outcome from the WHO *Global Health Estimates* (World Health Organization, 2017).

The WHO/ILO joint methodology will include a methodology for estimating the burden of melanoma and non-melanoma skin cancer (NMSC) (also known as keratinocyte carcinoma) from occupational exposure to solar ultraviolet (UV) radiation (UVR) if feasible, as one additional prioritized risk factor-outcome pair. To optimize parameters used in estimation models, a systematic review is required of studies on the prevalence of occupational exposure to the risk factor ('Systematic Review 1'), as well as a second systematic review and meta-analysis of studies with estimates of the effect of occupational exposure to solar UVR on melanoma and NMSC ('Systematic Review 2'). The term 'effect' is used throughout this protocol to include both association and causal effect. In the current paper, we present the protocol for these two systematic reviews, in parallel to presenting systematic review protocols on other additional risk factor-outcome pairs elsewhere (Descatha et al., 2018; Godderis et al., 2018; Hulshof et al., 2018; Li et al., 2018; Mandrioli et al., 2018; Rugulies et al., 2018; Teixeira et al., 2018; Tenkate et al., 2018). To our knowledge, this is the first systematic review protocol of its kind. The WHO/ILO joint estimation methodology and the burden of disease estimates are separate from these systematic reviews, and they will be described and reported elsewhere.

We refer separately to Systematic Reviews 1 and 2, because the two systematic reviews address different objectives and therefore require different methodologies. The two systematic reviews will, however, be harmonized and conducted in tandem. This will ensure that – in the later development of the methodology for estimating the burden of disease from this risk factor–outcome pair – the parameters on the risk factor prevalence are optimally matched with the parameters from studies on the effect of the risk factor on the designated outcome. The findings from Systematic Reviews 1 and 2 will be reported in two distinct journal articles. For this protocol and the second one in the series with occupational exposure to solar UVR as the risk factor (Tenkate et al., 2018), the Systematic Review 1 of the two different protocols will be performed jointly.

1.1. Rationale

To consider the feasibility of estimating the burden of melanoma and NMSC from occupational exposure to solar UVR, 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) (Stevens et al., 2016), WHO and ILO require a systematic review of studies on the prevalence of relevant levels of occupational exposure to solar UVR (Systematic Review 1), as well as a second systematic review and meta-analysis of studies with estimates of the relative effect of occupational exposure to solar UVR on melanoma and NMSC prevalence, incidence or mortality, compared with the theoretical minimum risk exposure level (Systematic Review 2). 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 exposure level in practice (Murray et al., 2004). These data and effect estimates should be tailored to serve as parameters for estimating the burden of melanoma and NMSC from occupational exposure to solar UVR in the WHO/ILO joint methodology.

Different contexts may result in different exposures and effects of these exposures on the health outcome. Work in the informal economy, for example, may lead to different exposures and exposure effects than does work in the formal economy. 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", but excluding "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" (p. 4) (International Labour Conference, 2015). Therefore, we will consider the formality of the economy studied in included studies in both systematic reviews.

1.1.1. Non-melanoma skin cancer

Globally, NMSC are the most common cancers in fair-skinned populations (Pelucchi et al., 2007). Solar UVR is the main cause of NMSC in fair-skinned people, responsible for an estimated 50–70% of squamous cell carcinoma (SCC) and 50–90% of basal cell carcinoma (BCC) (D'Orazio et al., 2013). Recent systematic review and meta-analytic evidence found that the risk among outdoor workers was raised for SCC and actinic keratoses by 77%, and for BCC by 43% respectively, compared with the general population (Bauer et al., 2011; Schmitt et al., 2011).

1.1.2. Cutaneous melanoma

Evidence on the effect on incident melanoma among outdoor workers has been described as unclear, with some studies reporting an inverse association with continuous UVR exposure in adult age (e.g. outdoor professions) as opposed to intermittent exposure (e.g. leisure time or childhood exposure) (Armstrong and Cust, 2017). We are not aware of a previous systematic review of the effect of occupational exposure to solar UVR on melanoma skin cancers. In IARC Monograph 100D (International Agency for Research on Cancer, 2012) the "objective cutaneous signs of skin damage" showed an "almost uniformly, strong positive association with melanoma", suggesting a possible inconsistency with the lack of evidence for a raised melanoma incidence in outdoor workers. Appendix A presents additional background information on occupational solar UVR exposure and both melanoma and NMSCs.

1.2. Description of the risk factor

The definition of the risk factor, the risk factor levels and the theoretical minimum risk exposure level are presented in Table 1, and they are explained below in more detail. Since the theoretical minimum risk exposure level is usually set empirically based on the causal epidemiological evidence, we will change the assumed level as evidence suggests. If several studies report exposure levels differing from the standard levels we define here, then, if possible, we will convert the reported levels to the standard levels and, if not possible, we will report analyses on these alternate exposure levels as supplementary information in the systematic reviews. In the latter case, our protocol will be updated to reflect our new analyses.

1.2.1. Risk factor definition

UVR, part of the spectrum of electromagnetic radiation emitted by the sun, is divided into three bands of different wavelengths: UVA 400–315 nm; (ii) UVB 315–280 nm; and (iii) UVC 280–100 nm (Lucas et al., 2006). However, the exact wavelengths at which divisions are constructed differ accross disciplines.

Artificial sources of UVR (e.g. lamps and welding) can include all UV bands (UVA, UVB and UVC), whereas terrestrial solar UVR only contains UVA and UVB bands. UVR in band C (280–100 nm) is totally filtered by the ozone layer, which also absorbs the majority (~90%) of UVB, while UVA passes through the atmosphere with little change. While all three types of UVR have differing effects on humans, UVA and UVB are primarily responsible for skin malignancies. UVR in band A (400–315 nm) has the longest wavelength and penetrates the skin more deeply, reaching the dermis and generating reactive oxygen species capable of damaging deoxyribonucleic acid (DNA). On the contrary, UVB is almost completely absorbed by DNA in the epidermis. While UVA penetrates the human skin more deeply than UVB, action spectra for biological responses indicate that it is radiation in the UVB range that is absorbed by DNA – subsequent damage to DNA appears to be a key factor in the initiation of the carcinogenic process in skin (Lucas et al., 2006). More information about the environmental and individual factors influencing solar UVR exposure and effects in human skin, including immunosuppression by UVR, can be found in Appendix A.

1.2.2. Risk factor levels

For solar UV exposure to the skin, the 'radiant exposure' (or dose) is commonly described in terms of a biological weighting for erythema (i.e. skin reddening), and can be expressed in two ways: (1) Minimal Erythemal Dose (MED), which provides the dose of UVR (particularly UVB) required to cause a minimal erythematous skin response within 24 h after exposure, with specific skin type (e.g. fair, dark) altering the response time (and dose required to produce one MED), which varies according to the Fitzpatrick scale (D'Orazio et al., 2013); or (2) Standard Erythema Dose (SED) which is more of a 'standardized dose', where 1 SED equals 100 Jm^{-2} of erythemally weighted UV irradiance (Diffey, 2002).

For occupational exposure the most widely used UV exposure limit was initially developed by the American Conference of Governmental Industrial Hygienists (ACGIH) and has been adopted internationally by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) (International Commission on Non-Ionizing Radiation Protection, 2012). This standard limit is based on threshold data (i.e. the minimum exposure needed to produce a specific biological effect) for erythema and photokeratitis, which are both acute effects. It describes 'allowed' daily (i.e. 8 h) exposure at each wavelength in the UV spectrum (i.e. the so-called 'UV Hazard Curve'), with the lowest (or limiting) dose being 30 Jm^{-2} at 270 nm. This is equivalent to approximately 1.0 to 1.33 SED per day in case of the solar spectrum. This is approximately one half of an MED for a fair skinned person (2.0 SED, skin type I and II) (Diffey, 2002). In our systematic reviews, we will use SED as the metric for exposure to UVR.

1.2.3. Theoretical minimum risk exposure level

Because of the ubiquitous nature of solar UVR, it is one of the few occupational exposures that everyone is exposed to, whether an outdoor worker or not. Fortunately, ongoing, regular exposure at or below the ACGIH/ICNIRP exposure standard/guideline for UVR is considered to produce an extremely small risk for the development of skin cancers. However, with this guideline representing a dose of 1.0 to 1.3 SED/day, it likely includes solar UV exposure of indoor workers, considering that the annual 'leisure' UV dose for, for example, the German population is currently considered to be 0.33 SED/day (Knuschke et al., 2004; Wittlich et al., 2016). Further, it has been calculated that the "tolerable" risk for SCC corresponds to 1.15 SED/day, with the "acceptable" risk at 0.115 SED/day (German Society of Occupational and Environmental

Table 1
Definitions of the risk factor, risk factor levels and the minimum risk exposure level.

Concept	Definition
Risk factor	Occupational exposure to solar UVR, defined as UVA and UVB from solar radiation reaching the worker's skin.
Risk factor levels	The occupational exposure limit for artificial UVR is recognized as being 30 Jm^{-2} (effectively weighted irradiance) according to ICNIRP and the European directive 2006/25/EC as a daily 8-hour value. This equates to a skin exposure of 1.0 and 1.33 Standard Erythemal Dose (SED; 1 SED = 100 Jm^{-2} of erythemally weighted irradiance) in the solar spectrum. 'Leisure' (i.e. non-occupational) exposure is considered to be roughly 1/3 of this. Two risk factor levels will be used: 1. Non-exposed (i.e. non-occupational exposure < 0.33 SED/day). 2. Exposed (occupational exposure ≥ 0.33 SED/day). If sufficient data are available, then additional risk factor levels will be constructed as multiples of the theoretical minimum risk exposure level (i.e. 0.33 SED/day). 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).
Theoretical minimum risk exposure level	A daily solar UVR exposure of < 0.33 SED/day (50° N/S), adjusted for latitude of the outdoor worker.

Medicine, 2017). Personal UV dosimetric measurements conducted with outdoor workers have shown a consistent trend for exposures to exceed the ACGIH/ICNIRP standard, often by many times (Gies et al., 2009; Hammond et al., 2009; Siani et al., 2011), with exposures of up to 5 SED/day common in German outdoor workers (Wittlich, 2017; Wittlich et al., 2016).

Overall, as we consider the theoretical minimum risk exposure level to represent no occupational exposure to solar UVR, for the purpose of this review we will use the value of 0.33 SED/day as the minimum risk exposure level, as this represents the recognized 'leisure' exposure to solar UV for the German population, and because 'adjustment' factors are available to account for latitude (Wittlich et al., 2016), therefore enabling baseline/comparator geographic exposure estimates.

1.3. Description of the outcome

The WHO *Global Health Estimates* group health outcomes into standard burden of disease categories (World Health Organization, 2017), based on the standard codes from the *International Statistical Classification of Diseases and Related Health Problems 10th Revision* (ICD-10) (World Health Organization, 2015). The two relevant WHO *Global Health Estimates* categories for this systematic review are "*II.A.8a Malignant skin melanoma*" (ICD-10 code: C43) and "*II.A.8b Non-melanoma skin cancer*" (C44) (World Health Organization, 2017). In line with the WHO *Global Health Estimates*, we define the health outcomes covered in Systematic Review 2 as melanoma and NMSC, defined as conditions with ICD-10 codes C43 and C44, respectively. Because the standard WHO burden of disease categories exclude actinic keratosis (i.e. in situ SCC or intraepidermal neoplasm), the systematic review will also exclude it. We will consider prevalence of, incidence of and mortality from melanoma and NMSC. This review covers all the relevant WHO *Global Health Estimates* categories.

1.4. How the risk factor may impact the outcome

Fig. 1 presents the logic model for our systematic review of the assumed causal relationship between occupational exposure to solar UVR and melanoma and NMSC. This logic model is an *a priori*, process-orientated one (Rehfuess et al., 2017) that seeks to capture the complexity of the risk factor-outcome causal relationship (Anderson et al., 2011).

Mechanistic or experimental evidence suggests that *occupational* exposure to solar UVR impacts melanoma and NMSC through direct (UVB) or indirect (UVA) DNA damage (e.g. photo-dimerization). Animal studies support a causal effect of the exposure to UVR on melanoma and NMSC (Appendix A).

2. Objectives

1. Systematic Review 1: To systematically review quantitative studies of any design on the prevalence of relevant levels of occupational exposure to solar UVR (i.e. ≥ 0.33 SED/day and < 0.33 SED/day) in the years 1960 to 2018 among working-age workers, disaggregated by country, sex, age (and, if possible, skin type) and industrial sector or occupation.
2. Systematic Review 2: To systematically review and meta-analyse randomized controlled trials, cohort studies, case-control studies and other non-randomized intervention studies including estimates of the relative effect of occupational exposure to solar UVR (≥ 0.33 SED/day) on melanoma and NMSC in any year among

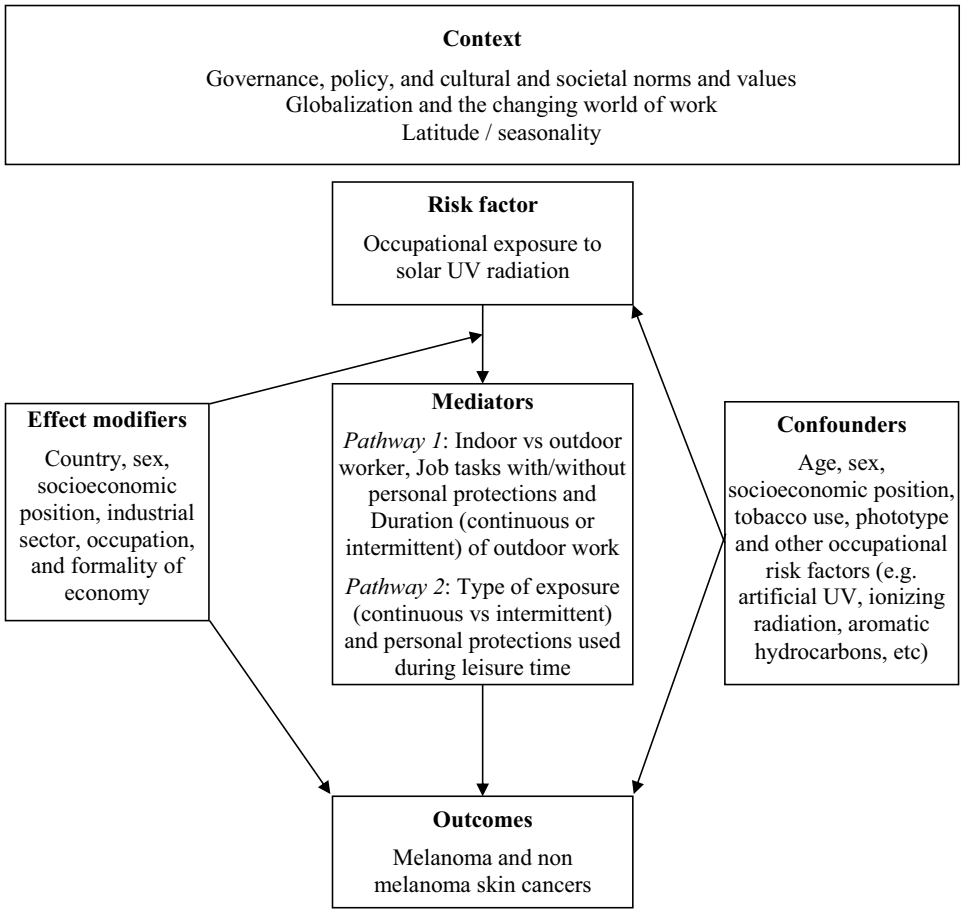

Fig. 1. Logic model of the causal relationship between occupational exposure to solar UVR and melanoma and NMSC.

working-age workers, compared with the minimum risk exposure level of < 0.33 SED/day.

3. Methods

We will apply the *Navigation Guide* (Woodruff and Sutton, 2014) methodology for systematic reviews in environmental and occupational health as our guiding methodological framework, wherever feasible. The guide applies established systematic review methods from clinical medicine, including standard Cochrane Collaboration methods for systematic reviews of interventions, to the field of environmental and occupational health to ensure systematic and rigorous evidence synthesis on environmental and occupational risk factors that reduces bias and maximizes transparency (Woodruff and Sutton, 2014). The need for further methodological development and refinement of the relatively novel *Navigation Guide* has been acknowledged (Woodruff and Sutton, 2014).

Systematic Review 1 may not map well to the *Navigation Guide* framework (Fig. 1 on page 1009 in Lam et al., 2016), which is tailored to hazard identification and risk assessment. Nevertheless, steps 1–6 for the stream on human data can be applied to systematically review exposure to risk factors. Systematic Review 2 maps more closely to the *Navigation Guide* framework, and we will conduct steps 1–6 for the stream on human data, but not conduct any steps for the stream on non-human data, although we will briefly summarize narratively the evidence from non-human data that we are aware of.

We have registered the protocol in PROSPERO under CRD42018094817. This protocol adheres with the preferred reporting items for systematic review and meta-analysis protocols statement (PRISMA-P) (Moher et al., 2015; Shamseer et al., 2015), with the abstract adhering with the reporting items for systematic reviews in journal and conference abstracts (PRISMA-A) (Beller et al., 2013). Any modification of the methods stated in the present protocol will be registered in PROSPERO and reported in the systematic review itself. Systematic Review 1 will be reported according to the GATHER guidelines (Stevens et al., 2016), and Systematic Review 2 will be reported according to the preferred reporting items for systematic review and meta-analysis statement (PRISMA) (Liberati et al., 2009). Our reporting of the parameters for estimating the burden of melanoma and NMSC from occupational exposure to solar UVR in the systematic reviews will adhere with the requirements of the GATHER guidelines (Stevens et al., 2016), because the WHO/ILO burden of disease estimates that may be produced consecutive to the systematic reviews must also adhere to these reporting guidelines.

3.1. Systematic Review 1

3.1.1. Eligibility criteria

The population, exposure, comparator and outcome (PECO) criteria (Woodruff and Sutton, 2014) are described below.

3.1.1.1. Types of populations. We will include studies of working-age (≥15 years) workers in the formal and informal economy. Studies of children (aged < 15 years) and unpaid domestic workers will be excluded. Participants residing in any WHO and/or ILO Member State and any industrial setting or occupation will be included. Appendix B provides a complete, but briefer overview of the PECO criteria.

3.1.1.2. Types of exposures. We will include studies that define occupational exposure to solar UVR in accordance with our standard definition (Table 1). Cumulative exposure may be the most relevant exposure metric in theory, but we will here prioritize a non-cumulative exposure metric because we do not have global exposure data on agreed cumulative exposure measures. We will include all studies where occupational exposure is measured, whether objectively (e.g. by means of dosimeters), or subjectively, including studies that used measurements by experts (e.g. scientists with subject matter expertise) and self-reports by the worker or workplace administrator or manager. If a study presents both objective and subjective measurements, then we will prioritize objective measurements. We will include studies with measures from any data source, including registry data.

We will include studies on the prevalence of occupational exposure to the risk factor, if it is disaggregated by country (defined as a WHO or ILO Member State), sex (two categories: female, male), age (ideally in 5-year age bands, such as 20–24 years) (and, if possible, also skin type [e.g. Fitzpatrick scale or colour]) and industrial sector (e.g., *International Standard Industrial Classification of All Economic Activities, Revision 4* [ISIC Rev. 4]) (United Nations, 2008) or occupation (as defined, for example, by the *International Standard Classification of Occupations 2008* [ISCO-08]) (International Labour Office, 2012). Criteria may be revised in order to identify optimal data disaggregation to enable subsequent estimation of the burden of disease.

We shall include studies with exposure prevalence data from 1960 until 31 July 2018. For optimal modelling of exposure, WHO and ILO require exposure data up to 2018, because recent data points help better estimate time trends, especially where data points may be sparse. The additional rationale for this data collection window is that the WHO and ILO aim to estimate burden of disease in the year 2015, and we believe that the lag time from exposure to outcome will not exceed 55 years; so in their models, the organizations can use the exposure data from as early as 1960 to determine the burden of melanoma and non-melanoma skin cancer 55 years later in 2015. To make a conclusive judgment on the best lag time to apply in the model, we will summarize the existing body of evidence on the lag time between exposure to solar UVR and melanoma and NMSC in the review. The exposure parameter should match the one used in Systematic Review 2 or can be converted to match it.

3.1.1.3. Types of comparators. There will be no comparator, because we will review risk factor prevalence only.

3.1.1.4. Types of outcomes. Occupational exposure to solar UVR.

3.1.1.5. Types of studies. This Systematic Review will include quantitative studies of any design, including cross-sectional studies. These studies must be representative of the relevant industrial sector, relevant occupational group or the national population. We will exclude qualitative, modelling and case studies, as well as non-original studies without quantitative data (e.g. letters, commentaries and perspectives).

Study records written in any language will be included. If a study record is written in a language other than those spoken by the authors of this review or those of other reviews (Descatha et al., 2018; Godderis et al., 2018; Hulshof et al., 2018; Li et al., 2018; Mandrioli et al., 2018; Rugulies et al., 2018; Teixeira et al., 2018; Tenkate et al., 2018) in the series (i.e. Arabic, Bulgarian, Chinese, Danish, Dutch, English, French, Finnish, German, Hungarian, Italian, Japanese, Norwegian, Portuguese, Russian, Spanish, Swedish and Thai), it will be translated into English. Published and unpublished studies will be included.

Studies conducted using unethical practices will be excluded from the review.

3.1.1.6. Types of effect measures. We will include studies with a measure of the prevalence of occupational exposure to solar UVR.

3.1.2. Information sources and search

3.1.2.1. Electronic academic databases. We (AM and MSP) will at a minimum search the following four electronic academic databases:

1. Ovid MEDLINE with Daily Update (1 January 1960 to 31 July 2018).

2. PubMed (1 January 1960 to 31 July 2018).
3. EMBASE (1 January 1960 to 31 July 2018).
4. Web of Science (1 January 1960 to 31 July 2018) with inclusion of 3 databases: Science Citation Index Expanded; Social Sciences Citation Index; and Arts and Humanities Citation Index.

The Ovid Medline search strategy for Systematic Review 1 is presented in Appendix C. We have tested and validated the search strategy for the four selected databases. The CISDOC and TOXNET databases were also tested, but their scopes were found to not sufficiently cover that of the systematic review. We will perform searches in electronic databases operated in the English language using a search strategy in the English language. Consequently, study records that do not report essential information (i.e. title and abstract) in English will not be captured. We will adapt the search syntax to suit the other electronic academic and grey literature databases. When we are nearing completion of the review, we will search the PubMed database for the most recent publications (e.g., e-publications ahead of print) over the last six months. Any deviation from the proposed search strategy in the actual search strategy will be documented.

3.1.2.2. Electronic grey literature databases. We (AM and MSP) will at a minimum search the following two electronic academic databases:

1. OpenGrey (http://www.opengrey.eu/).
2. Grey Literature Report (http://greylit.org/).

3.1.2.3. Internet search engines. We (AM and MSP) will also search the Google (www.google.com/) and GoogleScholar (www.google.com/scholar/) Internet search engines and screen the first 100 hits for potentially relevant records.

3.1.2.4. Organizational websites. The websites of the seven following international organizations and national government departments will be searched by AM and MSP:

1. International Labour Organization (www.ilo.org/).
2. World Health Organization (www.who.int).
3. European Agency for Safety and Health at Work (https://osha.europa.eu/en).
4. Eurostat (www.ec.europa.eu/eurostat/web/main/home).
5. China National Knowledge Infrastructure (http://www.cnki.net/).
6. Finnish Institute of Occupational Health (https://www.ttl.fi/en/).
7. National Institute of Occupational Safety and Health (NIOSH) of the United States of America, using the NIOSH data and statistics gateway (https://www.cdc.gov/niosh/data/).

3.1.2.5. Hand-searching and expert consultation. We (AM and MSP) will hand-search for potentially eligible studies in:

- Reference lists of previous systematic reviews.
- Reference lists of all study records of all included studies.
- Study records published over the past 24 months in the three peer-reviewed academic journals from which we obtain the largest number of included studies.
- Study records that have cited an included study record (identified in Web of Science citation database).
- Collections of the review authors.

Additional experts will be contacted with a list of included studies and study records, with the request to identify potentially eligible additional ones.

3.1.3. Study selection

Study selection will be carried out with Covidence (Babineau, 2014; Covidence, n.d.). All study records identified in the search will be downloaded, and duplicates will be identified and deleted. Afterwards, at least two review authors (AM and MSP) will independently screen against eligibility criteria titles and abstracts (step 1) and then full texts of potentially relevant records (step 2). A third review author (TL or TT) will resolve any disagreements between the study selectors. If a study record identified in the literature search was authored by a review author assigned to study selection or if an assigned review author was involved in the study, then the record will be re-assigned to another review author for study selection. In the systematic review, we will document the study selection in a flow chart, as per GATHER guidelines (Stevens et al., 2016).

3.1.4. Data extraction and data items

A data extraction form will be developed and piloted until there is convergence and agreement among data extractors. At a minimum, two review authors (out of: AM, CP, MSP and SB) will independently extract the data on occupational exposure to solar UVR, disaggregated by country, sex, age and industrial sector or occupation. A third review author (SMJ, TL or TT) will resolve conflicting extractions. At a minimum, we will extract data on study characteristics (including study authors, study year, study country, participants and risk factor exposure), study design (including study type and measurements of the risk factor and response rate), risk of bias (including missing data, as indicated by response rate and other measures) and study context. The estimates of the proportion of the population exposed to the occupational risk factor from included studies will be entered into and managed with, the Review Manager, Version 5.3 (Review Manager (RevMan), 2014) or DistillerSR (Evidence Partners, 2017) softwares.

We will also extract data on potential conflict of interest in included studies, including the financial disclosures and funding sources of each author and their affiliated organization. We will use a modification of a previous method to identify and assess undisclosed financial interests (Forsyth et al., 2014). Where no financial disclosure/conflict of interest is provided, we will search declarations of interest both in other records from this study published in the 36 months prior to the included study record and in other publicly available repositories (Drazen et al., 2010, 2009).

We will request missing data from the principal study author by email or phone, using the contact details provided in the principal study record. If no response is received, we will follow up twice via email, at two and four weeks.

3.1.5. Risk of bias assessment

Generally agreed methods (i.e. framework plus tool) for assessing risk of bias do not exist for systematic reviews: of input data for health estimates (The GATHER Working Group, 2016), for burden of disease studies, of prevalence studies in general (Munn et al., 2014) and of prevalence studies of occupational and/or environmental risk factors specifically (Krauth et al., 2013; Mandrioli and Silbergeld, 2015; Vandenberg et al., 2016). None of the five standard risk of bias assessment methods in systematic reviews for environmental and occupational health (Rooney et al., 2016) are applicable to assessing prevalence studies. The *Navigation Guide* does not support checklist approaches, such as (Hoy et al., 2012; Munn et al., 2014), for assessing risk of bias in prevalence studies.

We will use a modified version of the *Navigation Guide* risk of bias tool (Lam et al., 2016) that we developed specifically for Systematic Review 1 (Appendix D). We will assess risk of bias on the levels of the individual study and the entire body of evidence. As per our preliminary tool, we will assess risk of bias along five domains: (i) selection bias; (ii) performance bias; (iii) misclassification bias; (iv) conflict of interest; and (v) other biases. Risk of bias will be: “low”; “probably low”; “probably high”; “high” or “not applicable”. To judge the risk of bias in each domain, we will apply our *a priori* instructions (Appendix D).

All risk of bias assessors (AG, CA, FG, MW, SJ, SMJ, TL, AM, MSP

and TT) will trial the tool until they synchronize their understanding and application of each risk of bias domain, considerations and criteria for ratings. At least two study authors (AM, MSP) will then independently judge the risk of bias for each study by outcome, and a third author (AG, CA, FG, MW, SJ, SMJ, TL or TT) will resolve any conflicting judgments. We will present the findings of our risk of bias assessment for each eligible study in a standard 'Risk of bias' table (Higgins and Green, 2011). Our risk of bias assessment for the entire body of evidence will be presented in a standard 'Risk of bias summary' figure (Higgins and Green, 2011).

3.1.6. Synthesis of results

We will neither produce any summary measures, nor synthesise the evidence quantitatively. The included evidence will be presented in what could be described as an 'evidence map'. All included data points from included studies will be presented, together with meta-data on the study design, number of participants, characteristics of population, setting, and exposure measurement of the data point.

3.1.7. Quality of evidence assessment

There is no agreed method for assessing quality of evidence in systematic reviews of the prevalence of occupational and/or environmental risk factors. We will adopt or adapt the latest *Navigation Guide* instructions for grading (Lam et al., 2016), including criteria (Appendix E). We will downgrade for the following five reasons from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach: (i) risk of bias; (ii) inconsistency; (iii) indirectness; (iv) imprecision; and (v) publication bias (Schünemann et al., 2011). We will grade the evidence, using the three *Navigation Guide* quality of evidence ratings: "high", "moderate" and "low" (Lam et al., 2016). Within each of the relevant reasons for downgrading, we will rate any concern per reason as "none", "serious" or "very serious". We will start at "high" for non-randomized studies and will downgrade for no concern by nil, for a serious concern by one grade (−1), and for a very serious concern by two grades (−2). We will not up-grade or downgrade the quality of evidence for the three other reasons normally considered in GRADE assessments (i.e. large effect, dose-response and plausible residual confounding and bias), because we consider them irrelevant for prevalence estimates.

All quality of evidence assessors (AM, BA, MSP, RA and TL) will trial the application of our instructions and criteria for quality of evidence assessment until their understanding and application is synchronized. Two separate review author groups (i.e. AM, FG, MC and TT and BA, MSP, RA and TL, respectively) will independently judge the quality of evidence for the entire body of evidence by outcome. A third review author group (AG, CA, SK and SMJ) will resolve any conflicting judgments. In the systematic review, for each outcome, we will present our assessments of the risk for each GRADE domain, as well as an overall GRADE rating.

3.1.8. Strength of evidence assessment

To our knowledge, no agreed method exists for rating strength of evidence in systematic reviews of prevalence studies. We (AM, MSP and SMJ) will rate the strength of the evidence for use as input data for estimating national-level exposure to the risk factor. Our rating will be based on a combination of the following four criteria: (i) quality of the entire body of evidence; (ii) population coverage of evidence (WHO regions and countries); (iii) confidence in the entire body of evidence; and (iv) other compelling attributes of the evidence that may influence certainty. We will rate the strength of the evidence as either "potentially sufficient" or "potentially inadequate" for use as input data (Appendix F).

3.2. Systematic Review 2

3.2.1. Eligibility criteria

3.2.1.1. Types of populations. We will include studies of working-age (≥15 years) workers in the formal and informal economy. Studies of children (aged < 15 years) and unpaid domestic workers will be excluded. Participants residing in any WHO and/or ILO Member State and any industrial setting or occupation will be included. Appendix G provides a complete, but briefer overview of the PECO criteria.

3.2.1.2. Types of exposures. We will include studies that define solar UVR in accordance with our standard definition (Table 1). We will include all studies where occupational exposure to solar UVR was measured, whether objectively (e.g. by means of dosimeters) or subjectively, including studies that used measurements by experts (e.g. scientists with subject matter expertise) and self-reports by the worker or workplace administrator or manager. If a study presents both objective and subjective measurements, then we will prioritize objective measurements. We will include studies with measures from any data source, including registry data.

3.2.1.3. Types of comparators. The included comparator will be participants exposed to the theoretical minimum risk exposure level (Table 1). We will exclude all other comparators.

3.2.1.4. Types of outcomes. We will include studies that defined melanoma and NMSC in accordance with our standard definition of these outcomes (Table 1).

The following measurements of melanoma and NMSC will be regarded as eligible:

i) Diagnosis by a physician.
ii) Hospital discharge records.
iii) Registry data of treatment for melanoma and/or NMSC.
iv) Other relevant administrative data (e.g. records of sickness absence or disability).
v) Medically certified cause of death.

All other measure will be excluded from this systematic review.

We will include objective measures of melanoma and of NMSC including those of only BCC or SCC (e.g., diagnosed or measured by a dermatologist or by a trained occupational health practitioner, such as an occupational physician or nurse, using a validated tool), as well as subjective measures of the outcomes. If both subjective and objective measures are presented, we will prioritize the objective measures.

3.2.1.5. Types of studies. We will include studies that investigate the effect of occupational exposure to solar UVR on skin cancers for any years. Eligible study designs will be randomized controlled trials (including parallel-group, cluster, cross-over and factorial trials), cohort studies (both prospective and retrospective), case-control studies and other non-randomized intervention studies (including quasi-randomized controlled trials, controlled before-after studies and interrupted time series studies). We included a broader set of observational study designs than is commonly included, because a recent augmented Cochrane Review of complex interventions identified valuable additional studies using such a broader set of study designs (Arditi et al., 2016). As we have an interest in quantifying risk and not in qualitative assessment of hazard (Barroga and Kojima, 2007), we will exclude all other study designs (e.g. uncontrolled before-and-after, cross-sectional, qualitative, modelling, case and non-original studies).

Records published in any year and any language will be included. Again, the search will be conducted using English language terms, so that records published in any language that present essential information (i.e. title and abstract) in English will be included. If a record is

written in a language other than those spoken by the authors of this review or those of other reviews in the series (Descatha et al., 2018; Godderis et al., 2018; Hulshof et al., 2018; Li et al., 2018; Mandrioli et al., 2018; Rugulies et al., 2018; Teixeira et al., 2018; Tenkate et al., 2018), then the record will be translated into English. Published and unpublished studies will be included.

Studies conducted using unethical practices will be excluded (e.g., RCTs that deliberately exposed humans to a known risk factor to human health).

3.2.1.6. Types of effect measures. We will include measures of the relative effect of occupational exposure to solar UVR on the risk of having, developing or dying from melanoma and NMSC, compared with the theoretical minimum risk exposure level. In studies with low versus high exposure, the risk estimate may be assessed based on risk estimated in low versus high exposed workers. We will include relative effect measures such as risk ratios and odds ratios for mortality measures and hazard ratios for incidence measures (e.g., developed or died from skin cancers). Measures of absolute effects (e.g. mean differences in risks or odds) will be converted into relative effect measures, but if conversion is impossible, they will be excluded. To ensure comparability of effect estimates and facilitate meta-analysis, if a study presents an odds ratio, then we will convert it into a risk ratio, if possible, using the guidance provided in the Cochrane Collaboration's handbook for systematic reviews of interventions (Higgins and Green, 2011).

As shown in our logic framework (Fig. 1), we *a priori* consider the following variables to be potential effect modifiers of the effect of solar UVR on melanoma and NMSC: country, age, sex, socioeconomic position, industrial sector, occupation and formality of economy. As mediating factors we consider two groups of factors that affect the exposure-outcome relation through two different pathways, one related to work and one to personal factors (see Fig. 1).

If a study presents estimates for the effect from two or more alternative models that have been adjusted for different variables, then we will systematically prioritize the estimate from the model that we consider best adjusted, applying the lists of confounders and mediators identified in our logic model (Fig. 1). We will prioritize estimates from models adjusted for more potential confounders over those from models adjusted for fewer. For example, if a study presents estimates from a crude, unadjusted model (Model A), a model adjusted for one potential confounder (Model B) and a model adjusted for two potential confounders (Model C), then we will prioritize the estimate from Model C. We will prioritize estimates from models unadjusted for mediators over those from models that adjusted for mediators, because adjustment for mediators can introduce bias. For example, if Model A has been adjusted for two confounders, and Model B has been adjusted for the same two confounders and a potential mediator, then we will choose the estimate from Model A over that from Model B. We prioritize estimates from models that can adjust for time-varying confounders that are at the same time also mediators, such as marginal structural models (Pega et al., 2016), over estimates from models that can only adjust for time-varying confounders, such as fixed-effects models (Gunasekara et al., 2014), over estimates from models that cannot adjust for time-varying confounding. If a study presents effect estimates from two or more potentially eligible models, then we will explain specifically why we prioritized the selected model.

3.2.2. Information sources and search

3.2.2.1. Electronic academic databases. At a minimum, we (AM and MP) will search the four following electronic academic databases:

1. Ovid MEDLINE with Daily Update (1 January 1946 to 31 July 2018).
2. PubMed (1 January 1946 to 31 July 2018).
3. EMBASE (1 January 1947 to 31 July 2018).
4. Web of Science (1 January 1945 to 31 July 2018) with inclusion of three databases: Science Citation Index Expanded; Social Sciences Citation Index; and Arts and Humanities Citation Index.

The Ovid Medline search strategy for Systematic Review 2 is presented in Appendix H. We have tested and validated the search strategy for the four selected databases. The International Clinical Trials Register Platform, CISDOC and TOXNET databases were also tested, but their scopes were found to not sufficiently cover that of the systematic review. We will perform searches in electronic databases operated in the English language using a search strategy in the English language. We will adapt the search syntax to suit the other electronic academic and grey literature databases. When we are nearing completion of the review, we will search the PubMed database for the most recent publications (e.g., e-publications ahead of print) over the last six months. Any deviation from the proposed search strategy in the actual search strategy will be documented.

3.2.2.2. Electronic grey literature databases. At a minimum, we (AM and MSP) will search the two following electronic grey literature databases:

1. OpenGrey (http://www.opengrey.eu/).
2. Grey Literature Report (http://greylit.org/).

3.2.2.3. Internet search engines. We (AM and MSP) will also search the Google (www.google.com/) and GoogleScholar (www.google.com/scholar/) Internet search engines and screen the first 100 hits for potentially relevant records.

3.2.2.4. Organizational websites. The websites of the seven following international organizations and national government departments will be searched by AM and MSP:

1. International Labour Organization (www.ilo.org/).
2. World Health Organization (www.who.int).
3. European Agency for Safety and Health at Work (https://osha.europa.eu/en).
4. Eurostat (www.ec.europa.eu/eurostat/web/main/home).
5. China National Knowledge Infrastructure (http://www.cnki.net/).
6. Finnish Institute of Occupational Health (https://www.ttl.fi/en/).
7. United States National Institute of Occupational Safety and Health (NIOSH) of the United States of America, using the NIOSH data and statistics gateway (https://www.cdc.gov/niosh/data/).

3.2.2.5. Hand-searching and expert consultation. We (AM and MSP) will hand-search for potentially eligible studies in:

- Reference lists of previous systematic reviews.
- Reference lists of all study records of all included studies.
- Study records published over the past 24 months in the three peer-reviewed academic journals from which we obtain the largest number of included studies.
- Study records that have cited an included study record (identified in Web of Science citation database).
- Collections of the review authors.

Additional experts will be contacted with a list of included studies and study records, with the request to identify potentially eligible additional ones.

3.2.3. Study selection

Study selection will be carried out with Covidence (Babineau, 2014; Covidence, n.d.). All study records identified in the search will be downloaded, and duplicates will be identified and deleted. Afterwards, at least two review authors (AM and MSP) will independently screen against eligibility criteria titles and abstracts (step 1) and then full texts

of potentially relevant records (step 2). A third review author (CP or TT) will resolve any disagreements between the study selectors. If a study record identified in the literature search was authored by a review author assigned to study selection or if an assigned review author was involved in the study, then the record will be re-assigned to another review author for study selection. In the systematic review, we will document the study selection in a flow chart, as per PRISMA guidelines (Liberati et al., 2009).

3.2.4. Data extraction and data items

A data extraction form will be developed and trialled until data extractors reach convergence and agreement. At a minimum, two review authors (out of: AM, CP, MSP and SB) will extract data on study characteristics (including study authors, study year, study country, participants, exposure and outcome), study design (including summary of study design, comparator, epidemiological models used and effect estimate measure), risk of bias (including selection bias, reporting bias, confounding, and reverse causation) and study context (e.g. data on contemporaneous exposure to other occupational risk factors potentially relevant for deaths or other health loss from skin cancers). A third review author (SMJ, TL or TT) will resolve conflicts in data extraction. Data will be entered into and managed with the Review Manager, Version 5.3 (Review Manager (RevMan), 2014) or DistillerSR (Evidence Partners, 2017) softwares, but the Health Assessment Workspace Collaborative (HAWC) (Shapiro, 2013) may also be used in parallel or to prepare data for entry into RevMan 5.3.

We will also extract data on potential conflict of interest in included studies. For each author and affiliated organization of each included study record, we will extract their financial disclosures and funding sources. We will use a modification of a previous method to identify and assess undisclosed financial interest of authors (Forsyth et al., 2014). Where no financial disclosure or conflict of interest statements are available, we will search the name of all authors in other study records gathered for this study and published in the prior 36 months and in other publicly available declarations of interests (Drazen et al., 2010, 2009).

We will request missing data from the principal study author by email or phone, using the contact details provided in the principal study record. If we do not receive a positive response from the study author, we will send follow-up emails twice, at two and four weeks.

3.2.5. Risk of bias assessment

Standard risk of bias tools do not exist for systematic reviews for hazard identification in occupational and environmental health, nor for risk assessment. The five methods specifically developed for occupational and environmental health are for either or both hazard identification and risk assessment, and they differ substantially in the types of studies (randomized, observational and/or simulation studies) and data (e.g. human, animal and/or in vitro) they seek to assess (Rooney et al., 2016). However, all five methods, including the *Navigation Guide* (Lam et al., 2016), assess risk of bias in human studies similarly (Rooney et al., 2016).

The *Navigation Guide* was specifically developed to translate the rigor and transparency of systematic review methods applied in the clinical sciences to the evidence stream and decision context of environmental health (Woodruff and Sutton, 2014), which includes workplace environment exposures and associated health outcomes. The guide is our overall organizing framework, and we will also apply its risk of bias assessment method in Systematic Review 2. The *Navigation Guide* risk of bias assessment method builds on the standard risk of bias assessment methods of the Cochrane Collaboration (Higgins and Green, 2011) and the US Agency for Healthcare Research and Quality (Viswanathan et al., 2008). Some further refinements of the *Navigation Guide* method may be warranted (Goodman et al., 2017), but it has been successfully applied in several completed and ongoing systematic reviews (Johnson et al., 2016, 2014; Koustas et al., 2014; Lam et al., 2017, 2015, 2014; Rooney et al., 2016; Vesterinen et al., 2015). In our application of the *Navigation Guide* method, we will draw heavily on one of its latest versions, as presented in the protocol for an ongoing systematic review (Lam et al., 2016). Should a more suitable method become available, we may switch to it.

We will assess risk of bias 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) source population representation; (ii) blinding; (iii) exposure assessment; (iv) outcome assessment; (v) confounding; (vi) incomplete outcome data; (vii) selective outcome reporting; (viii) conflict of interest; and (ix) other sources of bias. While two of the earlier case studies of the *Navigation Guide* did not utilize outcome assessment as a risk of bias domain for studies of human data (Johnson et al., 2014; Koustas et al., 2014; Lam et al., 2014; Vesterinen et al., 2015), all of the subsequent reviews have included this domain (Johnson et al., 2016; Lam et al., 2017, 2016, 2015, 2014). Risk of bias or confounding ratings will be: “low”; “probably low”; “probably high”; “high” or “not applicable” (Lam et al., 2016). To judge the risk of bias in each domain, we will apply *a priori* instructions (Appendix I), which we have adopted or adapted from an ongoing *Navigation Guide* systematic review (Lam et al., 2016). For example, a study will be assessed as carrying “low” risk of bias from source population representation, if we judge the source population to be described in sufficient detail (including eligibility criteria, recruitment, enrollment, participation and loss to follow up) and the distribution and characteristics of the study sample to indicate minimal or no risk of selection effects. The risk of bias at study level will be determined by the worst rating in any bias domain for any outcome. For example, if a study is rated as “probably high” risk of bias in one domain for one outcome and “low” risk of bias in all other domains for the outcome and in all domains for all other outcomes, the study will be rated as having a “probably high” risk of bias overall.

All risk of bias assessors (BA, RA, MC, AG, FG, SMJ, SK, TL, AM, MSP and TT) will jointly trial the application of the risk of bias criteria until they have synchronized their understanding and application of these criteria. At least two study authors (out of: BA, RA, MC, FG, TL, AM, MSP and TT) will independently judge the risk of bias for each study by outcome. Where individual assessments differ, a third author (AG, SK and SMJ) will resolve the conflict. In the systematic review, for each included study, we will report our study-level risk of bias assessment by domain in a standard ‘Risk of bias’ table (Higgins and Green, 2011). For the entire body of evidence, we will present the study-level risk of bias assessments in a ‘Risk of bias summary’ figure (Higgins and Green, 2011).

3.2.6. Synthesis of results

We will conduct meta-analyses separately for estimates of the effect on prevalence, incidence and mortality. If we find two or more studies with an eligible effect estimate, two or more review authors (out of: BA, RA, TL, and MSP) will independently investigate the clinical heterogeneity of the studies in terms of types of studies, participants (including country, sex, age and industrial sector or occupation), level of risk factor exposure, comparator and outcomes. If we find that effect estimates differ considerably by country, sex and/or age, or a combination of these, then we will synthesise evidence for the relevant populations defined by country, sex and/or age, or combination thereof. Differences by country could include or be expanded to include differences by country group (e.g. WHO region or World Bank income group). If we find that effect estimates are clinically homogenous across countries, sexes and age groups, then we will combine studies from all of these populations into one pooled effect estimate that could be applied across all combinations of countries, sexes and age groups in the WHO/ILO joint methodology.

If we judge two or more studies for the relevant combination of country, sex and age group, or combination thereof, to be sufficiently clinically homogenous to potentially be combined quantitatively using

quantitative meta-analysis, then we will test the statistical heterogeneity of the studies using the I^2 statistic (Figueroa, 2014). If two or more clinically homogenous studies are found to be sufficiently homogenous statistically to be combined in a meta-analysis, we will pool the risk ratios of the studies in a quantitative meta-analysis, using the inverse variance method with a random effects model to account for cross-study heterogeneity (Figueroa, 2014). The meta-analysis will be conducted in RevMan 5.3, but the data for entry into these programmes may be prepared using another recognized statistical analysis programme, such as Stata. We will quantitatively combine neither data from studies with different designs (e.g. combining cohort studies with case-controls studies), nor unadjusted and adjusted models. We will only combine studies that we judge to have a minimum acceptable level of adjustment for confounders. If quantitative synthesis is not feasible, then we will synthesise the study findings narratively and identify the estimates that we judged to be the highest quality evidence available.

3.2.7. Additional analyses

If we source micro-data on exposure, outcome and potential confounding variables, we may conduct meta-regressions to adjust optimally for potential confounders.

If there is evidence for differences in effect estimates by country, sex, age, industrial sector and/or occupation, or by a combination of these variables, then we will conduct subgroup analyses by the relevant variable or combination of variables, as feasible. Where both studies on workers in the informal economy and in the formal economy are included, then we will conduct sub-group analyses by formality of economy. Findings of these subgroup analyses, if any, will be used as parameters for estimating burden of disease specifically for relevant populations defined by these variables. Where possible, we will also conduct subgroup analyses by study design (e.g. randomized controlled trials versus cohort studies versus case-control studies) and temporal direction for case-control and cohort studies (i.e. retrospective versus prospective). Subgroup analyses may also be conducted by different levels of solar UV exposure (e.g. quartiles of exposure and lifetime exposure in years) and specific types of melanoma and NMSC.

We will perform a sensitivity analyses that will include only studies judged to be of “low” or “probably low” risk of bias from conflict of interest; judged to be of “low” or “probably low” risk of bias; and with documented or approximated ICD-10 diagnostic codes. For meta-analyses with $I^2 \geq 75\%$, we may also conduct sensitivity analyses using two alternative meta-analytic models, namely the inverse variance heterogeneity (IVhet) (Doi et al., 2015a) and quality effects (QE) (Doi et al., 2015b) models.

3.2.8. Quality of evidence assessment

We will assess quality of evidence using a modified version of the *Navigation Guide* (Woodruff and Sutton, 2014) quality of evidence assessment tool (Lam et al., 2016). The tool is based on the GRADE approach (Schünemann et al., 2011) adapted specifically to systematic reviews in occupational and environmental health (Morgan et al., 2016). Should a more suitable method become available, we may switch to it.

We will assess quality of evidence for the entire body of evidence by outcome, with any disagreements resolved by a third review author. We will adopt or adapt the latest *Navigation Guide* instructions (Appendix E) for grading the quality of evidence (Lam et al., 2016). We will downgrade the quality of evidence for the following five GRADE reasons: (i) risk of bias; (ii) inconsistency; (iii) indirectness; (iv) imprecision; and (v) publication bias. If our systematic review includes ten or more studies, we will generate a funnel plot to judge concerns on publication bias. If it includes nine or fewer studies, we will judge the risk of publication bias qualitatively. To assess risk of bias from selective reporting, protocols of included studies, if any, will be screened to identify instances of selective reporting.

We will grade the evidence, using the three *Navigation Guide* standard quality of evidence ratings: “high”, “moderate” and “low” (Lam et al., 2016). Within each of the relevant domains, we will rate the concern for the quality of evidence, using the ratings “none”, “serious” and “very serious”. As per *Navigation Guide*, we will start at “high” for randomized studies and “moderate” for observational studies. Quality will be downgrade for no concern by nil grades (0), for a serious concern by one grade (−1) and for a very serious concern by two grades (−2). We will up-grade the quality of evidence for the following other reasons: large effect, dose-response and plausible residual confounding and bias. For example, if we have a serious concern for risk of bias in a body of evidence consisting of observational studies (−1), but no other concerns, and there are no reasons for upgrading, then we will downgrade its quality of evidence by one grade from “moderate” to “low”.

3.2.9. Strength of evidence assessment

We will apply the standard *Navigation Guide* methodology (Lam et al., 2016) to rate the strength of the evidence. The rating will be based on a combination of four criteria: (i) quality of the body of evidence; (ii) direction of effect; (iii) confidence in effect; and (iv) other compelling attributes of the data that may influence our certainty. The ratings for strength of evidence for the effect of solar UV exposure on melanoma and NMSC will be “sufficient evidence of toxicity/harmfulness”, “limited of toxicity/harmfulness”, “inadequate of toxicity/harmfulness” and “evidence of lack of toxicity/harmfulness” (Appendix J).

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Author contributions

II, NL, FP and APU had the idea for the systematic review. II, NL, FP and YU gathered the review team. FP led and all authors contributed to the development of the standard methodology for all systematic reviews in the series. FP led and all authors contributed to the development and writing of the standard template for all protocols in the series. SMJ is the lead reviewer of this systematic review. AM, MSP, SMJ and TL wrote the first draft of this protocol, using the protocol template prepared by FP, and AG, BA, CA, CP, FG, FP, IA, MW, RA, TT, SB, SK and YU made substantial contributions to the revisions of the manuscript. The search strategy was developed and piloted by AM and MSP in collaboration with a research librarian. SMJ, FP, BA, RA and TL are experts in epidemiology, SMJ is an occupational dermatologist, and FP is an expert in systematic review methodology. FP coordinated all inputs from the World Health Organization, International Labour Organization and external experts and ensured consistency across the systematic reviews of the series. SMJ is the guarantor of the systematic reviews.

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Appendices A, B, C, D, E, F, G, H, I and J. Supplementary data

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