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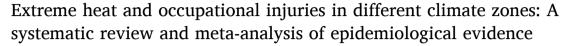
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Review article



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ABSTRACT

Background: The link between heat exposure and adverse health outcomes in workers is well documented and a growing body of epidemiological evidence from various countries suggests that extreme heat may also contribute to increased risk of occupational injuries (OI). Previously, there have been no comparative reviews assessing the risk of OI due to extreme heat within a wide range of global climate zones. The present review therefore aims to summarise the existing epidemiological evidence on the impact of extreme heat (hot temperatures and heatwaves (HW)) on OI in different climate zones and to assess the individual risk factors associated with workers and workplace that contribute to heat-associated OI risks.

Methods: A systematic review of published peer-reviewed articles that assessed the effects of extreme heat on OI among non-military workers was undertaken using three databases (PubMed, Embase and Scopus) without temporal or geographical limits from database inception until July 2020. Extreme heat exposure was assessed in terms of hot temperatures and HW periods. For hot temperatures, the effect estimates were converted to relative risks (RR) associated with 1 $^{\circ}$ C increase in temperature above reference values, while for HW, effect estimates were RR comparing heatwave with non-heatwave periods. The patterns of heat associated OI risk were investigated in different climate zones (according to Köppen Geiger classification) based on the study locations and were estimated using random-effects meta-analysis models.

Subgroup analyses according to workers' characteristics (e.g. gender, age group, experience), nature of work (e.g. physical demands, location of work i.e. indoor/outdoor) and workplace characteristics (e.g. industries, business size) were also conducted.

Results: A total of 24 studies published between 2005 and 2020 were included in the review. Among these, 22 studies met the eligibility criteria, representing almost 22 million OI across six countries (Australia, Canada, China, Italy, Spain, and USA) and were included in the meta-analysis. The pooled results suggested that the overall risk of OI increased by 1% (RR 1.010, 95% CI: 1.009-1.011) for $1\,^{\circ}$ C increase in temperature above reference values and 17.4% (RR 1.174, 95% CI: 1.057-1.291) during HW.

Among different climate zones, the highest risk of OI during hot temperatures was identified in Humid Subtropical Climates (RR 1.017, 95% CI: 1.014–1.020) followed by Oceanic (RR 1.010, 95% CI: 1.008–1.012) and Hot Mediterranean Climates (RR 1.009, 95% CI: 1.008–1.011). Similarly, Oceanic (RR 1.218, 95% CI: 1.093–1.343) and Humid Subtropical Climates (RR 1.213, 95% CI: 0.995–0.431) had the highest risk of OI during HW periods. No studies assessing the risk of OI in Tropical regions were found. The effects of hot temperatures on the risk of OI were acute with a lag effect of 0.995–0.9950 regions were found. The effects of hot temperatures on the risk of OI were acute with a lag effect of 0.9950 regions were found. The effects of hot temperatures and workers and workers in agriculture, forestry or fishing, construction and manufacturing industries were at high risk of OI during hot temperatures. Further young workers (age 0.950 years), male workers and those working in electricity, gas and water and manufacturing industries were found to be at high risk of OI during HW.

Conclusions: This review strengthens the evidence on the risk of heat-associated OI in different climate zones. The risk of OI associated with extreme heat is not evenly distributed and is dependent on underlying climatic conditions, workers' attributes, the nature of work and workplace characteristics. The differences in the risk of OI across different climate zones and worker subgroups warrant further investigation along with the development of climate and work-specific intervention strategies.

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1. Introduction

Climate change has led to a significant rise of 0.8 °C-0.9 °C in global mean temperature, leading to frequent and severe heatwaves (HW) (Glaser et al., 2016). Increasing temperatures and HW have and will continue to pose adverse effects on human health, ranging from minor discomfort to death, as documented in numerous epidemiological studies across the world (Amegah et al., 2016; Åström et al., 2011; Azongo et al., 2012; Song et al., 2017). It is predicted that the trend of increasing temperatures and frequent occurrences of HW will continue into the future placing populations at further risk. Recent studies have raised serious concerns about the impacts of extreme heat on workers' health (Kjellstrom et al., 2016; Yang et al., 2017). Workers, as opposed to the general public are usually required to work under exposed conditions for extended periods. The combined effects of prolonged exposure to heat and hot environments, physical work demands and work uniform requirements contribute to heat stress experienced by workers in several occupations and industries (Gao et al., 2018; McCarthy et al., 2018). Thermal exposure can elicit heat stress, acute impairment of work capacity, heat-related illness, loss of productivity and even death among workers (Cheung et al., 2016). Diminished performance and work capacity may further lead to an increased risk of occupational injuries (OI) in the workplace (Binazzi et al., 2019).

A growing body of epidemiological evidence suggests that the risk of OI increases at hot temperatures as compared to an intermediate 'comfortable' temperature range (Adam-Poupart et al., 2015; Ricco, 2018; Tawatsupa et al., 2013). A majority of studies assessing the risk of heat-related OI have found a curvilinear response with a steeper slope at higher temperature thresholds (Marinaccio et al., 2019; Martínez-Solanas et al., 2018; Varghese et al., 2019). Most of these studies were conducted in developed countries with Temperate Climates (Marinaccio et al., 2019; Spector et al., 2016; McInnes et al., 2017; Xiang et al., 2014), while two studies were from developing countries with Humid Subtropical Climates (Guangzhou, China) (Sheng et al., 2018; Ma et al., 2019). However, the thermal exposure thresholds at which the risk of OI increases varies from region to region because of the underlying climate. For example a study from Adelaide, Australia with a dry Warm Mediterranean Climate showed that 1 $^{\circ}\text{C}$ increase in maximum temperature (Tmax) above 14.2 $^{\circ}\text{C}$ and below 37 $^{\circ}\text{C}$ was associated with an increased risk of OI (Xiang et al., 2014), while in Guangzhou, China, Tmax above 30 °C was found to be linearly associated with an increased risk of OI (Sheng et al., 2018). Particularly noteworthy here are the differences in thermal exposure limits. It appears that the threshold above which the risk of OI increases is higher in Guangzhou than Adelaide, suggesting that the heat impacts vary. This geographic variability is due to the underlying local climatic conditions because human health is primarily affected by the long-term climate and seasonal trends rather than daily weather variability (Kalkstein et al., 1996). People are largely adapted to the local climate, in their physiology, culture and engineered supporting infrastructure (Nairn and Fawcett, 2015).

Previously conducted reviews have explored the risk of OI associated with heat exposure (Binazzi et al., 2019; Bonafede et al., 2016; Levi et al., 2018; Spector et al., 2019; Varghese et al., 2018; Xiang et al., 2013). Three comprehensive reviews of the literature (Spector et al., 2019; Varghese et al., 2018; Xiang et al., 2019; Varghese et al., 2018; Xiang et al., 2013) published until December 2019, provided evidence on the relationship between heat exposure and the risk of OI and identified specific individual and occupational characteristics that contribute to the vulnerability of workers. These reviews of ecological observational studies have indicated that a linear relationship exists between hot weather and the risk of OI. Further, male workers and young workers (age < 25 years) and those working in outdoor intensive industries such as agriculture, forestry and fishing and construction were found to be at high risk (Binazzi et al., 2019; Xiang et al., 2013).

Occupational injuries including both serious and traumatic injuries arising from slips, trips and falls, exposure to harmful objects, blunt

forces and hitting objects, wounds, lacerations and amputations, burns and minor cuts etc. have been reported to increase in hot weather conditions (Bonafede et al., 2016; Spector et al., 2019; Varghese et al., 2018). Varghese et al. (2018) shed light on the potential mechanisms of heat-associated risk of OI involving a combination of physiological and psycho-behavioral responses which upon interaction with other workplace hazards result in OI. Further, a systematic review (Bonafede et al., 2016) explored the associations between extreme weather conditions (both heat and cold) and OI. This systematic review included eight studies published till November 2014 in the qualitative synthesis and showed an association between high temperatures/HW and risk of workrelated injuries. More recently, Binazzi et al. (2019) carried out a metaanalysis to summarize the evidence on the heat associated risk of OI and identified specific subgroups of workers at higher risk. A total of eight studies published till October 2018 were included in this meta-analysis and estimated an increased risk of 0.5% (RR 1.005, 95% CI: 1.001-1.009) of OI associated with heat exposure. However, Binazzi et al. (2019) pooled estimates from eight studies irrespective of underlying climates and exposures variables (hot temperatures and HW). For example, the estimates from four city-based (Garzon-Villalba et al., 2016; McInnes et al., 2017; Xiang et al., 2014; Sheng et al., 2018) and three province/state-based studies (Adam-Poupart et al., 2015; Ricco, 2018; Spector et al., 2016) were pooled with that from a whole country based study (Martínez-Solanas et al., 2018), without considering the possible geographical variability of the effect estimates across different locations. Subgroup analyses based on a limited number of variables such as gender, age and industries revealed increased risk for male workers, young workers (with age < 25 years) and those working in the agricultural industry. Other characteristics such as work experience, physical demands of the occupation, business size and industries where heat has been shown previously to be problematic (e.g. electricity, gas, and water, transport etc.) were not considered.

Between 2018 and early 2020, multiple studies have been published concerning the heat-associated risk of OI and covering a range of occupations and geographical locations with diverse climates. While both previous systematic reviews (Binazzi et al., 2019; Bonafede et al., 2016) assessed the risk of bias in individual studies, the strength and quality of their synthesized evidence were not systematically assessed. We therefore systematically reviewed observational ecological studies regarding heat exposure, considering both hot temperatures and HW, and OI risk including more recent studies and undertook an extended meta-analysis using location-specific estimates at the city/province-level classified by Köppen Geiger climate zones. Our primary research question in terms of Population, Exposure, Comparator, Outcome and Study design (PECOS) (Morgan et al., 2018) was:

Among non-military workers (Population) what is the effect of extreme heat assessed in terms of hot temperatures and heatwaves (Exposure) estimated per 1 °C increase in temperature or HW vs non-HW periods (Comparator) on the incidence of Occupational Injuries (Outcome) in observational ecological studies (Study design)?

Further, we also aimed to address the following two specific research questions:

- 1. How does the risk of OI associated with extreme heat vary in different climate zones of the world?
- 2. Which workers are at high risk of OI associated with extreme heat in terms of workers' characteristics, nature of work and workplace characteristics?

2. Methods

2.1. Search strategy and selection criteria

A systematic review of published literature for studies that assessed the effects of extreme heat on OI was undertaken using three databases (PubMed, Embase and Scopus). A comprehensive search strategy focused on "Extreme Heat" and "Occupational Injuries" was developed in consultation with the University librarian (Tables A1-A3, Appendix A of Supplementary Material - SM). The search strategy was designed using the PECOS framework (Morgan et al., 2018; Moola et al., 2015). Briefly, it included keywords such as "hot temperatures" and "heatwaves", "occupations" and "industries", "occupational injuries", "risk assessment" and "epidemiological studies". The study selection criteria based on our PECOS statement is presented in Table 1. Studies were considered eligible after full-text evaluation, if: (a) they explicitly examined and quantitatively reported a risk estimate including odds ratios (OR), incidence rate ratios (IRR) or relative risks (RR) for the relationship between heat exposure (hot temperatures and HW) and OI in non-military workers and (b) they were peer-reviewed publications in English (Table 1). Studies were excluded if: (a) they examined the risk in military workers (b) they addressed process-generated heat, (c) they qualitatively evaluated heat exposure, for example in a questionnaire survey and (d) they were conference abstracts without full-text or non-English articles, editorials, or review articles. No additional filter was applied for publication date.

The search was initially run on November 23, 2019 and was last updated on July 20, 2020 before the finalization of this review.

2.2. Study selection process

Studies retrieved from the three electronic databases were imported into the Endnote X9 reference management system and duplicates were subsequently removed. The study selection process is shown in Fig. 1. All retrieved studies were then identified by initial screening of titles followed by abstract screening. If the information in titles or abstracts was not sufficient to decide on inclusion or exclusion of the study, then the full text was reviewed for eligibility. The studies were screened against inclusion exclusion criteria by two authors independently (SHF and BMV). Inconsistencies between the two authors were discussed for clarification and agreement on final reporting with the other authors. References in each of the identified papers were also examined for any additional studies that may have been missed in our electronic database searches. As the health impacts of HW are different from that of a single

Table 1
Studies eligibility criteria.

Outcome

Study

Design

Studies eligibility criteria based on PECOS elements All epidemiological studies assessing the risk of occupational injuries **Population** among non-military workers associated with extreme heat, published from database inception until July 20, 2020 were eligible for inclusion. Exposure All epidemiological studies where extreme heat was quantified in terms of hot temperature and HW. The following heat exposure metrics were considered: maximum temperature (Tmax), minimum temperature (Tmin), mean temperature (Tmean) or composite measures of the thermal indices that take into account additional atmospheric variables such as humidity, wind speed, and solar exposure (e.g. Wet Bulb Globe Temperature (WBGT), apparent temperature (AT), Humidex) and HW classifications. HW have been previously defined as extended periods of hot temperatures with three or more days above 35 $^{\circ}\text{C}$ or using indices such as Excess Heat Factor (EHF) to measure intensity, load and duration of HW events (Nairn and Fawcett, 2015). Comparator Study design did not use any comparators, however the risk is estimated with reference to lower level of exposure. For example for hot temperatures studies there are generally- reference temperatures or thresholds beyond which there is an increase in risk or is a comparison between temperature percentiles while for heatwave studies the reference

"Occupational Injuries" were defined as any personal injury (injury,

occupational accident (ABS, 2018). Occupational illnesses with long

latency periods, symptoms of heat stress and loss of productivity were

retrospective cohort studies and case-control studies were considered for

Observational studies including ecological studies, prospective and

illness or death) taking place at the workplace as the result of an

is made to non-heatwave periods.

inclusion

hot day, evidence available on the risk of OI associated with extreme heat were categorized into studies assessing the risk at hot temperature and studies assessing the risk during HW periods.

2.3. Data extraction

Relevant study characteristics were extracted from eligible hot temperature and HW studies into a Microsoft Excel spreadsheet. The characteristics included: authors, year of publication, location, (where the study was conducted), climate zones, region (Asia, Australia, Europe and North America), type of industry (agriculture, construction etc.) study population (smelter workers, disaster relief workers etc.), exposure metrics (Tmax, Tmin, Tmean, Humidex or WBGT etc.), minimum reference temperature, highest threshold temperature associated with risk, study design (time series or case crossover), type of statistical models (examples such as Distributed Lag Nonlinear Models or Generalized Additive Models etc.), number of injury records, study duration, time span (short < 5 years or long > 5 years), yearly trend (i.e. whole year or warm season only), effect estimates (RR/OR/IRR) and confidence intervals or mean difference and standard deviation.

Climate zones were extracted for each study location (city, state or provinces) from the 1 Km resolution Köppen Geiger climate classification maps (Beck et al., 2018) and was verified with the climate data developed for cities across the world (Climate-Data.org, Climate data for cities worldwide, 2020). To enable investigation of heat associated risk of OI in different climate zones, location-specific risk estimates were extracted at city, state or province level from the published studies. For studies reporting regional-level results (i.e. province or state level) or national level results, location-specific estimates were obtained from published tables, through textual/graphical descriptions and supplementary materials. When information from figures seemed imprecise, or when data seemed available but was not given in the articles, the relevant studies' authors were contacted at least twice to request for additional data. A unique combination of authors, year of publication and location was used to identify the location-specific effect estimates which were further classified into nine Köppen Geiger climate zones (Humid and Warm Continental, Warm Mediterranean, Hot Mediterranean, Oceanic, Humid Subtropical, Hot Semi-arid, Cold Semi-arid, Subarctic, Hot Deserts Climates) based on Köppen Geiger classification (Köppen and Geiger, 1930).

For hot temperature studies, the effect estimates were reported either as "1°C increase in temperature" (Adam-Poupart et al., 2015; Spector et al., 2016; McInnes et al., 2017; Xiang et al., 2014; Sheng et al., 2018) or as a "comparison between temperature percentiles" (e.g. 90th percentile vs 50th percentile (Varghese et al., 2019; Schifano et al., 2019) or as a "comparison between extreme heat and the reference value where the injury risk was minimal" (e.g. 99th percentile vs. the minimum injury temperature percentile (Marinaccio et al., 2019; Martínez-Solanas et al., 2018; Varghese et al., 2019). Different estimates of effect sizes (e.g. OR, RR, IRR and percent change) have been used to quantify the risk of OI in the reference studies. In studies where ORs were reported, (Ricco, 2018; Spector et al., 2016; McInnes et al., 2017; Schifano et al., 2019; Calkins et al., 2019; Ricco et al., 2020; Ricco et al., 2019) the effect estimates were converted to RR under the assumption that OR approximate RR when the outcome is rare (Diaz-Quijano, 2012). In one study (Rameezdeen and Elmualim, 2017), results were presented as effect sizes and p-values. The method of Altman and Bland (2011) was used to estimate the risk confidence intervals for that study. In another study by Martínez-Solanas et al. (2018) effect estimate sizes were not available numerically at the provincial level. The percentage change was manually estimated from the exposure-response graphs for each province from the study's supplementary material and was converted to RR and 95% confidence intervals.

All effect estimates for hot temperature studies were converted into a common exposure unit of 1 °C increase above reference temperature to quantitatively pool the estimates following the approach of Luo et al.

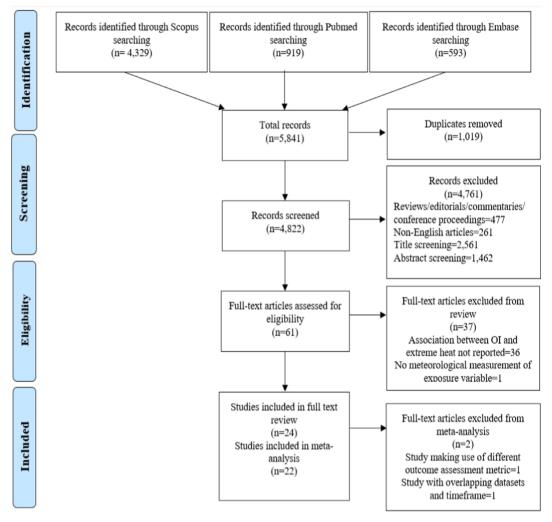


Fig. 1. Flow chart of the selection process to retrieve relevant studies (n = 24).

(2019). For studies assessing the risk using 1 $^{\circ}$ C increase in temperature, we recorded the reference temperature values and effect estimates associated with each 1 °C increase above the reference values. When percentile-based RR were given, we recorded the temperature values at the reference percentiles (e.g. 25th or 50th percentiles) and maximum percentiles (e.g. 75th, 95th or 99th) and the effect estimates between those percentile ranges. To quantify the effect estimates associated with a 1 °C increase in temperature above the reference value, we calculated the effect as the log RR divided by the range of temperature values at reference percentiles and maximum percentile in each city assuming a log-linear association of OI and heat beyond reference temperature (Luo et al., 2019; Ma et al., 2014; Sun et al., 2018). For HW studies, the effect estimates were extracted as RR and no conversion was performed as they compared the risk of OI in HW versus non-HW periods. For studies that focused on the same city during the same time period but stratified their analysis based on subgroups (e.g. one study assessing the impacts of heat on migrants workers (Ricco et al., 2019) and stratified their analysis into Islamic and non-Islamic holiday periods), we pooled the RRs using fixedeffect models to arrive at one estimate for city and time specific period.

2.4. Assessment of evidence

We used the Navigation Guide framework (Johnson et al., 2014; Johnson et al., 2016) to assess the strength of evidence in the reviewed articles. This framework offers a rigorous and transparent methodology for translating environmental studies including separate guidelines specifically for observational studies (Johnson et al., 2014; Johnson

et al., 2016; Goodman et al., 2017; Woodruff and Sutton, 2014). The assessment of evidence was carried out in three steps for both hot temperatures studies and HW studies: Step 1: Assessment of risk of bias in individual studies, Step 2: Assessment of quality of evidence across the studies and Step 3: Assessment of the strength of evidence across the studies for each outcome type.

Each stage of assessment was carried out by two authors independently (SHF and BMV) resolving any disagreement through discussion.

2.4.1. Step 1: Assessment of risk of bias in individual studies

The risk of bias across individual studies was assessed in the following domains: exposure assessment, outcome assessment, recruitment/selection strategy, confounding bias, incomplete outcome data, selective reporting and conflict of interest based on the predefined criteria. A predefined, unequivocal criteria was developed in each of the domains, modified from (Johnson et al., 2014; Woodruff and Sutton, 2014; Achilleos et al., 2017) (Appendix B of SM). Each study was rated as having "Low" (L), "Probably Low" (PL), "Probably High" (PH) or "High" (H) probability of bias. Any disagreements among the reviewers were resolved through discussions until a consensus on quality was reached.

2.4.2. Step 2: Assessment of quality of evidence across the studies

The Navigation Guide framework follows the approach developed by the Grading of recommendations, assessment, development and evaluation methods (GRADE), i.e. first assigning a pre-specified rating to the body of evidence and then considering adjustments (upgrading and downgrading) based on the characteristics of the included studies (Johnson et al., 2016; Balshem et al., 2011). The quality ratings are not additive scores but serve as qualitative guidance in assessing the overall quality of evidence (Johnson et al., 2016). GRADE guidelines evaluate clinical interventions and experimental human studies i.e. randomized control trials as "high" quality of evidence (Guyatt et al., 2011) and assign "low" quality to observational studies (Balshem et al., 2011). However, not all observational studies are of low quality (Johnson et al., 2014; Viswanathan et al., 2013) and the decision in the context of environmental health is primarily dependent on human observational data (Johnson et al., 2014). Therefore, in line with other methodological reviews (Johnson et al., 2014; Viswanathan et al., 2013) we initially assigned "moderate" quality to the overall body of evidence across all observational studies, in recognition of the value and limitations of such data in examining the associations between environmental exposures and health outcomes.

The upgrading and downgrading of the overall body of evidence is based on eight specific factors including: (1) risk of bias, (2) indirectness, (3) inconsistency, (4) imprecision, (5) publication bias, (6) large magnitude of effect, (7) dose response and (8) whether confounding minimizes the effect. These eight factors are based on GRADE guidelines (Johnson et al., 2014; Balshem et al., 2011) and their criteria for evaluation of the quality of evidence is detailed in Table C1, Appendix C of SM. Various statistical tests were performed to check the overall quality of evidence for risk of bias across the studies, inconsistencies (measured in terms of heterogeneity) and risk of publication bias (Higgins et al., 2003; Higgins and Green, 2008). As a result, the possible ratings were 0 (no change from initial quality rating), -1 (1 level downgrade) or -2 (2 level downgrade); +1 (1 level upgrade) or +2 (2 level upgrade).

Each reviewer independently evaluated the quality of evidence and then compared the ratings and rational for each quality factor. The downgrading and upgrading were conservative, and only when there was a compelling evidence to do so. The weighting of downgrades and upgrades in the overall quality assessment was done after thorough judgements and evidence from statistical tests.

2.4.3. Step 3: Assessment of strength of evidence across the studies

We rated the strength of the body of evidence provided in reviewed papers based on four considerations: (1) "quality of the body of evidence" (i.e. the study ratings from steps 1 and 2 of the assessment); (2) "direction of effect" (i.e. consistency in findings across studies on the risk of OI associated with hot temperatures or HW); (3) "confidence in the effects" (i.e. the likelihood of a new study changing our conclusions); and (4) "any other attributes that affect certainty", as highlighted by Johnson and colleagues (Johnson et al., 2016; Johnson et al., 2014; Woodruff & Sutton, 2014). We used these considerations to assign the overall strength rating, according to the definitions specified in the Navigation Guide for "sufficient evidence", "limited evidence", "inadequate evidence" or "lack of evidence" (Table C2, Appendix C of SM).

2.5. Synthesis of results

Quantitative synthesis was conducted in the form of meta-analysis and forest plots for studies assessing the risk during hot temperatures and HW periods. The meta-analyses were further classified into different climate zones for both categories of heat exposures (where possible). In case of studies not suitable for inclusion in the meta-analysis, we synthesized the study findings narratively and added these to the relevant climate zone results section.

2.5.1. Meta-analyses

There were two steps in the statistical analysis to meet the specific research questions of the study: (1) separately pooling estimates for hot temperatures and HW overall and by climate zones using random-effects models; and (2) performing subgroups analysis.

We estimated the pooled RR of OI associated with exposure to hot

temperature overall and separately for each of the climate zones where possible (when total number of city/province-specific effect estimates (K) were greater than equal to two i.e. $K \ge 2$). While different temperature metrics were used in the included studies, we pooled the RR regardless of the exposure metric due to the strong correlation between different measurements of temperature which suggests that on average, they have the similar predictive ability (Varghese et al., 2019).

For HW studies separate meta-analyses were conducted to pool RR of OI during HW compared to non-HW periods overall and in each climate zone where possible (i.e. K \geq 2). The studies included in this review used different definitions of HW. In some studies, HW were defined as Tmax \geq 35 °C for three or more consecutive days (Ricco, 2018; Ricco et al., 2020; Ricco et al., 2019; Rameezdeen and Elmualim, 2017; McInnes et al., 2018; Xiang et al., 2014). Varghese et al. (2019, 2018) used the dimensionless location-specific EHF index to assess HW, developed by Nairn and Fawcett (2015). EHF accounts for both short-term and long-term temperature anomalies by comparing the location specific three day Tmean with the 95th percentile of Tmean and the preceding 30 days Tmean (Nairn and Fawcett, 2015; Scalley et al., 2015). EHF is thus a potentially useful indicator to assess the effect of HW at a local population level on health outcomes.

While the HW definitions used in these studies differ, they quantify the risk of heat-related OI in relation to temperatures above the 95th percentile (i.e. 35 °C) (Rameezdeen and Elmualim, 2017; McInnes et al., 2018; Xiang et al., 2014). That is also captured by the studies using the EHF definition (Varghese et al., 2019; Varghese et al., 2018). Hence, we combined all the HW studies together for meta-analysis and presented them separately for different climate zones (where possible). It should be noted that for HW studies temperature variable was not included in the models and all studies modelled HW as the lagged effect of three or more days of hot temperatures. A random-effects meta-analysis was performed to obtain pooled results in different climate zones for both hot temperatures and HW studies considering the heterogeneity in included studies (for example based on different study designs, geographical locations, workforce characteristics etc.). Random-effects models assume that there may be different underlying true effects estimated in each trial which are distributed about an overall mean and are appropriate when heterogeneity between studies is anticipated. The I² statistic was calculated to quantify the degree of heterogeneity (Higgins et al., 2003). I^2 values of 0-25%, 25-50% and >50% were taken as indicative of low, moderate and high heterogeneity, respectively (Higgins et al., 2003).

In addition to I², we also used the 80% prediction intervals (PI) to assess heterogeneity between studies in line with previous systematic reviews (Orellano et al., 2020; Lee et al., 2020). We considered severe heterogeneity when the 80% PI contained unity and was twice the width of confidence intervals. A series of sensitivity analyses were conducted to explore the potential causes of heterogeneity using overall pooled estimates from all studies. Leave-one-out analysis was performed by iteratively removing one study at a time to confirm that our findings were not driven by any single study. Further, a set of sensitivity analyses were also conducted to calculate the pooled estimates for hot temperature studies based on different exposure metrics (Tmax, Tmean, thermal indices), exposure assessment datasets (single/multiple weather station data vs gridded, geolocated or satellite data) and unit of estimate (1 °C increase in temperature vs comparing percentiles). For HW studies sensitivity analysis was carried out based on exposure assessment datasets and different definitions of HW. Publication bias was evaluated for both hot temperature and HW studies (where possible) using Funnel plots, Begg's and Egger's tests (Egger et al., 1997). We further used Duval and Tweedie's Trim and Fill procedure (Duval and Tweedie, 2000) with random-effects model to recompute the pooled effect sizes after adjusting for small study bias.

2.5.2. Subgroup analyses

Subgroup analyses were conducted by workers characteristics (such

as gender, age, experienced vs new workers), nature of work (such as physical demands and location of work outdoors and indoors) and workplace characteristics (such as type of industries and business size). Additional subgroup analysis based on study characteristics (such as region, study design and modelling techniques) was also carried out. To accommodate the different age group categories across included studies, we stratified pooled estimates for different age groups as age below 35 years and above 35 years and excluded Adam-Poupart et al. (2015) and Ricco et al. (2020) as the age groups did not match with other studies. Subgroup analysis by workers, nature of work, and workplace characteristics was not conducted in different climate zones because of limited number of studies (K < 2).

All analyses were performed using 'Metan' command in Stata version 15 (Stata Corp 2013, Harris et al., 2008).

3. Results

3.1. Included studies

Our search retrieved a total of 5841 records. After eliminating duplicate records, 4822 unique records remained. Another 738 articles were excluded because they were either reviews, editorials, conference papers or in other languages. A total of 4023 articles out of the remaining 4084 were excluded as a result of initial screening of titles and abstracts based on inclusion and exclusion criteria. The remaining 61 articles were assessed for full-text eligibility. Thirty-seven articles were excluded because they did not report an association between extreme heat and risk of OI or did not use a direct measure of extreme heat to quantify the risk. The remaining 24 articles were selected for the full-text review as shown in Fig. 1.

3.2. Characteristics of included studies

All studies included in the full text review were published in the past fifteen years between January 2005 and July 2020, although no date restriction was applied to the search. All studies used either a time series

(n = 14) or case-crossover (n = 10) study designs. Two nationwide studies (Marinaccio et al., 2019; Martínez-Solanas et al., 2018) estimated the location-specific risk in all provinces of Italy and Spain. Three studies from Italy and Australia were multi-city studies representative of different climates, and 19 studies were representative of only one city/ state/province from various countries such as Australia, Canada, USA, and China. Together, all studies encompass nine climate zones, with a majority of studies representative of mid-latitude temperate climatic zones. Fig. 2 shows the geographic distribution of studies within different climate zones. Sixteen studies were focused on all workers, whereas, eight studies were focused on specific group of workers such as agriculture workers (Ricco, 2018; Spector et al., 2016), construction workers (Calkins et al., 2019; Ricco et al., 2020; Rameezdeen and Elmualim, 2017), aluminum smelter workers (Fogleman et al., 2005), disaster relief workers (Garzon-Villalba et al., 2016) and migrant workers (Ricco et al., 2019).

Sixteen studies assessed the risk of OI in hot temperatures only, while three studies estimated the risk in both hot temperatures and HW periods, and five studies assessed the risk exclusively during HW. In total, 19 studies were used to assess the risk of OI associated with hot temperatures. The study characteristics are given in Table 2. Eight studies were used to assess the risk of OI during HW periods, and their study characteristics are presented in Table 3.

3.3. Assessment of evidence

3.3.1. Assessment of risk of bias in individual studies

The risk of bias assessment of the included studies (hot temperature and HW studies) is summarized in Figs. 3 and 4. Detailed risk of bias assessment of all individual studies is presented in Tables D1–D24, Appendix D of SM.

3.3.1.1. Hot temperature studies. Two out of 19 (11%) hot temperature studies (Sheng et al., 2018; Ma et al., 2019) assessing the risk of OI had a "probably high" risk of bias in recruitment/selection strategy, as the baseline data were representative of only 54% of the workers'

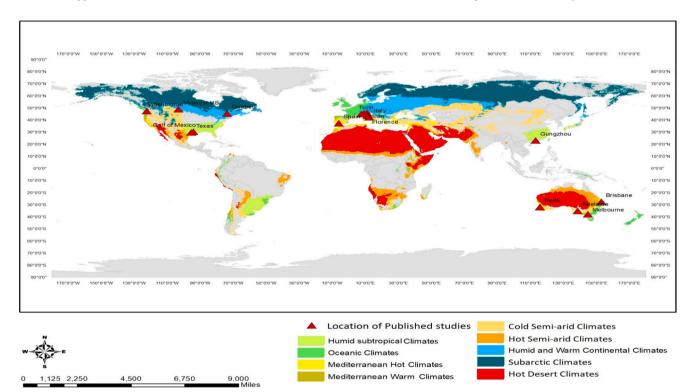


Fig. 2. Geographic distribution of published studies included in the review (n = 24) within nine climate zones.

 $\label{eq:conditions} \textbf{Table 2} \\ \textbf{Study characteristics and key findings of all studies assessing the risk of OI in hot temperature conditions (n = 19).} \\$

First Author, Year	Location	Climate	Study Population	Study Design	Exposure metric and source	Key findings ES(CI)
Fogleman et al., 2005	Midwest US	Humid and Warm Continental Climates	Aluminum smelter workers	TS	Daily Heat Index Comparing Percentiles: Ref Heat Index: 13.5 Threshold Heat Index: 38	RR: 1.050 (1.024–1.076)
Morabito et al., 2006	Tuscany, Italy	Hot Mediterranean Climates	All occupations	TS	Daily maximum AT Daily average AT Maximum AT \geq 31.1 °C	$X^2 = 9.3$ P-value = 0.025 Reversed U shape response
Xiang et al., 2014	Adelaide, Australia	Warm Mediterranean Climates	All occupations	TS	1 °C increase in Tmax	Revised to single response IRR: 1.002 (1.001–1.004) Gender M: 1.004 (1.002–1.006) F: 0.998 (0.994–1.001) Age ≤24: 1.005 (1.002–1.008) 25–34: 1.002 (0.999–1.003) 35–54: 1.001 (0.999–1.003) ≥55: 1.000 (0.997–1.003) Industries Agriculture: 1.007 (1.001–1.013) Construction: 1.006 (1.002–1.011) Reverse U shaped response with no lagged effect
Adam-Poupart et al., 2015	Quebec, Canada	Humid and Warm Continental Climates: Bas-Saint Laurent, Capitale Nationale, Maurice, Estrie, Montreal, Outaoais, Abitibi- Temiscamingue, Chaudere-Appalaches, Laval, Lanaudiere, Laurentides, Montrege Subarctic: Sanguenay-Lac-Saint, Jaen, Cote- Nord, Nord-du-Quebec, Gaspesia-lies-de-la- Madeleine	All occupations	TS	1 °C increase in Tmax	Hint is tagget eypter IRR: 1.002 (1.001–1.003) Gender M: 1.003 (1.002–1.005) F: 1.000 (0.998–1.003) Age 15–24: 1.008 (1.005–1.010) 25–44: 1.003 (1.001–1.004) ≥45: 1.000 (0.999–1.001) Industries Forestry and logging: 1.011 (1.001–1.020) Construction: 1.003 (1.000–1.006) Linear and lagged response
Garzon- Villalba et al., 2016	Gulf of Mexico, US	Humid Subtropical Climates	Disaster relief workers	TS	1 °C increase in WBGTmax	RR: 1.060 (1.040–1.070) No delayed effect for acute injuries
Spector et al., 2016	Washington, US	Warm Mediterranean Climates	Agriculture Workers	CCO	1 °C increase in Humidex	OR: 1.010 (1.010–1.020) Reverse U shaped curve
Martínez- Solanas et al., 2018	Spain	Oceanic: Alava, Asturias, Burgos, Cantabria, Guipzcoa, Huesca, La Rioja, Leon, Lugo, Navarra, Palencia, Soria, Teruel, Vallodoid, VizcayaWarm Mediterranean: A coruna, Avila, Pontevedra, Salamanca, Segovia, Hot Mediterranean: Badajoz, Barcelona, Caceres, Cadiz, Cordoba, Cuenca, Granada, Girona, Guadalajara, Huelva, Jaen, Madrid, Malaga, Ourense, Sevilla, Tarragona Hot Semi-arid: Alicante, Murcia, Santa Cruz de Tenerife, Cold Semi-arid: Albacante, Almeria, Castellon, Ciudad Real, Illes Balears, Lleida, Toledo, Valencia, Zamora, Zaragoza. Hot Desert: Las Palmas	All occupations	CCO	Comparing percentiles: Average Ref Tmax: 14.98 °C Average Threshold Tmax: 34.9 °C	Overall RR: 1.004 (1.003–1.005) Gender M: 1.004 (1.003–1.005) F: 1.002 (1.000–1.003) Age ≤24: 1.005 (1.003–1.006) 25–34: 1.003 (1.002–1.004) 35–54: 1.003 (1.002–1.004) ≥55: 1.002 (1.001–1.004) Industries Agriculture: 1.012 (1.010–1.015) Construction: 1.004 (1.002–1.005) U shaped trend and lag effect of 1 or 2 days and to less extent 3and 4 days
McInnes et al., 2017	Melbourne, Australia	Oceanic Climates	All occupations	CCO	1 °C increase in Tmax	extent 3and 4 days OR: 1.002 (0.999–1.004) Gender M: 1.003 (1.000–1.006) F: 0.999 (0.994–1.005) Age <25: 1.008 (1.001–1.015) (continued on next page)

Table 2 (continued)

First Author, Year	Location	Climate	Study Population	Study Design	Exposure metric and source	Key findings ES(CI)
						25–34: 1.002 (0.996–1.007) 35–44: 1.004 (0.999–1.009) 45–54: 0.999 (0.994–1.003)
Sheng et al., 2018	Guangzhou, China	Humid Subtropical Climates	All occupations	CCO	1 °C increase in daily Tmax and Tmin	≥55: 0.998 (0.987–1.002) RR: 1.014 (1.012–1.017) Gender M: 1.014 (1.011–1.016) F: 1.015 (1.008–1.021) Age ≤24: 1.005 (0.998–1.012) 25–34: 1.018 (1.013–1.024) 35–44: 1.021 (1.017–1.024) 45–54:1.009 (1.001–1.016) ≥55: 0.989 (-) Industries Manufacturing: 1.019 (1.015–1.022) Finance, property and business: 1.014 (1.009–1.019)
Ricco, 2018	Trento, Italy	Humid Subtropical Climates	Agricultural workers	TS	Comparing percentiles, Ref Tmax: 33.2 °C Threshold Tmax > 37.1 °C	RR: 1.034 (1.007–1.060) Lagged effect and linear increase
Calkins et al., 2019	Washington, US	Warm Mediterranean Climates	Construction Workers	CCO	1 °C increase in dry bulb temperature	OR: 1.007 (1.005–1.009) Age 18–24: 1.008 (1.004–1.014) 25–34: 1.005 (1.002–1.008) 35–44: 1.003 (0.98–1.005) 45–54: 1.004 (0.99–1.008) ≥55: 1.010 (1.002–1.080) Linear increase in risk
Dillender, 2019	Texas, US	Humid Subtropical Climates	All occupations	TS	Comparing percentiles, Ref Tmax: 15.5 °C Threshold Tmax > 37.7 °C	RR: 1.019 (1.009–1.027) Age Statistically significant risk in workers younger then 40 years of age at 37.7 °C
Ma et al., 2019	Guangzhou, China	Humid Subtropical Climates	All occupations	TS	Comparing percentiles, Ref WBGTmax: 24 °C Threshold WBGTmax > 30 °C	RR: 1.023 (1.008–1.033) Gender M: 1.023 (1.015–1.034) F: 1.021 (1.001–1.042) Age <35: 1.021 (1.006–1.035) 35–44: 1.024 (1.009–1.041) >44: 1.023 (0.998–1.046) No evidence of delayed effect between WBGTmax and OI
Marinaccio et al., 2019	All provinces of Italy (110)	Oceanic: Aosta, Arezzo, Belluno, Biella, Bolzano, Campobasso, Como, Cuneo, L'Aquilla, Varese, Verbano-Cusio-Ossola, Warm Mediterranean: Ogliastra, Potenza, Humid Subropical: Alessandria, Ancona, Ascoli Piceno, Asti, Barletta-Andria-Trani, Bergamo, Bologna, Brescia, Chieti, Cremona, Fermo, Ferrara, Foggia, Forlì-Cesena, Genova, Gorizia, Macerata, Lecco, Mantova, Milano, Modena, Monza e della, Brianza, Novara, Padova, Parma, Pavia, Perugia, Pesaro e Urbino, Pescara, Piacenza, Pordenone, Ravenna, Reggio nell'Emilia, Rieti, Rimini, Rovigo, Sondrio, Teramo, Trento, Torino, Treviso, Trieste, Venezia, Udine, Vercelli, Verona, Vicenza Hot Mediterranean: Agrigento, Avellino, Bari, Benevento, Brindisi, Cagliari, Caltanissetta, Carbonia-Iglesias, Caserta, Catania, Catanzaro,	Specific occupations	TS	Comparing percentiles: Average Ref Tmean (25th Percentile): 11.5 °C Average Threshold Tmean (75th Percentile): 20.5 °C	Overall RR: 1.017 (1.015–1.020) Gender M: 1.019 (1.015–1.023) F: 1.007 (1.002–1.013) Age 15–34: 1.023 (1.017–1.027) 35–60: 1.013 (1.009–1.060) >60: 0.989 (0.974–1.007) Industries Construction: 1.027 (1.020–1.033) Lag effect up to 2 days and U shaped relationship between daily mean temperature and OI

Table 2 (continued)

First Author, Year	Location	Climate	Study Population	Study Design	Exposure metric and source	Key findings ES(CI)
Ricco et al., 2019	Trento, Italy	Cosenza, Crotone, Enna, Firenze, Frosinone, Grosseto, Imperia, Isernia, La Spezia Latina Lecce Livorno, Lodi, Lucca, Massa Carrara, Matera, Medio Campidano Messina, Napoli Nuoro Olbia-Tempio Oristano Palermo Pistoia, Prato,Pisa, Ragusa, Reggio di Calabria, Roma, Salerno, Sassari Savona Siena Siracusa Terni, Trapani, Vibo Valentia, Viterbo, Cold Semi Arid: Tarranto, Humid Subtropical Climates	All occupations in Migrant workers in comparison to local workers	TS	Pooled the estimates for Islamic and non-Islamic holiday periods for warm season Ref Tmax: 21.4 °C Threshold Tmax > 25 °C	RR: 0.965 (0.871–1.035)
Schifano et al., 2019	Turin, Milan and Rome, Italy	Humid Subtropical: Turin and Milan Hot Mediterranean: Rome	All occupations	cco	Comparing percentiles, Turin: Ref Tmax:26 °C Threshold Tmax:33 °C Milan: Ref Tmax:21 °C Threshold Tmax:34 °C Rome: Ref Tmax:24 °C Threshold Tmax:32 °C	Turin RR: 1.002 (0.998–1.008) Industries Agriculture: 0.976 (0.927–1.063) Construction: 1.009 (0.992–1.027) Electricity: 1.063 (0.992–1.135) Transportation: 1.000 (0.983–1.017) Milan RR: 1.000 (0.998–1.003) Industries Agriculture: 0.998 (0.946–1.067) Construction: 1.005 (0.997–1.021) Electricity: 1.034 (1.002–1.066) Transportation: 1.003 (0.996–1.010) Rome RR: 1.000 (0.998–1.002) Industries Agriculture: 1.004 (0.975–1.035) Construction: 1.007 (1.001–1.014) Electricity: 1.000 (0.979–1.020) Transportation: 1.004
Varghese et al., 2019	Adelaide, Australia	Warm Mediterranean Climates	All occupations	cco	Comparing percentiles, Ref Tmax: 25 °C Threshold Tmax: 40.6 °C	(1.000–1.016) RR: 1.016 (1.010–1.023) Gender M: 1.015 (1.007–1.023) F: 1.019 (1.008–1.030) Age 15–24: 1.026 (1.011–1.041) 25–34: 1.004 (0.990–1.018) 35–54: 1.021 (1.011–1.030) >55: 1.011 (0.993–1.028) Industries Agriculture: 1.091 (1.014–1.169) Electricity: 1.141 (1.067–1.215) Non-Linear Increase in risk (J shaped curve)
Varghese et al., 2019	Melbourne Brisbane Perth, Australia	Oceanic: Melbourne Humid Subtropical: Brisbane Hot Mediterranean: Perth	All occupations	CCO	Comparing percentiles, Melbourne: Ref Tmax: 20 °C Threshold Tmax > 38.9 °C Brisbane:	Melbourne RR: 1.006 (1.001–1.011) Gender M: 1.003 (0.996–1.010) F: 1.012 (1.003–1.021) Age (continued on next page)

Table 2 (continued)

First Author, Year	Location	Climate	Study Population	Study Design	Exposure metric and source	Key findings ES(CI)
				Design	Ref Tmax: 26.7 °C Threshold Tmax > 34.7 °C Perth: Ref Tmax: 23.7 °C Threshold Tmax > 40.1 °C	15–24: 1.007 (0.992–1.022) 25–34: 1.011 (1.000–1.023) 35–54: 1.005 (0.998–1.013) >55: 1.002 (0.989–1.015 Industries Transport and warehousing: 1.024 (1.008–1.040) Brisbane RR: 0.997 (0.985–1.010) Gender M: 1.001 (0.985–1.016) F: 0.992 (0.972–1.013) Age 15–24: 1.018 (0.986–1.049) 25–34: 1.006 (0.978–1.031) 35–54: 0.998 (0.981–1.016) >55: 0.962 (0.929–0.993 Industries Agriculture: 1.080 (0.958–1.201) Perth RR: 1.009 (1.001–1.018) (Traumatic injuries only) Gender M: 1.004 (0.997–1.010) F: 0.994 (0.985–1.004) Age 15–24: 1.008 (0.996–1.020) 25–34: 0.994 (0.983–1.005) 35–54: 1.001 (0.993–1.009) >55: 0.998 (0.984–1.013 Industries Electricity, gas and water 1.025 (0.978–1.074) Non-Linear relationship an the impacts of hot
ticco et al., 2020	Trento, Italy	Humid Subtropical Climates	Construction workers	TS	Comparing percentiles, Ref Tmean: 21 $^{\circ}$ C Threshold Tmax $>$ 25.3	acute RR: 1.031 (1.013–1.040) Age <20: 1.115 (1.016–1.213 20–29: 1.088 (1.042–1.134) 30–39: 1.046 (1.000–1.092) 40–49: 1.057 (1.006–1.107) ≥50: 0.983 (0.910–1.057 Lagged effect and linear

Note: All values are converted to increase in risk associated with 1 °C increase in temperature above reference value. Risk is estimated in terms of overall risk and risk in subgroups such as age, gender and type of industries where available. * Two studies (Marinaccio et al., 2019; Martínez-Solanas et al., 2018) are representative of nationwide estimates. The results given in this table represent the overall estimates. Risk is measured in terms of effect sizes and confidence intervals ES(CI). For exposure metrics, following abbreviations were used: AT (Apparent temperature), WBGT (Wet Bulb Globe Temperature) and study design TS (Time Series), CCO (case crossover).

population. Sixty eight percent of the hot temperature studies (Adam-Poupart et al., 2015; Ricco, 2018; Martínez-Solanas et al., 2018; Varghese et al., 2019; Garzon-Villalba et al., 2016; Schifano et al., 2019; Varghese et al., 2019; Fogleman et al., 2005; Morabito et al., 2006; McInnes et al., 2017; Xiang et al., 2014; Sheng et al., 2018; Ma et al., 2019) had "probably high" risk in exposure assessment. A majority of the studies used meteorological data from a single weather station or an

average of multiple stations. Relatively few studies used gridded data (Spector et al., 2016; Calkins et al., 2019; Dillender, 2019) or satellite data (Marinaccio et al., 2019) or geolocated data (Ricco et al., 2020; Ricco et al., 2019) for exposure assessment. For outcome assessment, all studies had "probably low" to "low" risk of bias because of the use of national or regional databases that used standard measures of OI, although underreporting is possible. Around 32% of the studies (Ricco,

 Table 3

 Study characteristics and key findings of all studies assessing the risk of OI during HW periods.

First Author, Year	Location	Climate	Study Population	Study Design	Exposure metric and source	Key findings ES(CI)
Xiang et al., 2014	Adelaide, Australia	Warm Mediterranean Climates	All occupations	TS	HW (3 consecutive days Tmax \geq 35 °C)	IRR: 0.983 (0.943–1.024) Gender M: 1.001 (0.947–1.012) F: 0.935 (0.897–0.974) Age ≤ 24 1.035 (0.981–1.091) 25–34 0.973 (0.928–1.019) 35–54 0.951 (0.898–1.007) ≥55 1.024 (0.940–1.115) Industries Agriculture 1.447 (1.125–1.861) Electricity, gas and water 1.297 (1.049–1.604)
Rameezdeen and Elmualim, 2017	Adelaide, Australia	Warm Mediterranean Climates	Construction workers	TS	HW (3 consecutive days Tmax \geq 35 °C)	IRR: 0.970 (0.960–1.010)
McInnes et al., 2018	Melbourne, Australia	Oceanic Climates	All occupations	cco	HW (3 consecutive days Tmax \geq 35 °C)	OR: 1.090 (0.870–1.360) Gender M: 1.170 (0.900–1.510) F: 0.930 (0.610–1.420) Age <35: 0.970 (0.650–1.450) 35–49: 1.280 (0.930–1.780) ≥50: 0.940 (0.590–1.480)
Ricco, 2018	Trento, Italy	Humid Subtropical Climates	Agriculture workers	TS	HW (3 consecutive days Tmax \geq 35 °C)	OR: 1.090 (1.020–1.170)
Varghese et al., 2018	Adelaide, Australia	Warm Mediterranean Climates	All occupations	CCO	EHF (moderate/high-severity HW days)	RR: 1.080 (1.010–1.160) Gender M: 1.130 (1.030–1.230) F: 0.990 (0.870–1.130) Age 15–24: 1.150 (0.970–1.360) 25–34: 1.110 (0.950–1.300) 35–54: 1.080 (0.970–1.200) >55: 0.970 (0.78–1.18)
Ricco et al., 2019	Trento, Italy	Humid Subtropical Climates	All occupations in migrant workers	TS	Risk of OI in migrant workers during HW (3 consecutive days Tmax \geq 35 °C)	OR: 1.749 (1.014–3.017)
Varghese et al., 2019	Melbourne, Australia Brisbane, Australia Perth, Australia	Oceanic: Melbourne Humid Subtropical: Brisbane Hot Mediterranean: Perth	All occupations	CCO	EHF (moderate/high-severity HW days)	Melbourne RR: 1.250 (1.220–1.280) Gender M: 1.290 (1.250–1.330) F: 1.180 (1.150–1.230) Age 15–24: 1.270 (1.190–1.350) 25–34: 1.310 (1.240–1.370) 35–54: 1.260 (1.220–1.300) >55: 1.180 (1.120–1.240) Brisbane RR: 1.450 (1.420–1.480) Gender M: 1.500 (1.460–1.540) F: 1.350 (1.300–1.400) Age 15–24: 1.550 (1.470–1.630) 25–34: 1.560 (1.490–1.630) 35–54: 1.420 (1.370–1.460) >55: 1.300 (1.230–1.370) Perth RR: 1.260 (1.240–1.290) Gender (continued on next page)

Table 3 (continued)

First Author, Year	Location	Climate	Study Population	Study Design	Exposure metric and source	Key findings ES(CI)
						M: 1.290 (1.260-1.320)
						F: 1.200 (1.160-1.240)
						Age
						15–24: 1.290
						(1.230-1.350)
						25-34: 1.270
						(1.220-1.330)
						35-54: 1.260
						(1.220-1.300)
						>55: 1.210 (1.150-1.280
ticco et al., 2020	Trento, Italy	Humid Subtropical	Construction workers	TS	HW (3 consecutive days Tmax ≥	OR: 1.230 (1.144-1.322)
		Climates			35 °C)	Age
						< 20: 1.892 (1.449–2.470
						20-29: 1.125
						(1.971-1.305)
						30-39: 1.168
						(1.020-1.337)
						40-49: 1.323
						(1.146-1.527)
						≥50: 1.156 (0.958–1.396

Note: Risk is estimated in terms of overall risk and risk in subgroups such as age, gender and type of industries where available. Risk is measured in terms of effect sizes and confidence intervals ES(CI).

2018; Xiang et al., 2014; Ma et al., 2019; Garzon-Villalba et al., 2016; Fogleman et al., 2005; Morabito et al., 2006) had "probably high" risk of confounding bias because some of the critical confounders (Peng et al.,

2006) such as seasonality, time trends, day of the week, size of the workforce and additional confounders such as weather parameters and holidays were not taken into account. All studies had a "probably low"

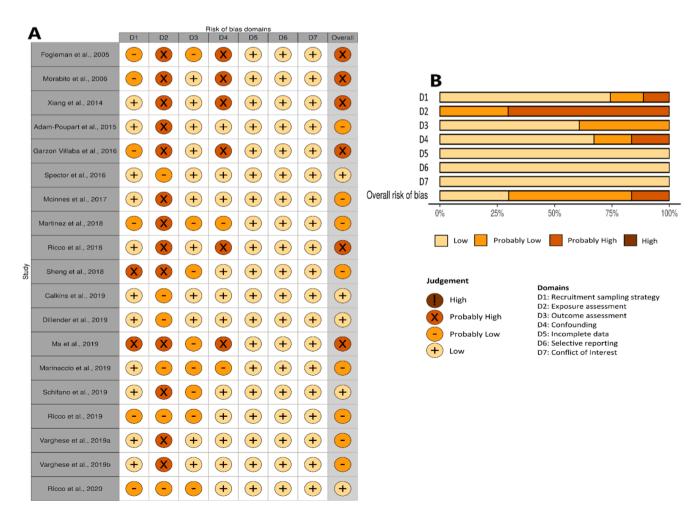


Fig. 3. Summary of the risk of bias assessment in the individual studies (hot temperatures studies n = 19) (A) shows the traffic plot of individual assessments and (B) shows the percentage plot given as percentages across all included hot temperature studies). Note: The probability of bias is assessed as High (H), Probably High (PH), Probably Low (PL) and low (L). The plots were created using Risk of Bias Visualization (ROBVIS) tool (McGuinness and Higgins, 2020).

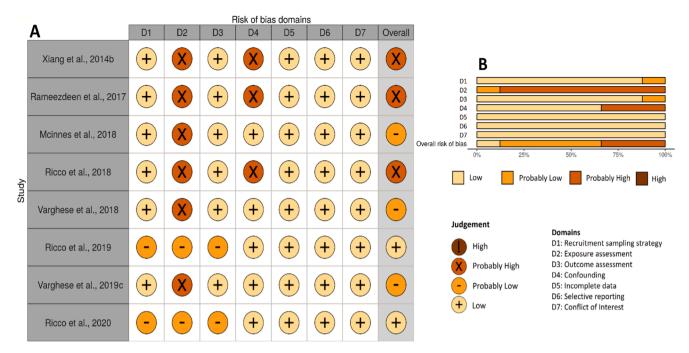


Fig. 4. Summary of the risk of bias assessment in the individual studies (HW studies n = 8) (A) shows the traffic plot and (B) shows the percentage plot given as percentages across all included HW studies. Note: The probability of bias is assessed as High (H), Probably High (PH), Probably Low (PL) and low (L). The plots were created using Risk of Bias Visualization (ROBVIS) tool (McGuinness and Higgins, 2020).

risk of bias in other domains i.e. incomplete datasets, selective reporting and conflict of interest.

3.3.1.2. Heatwave studies. All HW studies were found to be at "low" risk of recruitment/selection bias. Seventy five percent of HW studies (Ricco, 2018; Rameezdeen and Elmualim, 2017; McInnes et al., 2018; Xiang et al., 2014; Varghese et al., 2019; Varghese et al., 2018) had "probably high" risk in exposure assessment. For outcome assessment, all studies had "low" to "probably low" risk of bias. Thirty eight percent of HW studies (Ricco, 2018; Rameezdeen and Elmualim, 2017; Xiang et al., 2014) had "probably high" risk of confounding bias because some of the critical confounders such as seasonality, time trends, day of the week, size of the workforce and additional confounders such as weather parameters and holidays were not taken into account. All studies had a "low" probability of bias in other domains: incomplete datasets, selective reporting and conflict of interest.

3.3.2. Assessment of quality of evidence across the studies

The description and rationale of the assessment of the overall certainty of evidence assessing the risk of OI associated with extreme heat (hot temperatures and HW) is given in Table 4.

3.3.2.1. Hot temperature studies. The certainty of evidence for hot temperature studies was not downgraded for any of the downgrading factors but was upgraded for dose response category as all studies suggested an exposure response gradient. The overall certainty of evidence was therefore upgraded to "high" for the observational studies assessing the risk of OI associated with hot temperatures.

3.3.2.2. Heatwave studies. We downgraded the certainty of evidence for HW studies for high risk of bias and inconsistencies and upgraded the certainty of evidence for dose response category. The overall quality of evidence was therefore downgraded to "low" for the observational studies assessing the risk of OI associated with heatwaves.

3.3.3. Assessment of strength of evidence across the studies The quality of the body of evidence was found to be "high" for hot

temperature studies and "low" for HW studies (Table 4).

3.3.3.1. Hot temperature studies. The direction of the effect estimates indicated an increase in the risk of OI with exposure to hot temperatures. There is high confidence in effect estimates and it is unlikely that a new study would make the results of the meta-analysis null or statistically insignificant for evidence. The assessment of strength of evidence suggested that there was "sufficient" evidence that exposure to hot temperatures affect OI in non-military workers.

3.3.3.2. Heatwave studies. The direction of the effect estimates indicated an increase in the risk of OI with exposure to HW. However, the assessment of strength of evidence suggested that there was "limited" evidence that exposure to HW affects OI in non-military workers.

3.4. Synthesis of findings on extreme heat exposure on OI

Extreme heat exposure were assessed in terms of hot temperatures and HW. The following sections synthesize the evidence for hot temperature and HW studies in different climate zones (where possible).

3.4.1. Hot temperatures and the risk of OI

In total, 194 observations from 17 studies were considered for the meta-analysis in nine different climate zones. Two studies were excluded from the meta-analysis; Morabito et al., (Morabito et al., 2006) used a different outcome assessment metric and Ma et al., (Ma et al., 2019) was excluded because of the use of overlapping datasets. A summary of our meta-analysis results for all included hot temperature studies is presented in Table 5. For every 1 °C increase above reference temperature (mean reference temperature across all observations = 20.9 °C), the heat associated risk of OI increased by 1% (RR 1.010, 95% CI: 1.009–1.011). The results of meta-analyses by each climate zone are further presented in next sections.

3.4.1.1. Humid Subtropical Climates. Based on 56 effect estimates from nine studies (Ricco, 2018; Marinaccio et al., 2019; Varghese et al., 2019; Sheng et al., 2018; Garzon-Villalba et al., 2016; Schifano et al., 2019;

Table 4 Summary of findings, quality of evidence and strength of evidence for hot temperature exposure (n = 19) and HW periods (n = 8) and the risk of OI.

0. 11.	_	rature studies (n = 19)		e studies $(n = 8)$
Quality factor	Ratings	Rationale	Ratings	
Categories				
Downgrade consider				
Risk of Bias across studies	(0)	We have found "probably high risk of bias" for 32% of the studies. The sensitivity analysis of high risk of bias studies revealed statistical differences between studies with low/probably low versus probably high risk of bias, but majority of studies showing high risk of bias had small weight on the results, therefore we did not downgrade for risk of bias (Fig. E1, Appendix E of SM).	(-1)	We have found "probably high risk of bias" in 38% of studies is overall risk of bias. The sensitivity analysis of high risk of bias studies revealed significant statistical differences between studies with low/probably low versus probably high risk of bia (Fig. F1, Appendix F of SM). Therefore we downgraded the rating based on risk of bias assessment.
ndirectness	(0)	Most studies are representative of appropriate proportion of population of interest. OI were identified under standard definitions in most studies. Direct measures of exposure are used in most studies.	(0)	Most studies are representative of appropriate proportion of population of interest. OI were identified under standard definitions in most studies. Direct measures of exposure are used in most studies.
inconsistency imprecision Publication Bias	(0) (0) (0)	The evidence of quality was not downgraded for inconsistencies. The 1² value of heterogeneity was found to be 1² = 95.1% for overall all hot temperatures studies but 80% prediction intervals did not contain unity and were narrow as compared to confidence intervals (Fig. E2, Appendix E of SM). Further, "Leave One Out Analysis" also showed that the risk estimates were not significantly affected by individual studies (Table E1, Appendix E of SM). Sensitivity analysis based on exposure metrics (such as Tmax, Tmin, or thermal indices) indicated slightly higher estimates for studies that used heat indices instead of Tmax and Tmean. Different exposure assessment datasets (such as single or average weather station data or gridded/geolocated or satellite data) or the unit of estimate (i.e. 1 °C increase in temperature or comparing percentiles) (Table E2, Appendix E of SM) did not reveal major differences. It should also be noted that the 1² value of heterogeneity reduced to 89.3% after classifying the studies into different climate zones and standardizing the data and conversion to increase in risk per 1 °C temperature (Table E3, Appendix E of SM). Most studies had sufficiently narrow confidence intervals. Funnel plots of hot temperature studies (Fig. E3, Appendix E of	(-1) (0) (0)	Considerable heterogeneity was found across the studies, $I^2=98.9\%$. Moreover, prediction intervals contain unity and are double of confidence intervals (Fig. F2, Appendix F of SM). Therefore we downgraded the quality of evidence for heterogeneity. Leave One Out Analysis and Sensitivity analysis based on different exposure assessment datasets (such as single or average weather station data or gridded/geolocated or satellite data) and different HW definitions (i.e. three or more days of Tmax ≥ 35 °C or heat indices such as EHF) are given in Table F1 and F2, Appendix F of SM. The results indicated higher estimates for studies using EHF definition of HW.
лысацоп віаѕ	(0)	Funnel plots of not temperature studies (Fig. E.S., Appendix E of SM) showed an asymmetrical distribution and Egger's test were significant (p = 0.015), indicating a potential risk of publication bias. The Trim and Fill method was carried out imputing three studies adding to a total of 21 hot temperature studies (Fig. E4, Appendix E of SM) to adjust for pooled RR from small study bias. The observed pooled RR was 1.010 (95% CI: 1.007–1.013) and the imputed point RR was very similar (1.009, 95% CI: 1.006–1.012). Therefore we did not downgrade the quality of evidence for potential risk of publication bias.	(0)	Number of studies included in the meta-analysis were too smal (<10) for a statistical evaluation of potential publication bias.
Jpgrade considerati	ons			
arge effect	(0)	Overall effect magnitude (RR) was below 2 (RR < 2) times	(0)	Overall effect magnitude (RR) was below 2 (RR < 2) times
magnitude Pose response	(1)	increase in the outcome prevalence in all studies. All of the studies suggested an exposure–response gradient, i.e. exposure to high temperatures increases the risk of OI in most instances.	(1)	increase in the outcome prevalence in all studies. All of the studies suggested an exposure–response gradient, i.e exposure to HW increases or decreases the risk of OI.
Confounding minimizes effect	(0)	Time series and case crossover study design take into account the potential confounders by modeling and by design. However, we identified some studies that might have residual confounding because they did not account for all potential confounders. We do not expect that omission of any of these confounders would have led to underestimating our meta-analysis association estimate and therefore did not upgrade for this consideration.	(0)	We identified some studies that might have residual confounding because they did not account for all potential confounders. However, we do not expect that omission of any o these confounders would have led to underestimating our meta analysis association estimate and therefore we did not upgrade for this consideration.
Summary of Quality		Moderate (0) (0) (0) (1) Web Programme	Loui	Madagata (0) (7 1) (7 1) (7 1) 1 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
Overall quality of evidence Summary of	High NA	Moderate+ $(0)+(0)+(0)+(+1)$ = High - Downgrading and upgrading, brought the quality of studies to "high". Studies included in meta-analysis provided consistent results i.e.	Low	Moderate+ $(0)+(-1)+(-1)+(+1) = \text{Low}$ - Downgrading and upgrading, brought the quality of studies to "low". Studies included in meta-analysis provided consistent results i.e
findings for Meta- analysis		the risk of OI increases with hot temperatures.		the risk of OI increases during HW periods.
trength of evidence	assessment			
Quality of evidence Direction of effect	NA NA	High Risk of OI increase among workers with increasing exposure to	NA NA	Low Risk of OI increase among workers with increasing exposure to
estimates Confidence in effect estimates	NA	hot temperatures. It is unlikely that a new study would have an effect estimate that would make the results of the meta-analysis null or insignificant.	NA	HW. The evidence is limited
Other aspects Overall strength of evidence	NA Sufficient	None Overall, we rated the strength of evidence as "sufficient". We found that that there is a positive association between hot	NA Limited	None Overall, we rated the strength of evidence as "limited". A causa interpretation of the positive association observed in the body o (continued on next page)

Table 4 (continued)

Quality factor Categories	Hot tempe Ratings	rature studies (n $= 19$) Rationale	Heatwave Ratings	studies $(n=8)$
		temperatures and OI, and conclude with reasonable confidence that chance, bias and confounding could be ruled out as an explanation for the association. The available evidence included results from one or more well-designed, well-conducted studies, and we believe that our conclusion is unlikely to be strongly affected by the results of future studies		evidence on exposure and the outcome is credible, but chance, bias, or confounding could not be ruled out with reasonable confidence.

Note: Two studies (Ma et al., 2019; Morabito et al., 2006) were removed from the meta-analysis and therefore were not included in heterogeneity and publication bias tests

Ricco et al., 2020; Ricco et al., 2019; Dillender, 2019) included in the meta-analysis, Humid Subtropical Climates had the highest risk of OI during warm periods. An increased risk of 1.7% (RR 1.017, 95% CI: 1.014–1.020) was found to be associated with 1 °C increase in temperature above reference value (Table 5 and Fig. G1, Appendix G of SM). The results were consistent across various studies with risk of OI ranging from 1% to 1.7% in majority of instances. However, Dillender (2019) and Marinaccio et al. (2019) estimated slightly increased risk in Texas (1.6%) and a few provinces of Italy (up to 6.6%) respectively. Garzon-Villalba et al. (2016) found a particularly higher risk (around 6%) for disaster relief workers. One study Morabito et al. (2006) was not included in the meta-analysis but also suggested an increased incidence in occupational accidents on days characterized by hot weather conditions in Tuscany Italy.

The exposure response relationship was found to be linear (Ma et al., 2019; Garzon-Villalba et al., 2016) and delayed with lag effect of up to two days (Ricco, 2018; Ricco et al., 2020).

3.4.1.2. Oceanic Climates. In temperate Oceanic Climates, 28 effect estimates from four studies (McInnes et al., 2017; Marinaccio et al., 2019; Martínez-Solanas et al., 2018; Varghese et al., 2019) were used to estimate the pooled RR. An overall 1% increased risk of heat-related OI (RR 1.010, 95% CI: 1.008–1.012) was noted for each 1 $^{\circ}$ C increase in temperature above reference value (Table 5 and Fig. G2, Appendix G of SM). All studies reported an increased risk of OI associated with hot temperatures ranging from 0.1% to 4.8%. For instance in Melbourne, Australia, Varghese et al. (2019) reported a 0.6% increased risk of OI (above Tmax 20 °C) and McInnes et al. (2017) discovered a 0.2% increased risk with each 1 °C increase in temperature above Tmax of 14 °C (Table 2). Consistent with this, Martínez-Solanas et al. (2018) found an increased risk ranging between 0.3 and 0.9% (above Tmax 12 °C) in various provinces of Spain. Marinaccio et al. (2019) particularly found an increased risk above 1.4% in most provinces of Italy (above Tmean 7.5 °C). Studies (Martínez-Solanas et al., 2018; Varghese et al., 2019) that assessed the exposure-response curve in oceanic climates found a linear increase in the risk and the effects were found to be acute (Varghese et al., 2019).

3.4.1.3. Hot Mediterranean Climates. Sixty seven effect estimates from four studies (Schifano et al., 2019; Marinaccio et al., 2019; Martínez-Solanas et al., 2018; Varghese et al., 2019) were included in the meta-analysis. The pooled RR of heat-attributable OI was estimated to be 0.9% (RR 1.009, 95% CI: 1.008–1.011) with each 1 °C increase in temperature above reference value in these regions (Table 5 and Fig. G3, Appendix G of SM). All four studies reported positive associations between extreme heat and OI. The risk of OI varied between 0.1 and 0.9% in most instances in three studies (Martínez-Solanas et al., 2018; Varghese et al., 2019; Schifano et al., 2019), while Marinaccio et al. (2019) estimated a higher effect of OI up to 9% in many Provinces of Italy including Rome. All four studies indicated a linear increase in the risk of injuries in Hot Mediterranean Climates. Two nation-wide studies predominantly from Hot Mediterranean Climates revealed a lag effect up to

two days (Marinaccio et al., 2019; Martínez-Solanas et al., 2018) and up to four days in some instances (Martínez-Solanas et al., 2018).

3.4.1.4. Warm Mediterranean Climates. Our pooled estimates of 11 effect estimates from six studies (Marinaccio et al., 2019; Martínez-Solanas et al., 2018; Spector et al., 2016; Xiang et al., 2014; Varghese et al., 2019; Calkins et al., 2019) in Warm Mediterranean Climates suggested an increased risk of 0.6% (RR 1.006, 95% CI: 1.004-1.007) for OI for each 1 °C increase in temperature above reference value (Table 5 and Fig. G4, Appendix G of SM). All studies reported an increased risk of OI (ranging between 0.1% - 1.7%) and the results were consistent across the studies. For example, in Adelaide, Australia, a time-series study by Xiang et al. (2014) reported 0.2% increased risk of OI with every 1 °C increase in Tmax (above 14 °C) during warm periods. Similarly, Varghese et al. (2019) observed an increase in the OI risk of 1.7% during hot summers (above Tmax 25 °C). In Washington State, Spector et al. (2016) reported an increased risk of OI (1% per 1 $^{\circ}\text{C}$ increase in humidex) for agricultural workers; while Calkins et al. (2019) noted an increased risk of 0.7% per 1 $^{\circ}$ C increase in dry temperature for construction workers.

Five studies (Martínez-Solanas et al., 2018; Spector et al., 2016; Xiang et al., 2014; Varghese et al., 2019; Calkins et al., 2019) assessed the exposure–response curve in Warm Mediterranean Climates and reported mixed results. All studies reported a linear increase in risk above reference temperatures during warm seasons; however two studies (Spector et al., 2016; Xiang et al., 2014) reported a decline in the risk of OI at extremely hot temperatures indicating a reverse U-shaped curve.

3.4.1.5. Hot Semi-Arid Climates. One nation-wide study from Spain (Martínez-Solanas et al., 2018) provided three effect estimates for meta-analysis in Hot Semi-arid Climates. The results suggested a statistically significant risk of OI (RR 1.005, 95% CI: 1.004–1.007) with each 1 °C increase in hot temperatures above reference temperatures (Table 5 and Fig. G5, Appendix G of SM). The exposure–response relationship assessed by Martínez-Solanas et al. (2018) in various semi-arid provinces of Spain indicated a linear increase in the risk of OI.

3.4.1.6. Cold Semi-arid Climates. Eleven estimates from Italy and Spain (Marinaccio et al., 2019; Martínez-Solanas et al., 2018) were used in meta-analysis of Cold Semi-arid climates. An increased risk of 0.5% (RR 1.005, 95% CI: 1.004–1.005) associated with 1 $^{\circ}$ C increase in temperature above reference values was found in these climates (Table 5 and Fig. G6, Appendix G of SM). The exposure response relationship was found to be linear in all instances.

3.4.1.7. Humid and Warm Continental Climates. Our meta-analysis results of 13 effect estimates from two studies (Adam-Poupart et al., 2015; Fogleman et al., 2005) identified a 0.3% increase in OI (RR 1.003, 95% CI: 1.001–1.004) in Humid and Warm Continental Climates with 1 °C increase above reference temperature (Table 5 and Fig. G7, Appendix G of SM). Adam-Poupart et al., (Adam-Poupart et al., 2015) assessed the exposure—response curve and observed a linear and lagged effect of up to

Table 5 Random-effects meta-analysis estimates of RR and (95% CI) for risk of OI at hot temperatures ($n=17^*$).

Climate Zones (Studies)	Risk of OI RR(95% CI)	
Humid Subtropical Climates (Ricco, 2018; Marinaccio et al., 2019; Varghese et al., 2019; Sheng et al., 2018; Garzon-Villalba et al., 2016; Schifano et al., 2019; Ricco et al., 2020; Ricco et al., 2019; Dillender, 2019)	1.017 (1.014–1.020)	$K = 56$ $I^2 = 89.8\%$ $P < 0.001$ $N = 2,352,778**$
Oceanic Climates (McInnes et al., 2017; Marinaccio et al., 2019; Martínez-Solanas et al., 2018; Varghese et al., 2019)	1.010 (1.008–1.012)	$K = 28$ $I^2 = 91.3\%$ $P < 0.001$ $N = 2.842.807**$
Hot Mediterranean Climates (Schifano et al., 2019; Marinaccio et al., 2019; Martínez-Solanas et al., 2018; Varghese et al., 2019)	1.009 (1.008–1.011)	$K = 67$ $I^2 = 86.5\%$ $P < 0.001$ $N = 10,716,074**$
Warm Mediterranean Climates (Marinaccio et al., 2019; Martínez-Solanas et al., 2018; Spector et al., 2016; Xiang et al., 2014; Varghese et al., 2019; Calkins et al., 2019)	1.006 (1.004–1.007)	$K = 11$ $I^2 = 75.3\%$ $P < 0.001$ $N = 1,262,274**$
Hot Semi-arid Climates (Martínez-Solanas et al., 2018)	1.005 (1.004–1.007)	$K = 3$ $I^2 0.0\%$ $P = 0.918$ $N = 1,347,551$
Cold Semi-arid Climates (Marinaccio et al., 2019; Martínez-Solanas et al., 2018)	1.005 (1.004–1.005)	$K = 1,617,661$ $K = 11$ $I^2 = 0.0\%$ $P = 0.816$ $N = 2,958,103**$
Humid and Warm Continental Climates (Adam-Poupart et al., 2015; Fogleman et al., 2005)	1.003 (1.001–1.004)	$K = 13$ $I^2 = 53.1\%$ $P = 0.012$ $N = 350,196**$
Subarctic Climates (Adam-Poupart et al., 2015)	1.000 (0.996–1.005)	$K = 4$ $I^2 = 20.8\%$ $P = 0.286$ $N = 24,439$
Hot Desert Climates (Martínez-Solanas et al., 2018)	1.004 (1.001–1.008)	K = 1 N = 416,609
Overall	1.010 (1.009–1.011)	$N = 416,609$ $K = 194$ $I^2 = 89.3\%$ $P < 0.001$ $N = 22.270.831$

Note: *Two studies were (Ma et al., 2019; Morabito et al., 2006) not included in meta-analyses. K represents the number of city/province-specific estimates, and meta-analysis is conducted when $K \geq 2$. I^2 is the heterogeneity score. P is the P-value of X^2 test of heterogeneity. N represents the total number of injury records. **The sample size was not obtainable for province specific observations for two studies; Schifano et al. (2019) and Marinaccio et al. (2019) representative of different climate zones.

two days in the risk of OI associated with hot temperatures.

3.4.1.8. Subarctic Climates. One study (Adam-Poupart et al., 2015) conducted in sixteen health regions of Quebec Province, Canada provided four estimates of risk of OI associated with hot temperatures in Subarctic Climates. No association was found between OI and hot temperatures in these mild to cool summer regions (RR 1.000, 95% CI: 0.996–1.005) (Table 5 and Fig. G8, Appendix G of SM).

3.4.2. Heatwaves and the risk of OI

The impacts of heat exposure on the risk of OI were pronounced during HW periods. Ten effect estimates from eight studies were used to estimate the risk of OI during HW (Ricco, 2018; Ricco et al., 2020; Ricco et al., 2019; Rameezdeen and Elmualim, 2017; McInnes et al., 2018;

Xiang et al., 2014; Varghese et al., 2019; Varghese et al., 2018). The overall effect estimate was 17.4% (RR 1.174, 95% CI: 1.057–1.291) during HW periods. Further, among climate zones, the risk of OI was found to be highest in Oceanic Climates and Humid Subtropical Climates (Table 6 and Figs. H1–H3, Appendix H of SM).

3.5. Subgroup analyses

3.5.1. Subgroup analysis of hot temperatures

Subgroup analyses of workers' characteristics, nature of work and workplace characteristics identified specific group of workers which are at high risk during hot weather conditions. Summary of the subgroup analysis is given in Table 7. Male workers and young workers (age < 35 years) were found to be at high risk of OI during high temperatures. Outdoor intensive industries including: agriculture and construction were found to be at highest risk of OI although indoor industries such as manufacturing industries also had significant risk of OI associated with hot temperatures. Physical workload was also an important factor contributing towards increased risk of OI in hot weather conditions. Among various types of businesses, small and medium sized businesses were at high risk of OI associated with hot temperatures.

Further, subgroup analysis based on study characteristics (Table I1, Appendix I of SM) revealed that workers in North America and Asia were at higher risk of OI, however caution must be taken in interpreting the results because of small number of studies. Time series study design estimated higher values for heat attributable risk of OI. Studies using Distributed lag nonlinear models (n=6) and those using other models (n=11) (such as generalized linear models, condition logistics regression, generalized estimated equation) estimated similar risk of OI (Table I1, Appendix I of SM).

3.5.2. Subgroup analysis of heatwaves studies

Male workers, young workers (age < 35 years) and new workers were found to be at higher risk of OI associated with HW periods. Moreover, indoor industries had higher effect estimates for the risk of OI as compared to outdoor industries, high risk industries during HW included: Electricity gas and water and manufacturing. A summary of the subgroup analysis of HW studies is given in Table 8.

4. Discussions

4.1. Summary of research findings

Our systematic evaluation of the available literature representing around 22 millions of OI showed that the risk of OI associated with extreme heat has been extensively studied across different countries in nine climate zones. All studies suggested that working in hot environmental conditions increased the likelihood of experiencing OI (overall 1% increase in risk with 1 °C increase in temperature above reference value). Furthermore during extended periods of HW the risk of OI significantly increased by 17.4%. The additional classification of the available literature into different climate zones suggested that the risk of OI is not uniformly distributed and showed a geographic pattern associated with underlying local climate conditions. The heat associated risk of OI was highest in temperate climates with hot summers (for example Humid Subtropical Climates and Hot Mediterranean Climates) and in temperate climates with warm summers (for example Oceanic Climates). Subgroup analysis further revealed that male workers and young workers were at highest risk of OI during hot weather conditions. Among various industries; outdoor intensive industries such as agriculture and construction were at high risk during high temperatures, while electricity, gas and water supply, and manufacturing industries were at high risk during HW. The available evidence includes results from one or more well-designed and well-conducted studies. Overall, the strength of evidence across the studies was found to be sufficient for hot temperature studies but limited for HW studies.

4.2. Main findings in different climate zones

The results from the statistical analyses from various climate zones indicate that the risk of OI increased by 1.7% with 1 $^{\circ}\text{C}$ increase in temperature above reference value in Humid Subtropical Climates. Average reference temperature associated with risk of OI was found to be 13.3 °C (Ricco, 2018; Marinaccio et al., 2019; Varghese et al., 2019; Ricco et al., 2020; Ricco et al., 2019; Dillender, 2019). High humidity during warm periods plays a significant role in the risk of OI in these climates. Humidity limits bodily heat loss at hot temperatures, which leads to heat stress and an increased risk of OI (Xiang et al., 2014; Lucas et al., 2014). Similarly, temperate Hot Mediterranean Climates with hot summers and Oceanic Climates with warm summers were also found to be at increased risk of OI, ranging from 0.9 to 1% with 1 $^{\circ}$ C increase above reference temperature. Previously conducted multi-country analyses (Di Napoli et al., 2018; Gasparrini et al., 2015) on temperature and health associations from similar climates (for example from Spain, UK, France) also indicated increased risk of health outcomes associated with heat stress in these climate zones. Mediterranean climates are characterized by dry summers with several extremely hot days. Studies revealed that these regions are vulnerable to an increasing number of hot days under the climate change scenarios which can potentially contribute to increased risk in future (Hanna et al., 2011). The evidence is limited from Hot Semi-arid and Hot Desert Climates but our results indicate a high risk in these climate zones and warrant further investigations.

The impacts of hot temperatures on OI were estimated to be acute with a lag effect of 1 or 2 days and to a lesser extent 3–4 days (Ricco, 2018; Marinaccio et al., 2019; Martínez-Solanas et al., 2018). Understanding such lagged effects is important as it would help local Occupational Health Safety regulators and industries to take preventative actions. The exposure–response relationship was found to be linear or

Table 6 Random-effects meta-analytic estimates of RR and (95% CI) for risk of OI during HW (n = 8).

Climate Zones (Studies)	Risk of OI RR(95%CI)	
Oceanic Climate (McInnes et al., 2018; Varghese et al., 2019)	1.218 (1.093–1.343)	$K = 2$ $I^2 =$ 38.0% $P = 0.204$ $N =$ $155,734$
Humid Subtropical Climates (Ricco, 2018; Ricco et al., 2020; Ricco et al., 2019; Varghese et al., 2019)	1.213 (0.995–1.431)	$K = 4 I^2 = 96.9% P < 0.001 N = 180,114$
Warm Mediterranean Climates (Rameezdeen and Elmualim, 2017; Xiang et al., 2014; Varghese et al., 2018)	1.088 (0.860–1.316)	$K = 3$ $I^2 =$ 99.4% $P < 0.001$ $N =$ $392,875$
Hot Mediterranean Climates (Varghese et al., 2019)	1.260 (1.235–1.283)	K = 1 - - N = 12,207
Overall	1.174 (1.057–1.291)	$K = 10$ $I^2 =$ 98.9% $P < 0.001$ $N =$ $740,930$

Note: K represents the number of city/province-specific observations, and meta-analysis is conducted when $K \geq 2$. I^2 is the heterogeneity score. P is the P-value of X^2 test of heterogeneity. N represents the total number of injury records.

curvilinear in the majority of the studies (Adam-Poupart et al., 2015; Marinaccio et al., 2019; Martínez-Solanas et al., 2018; Varghese et al., 2019; Varghese et al., 2019; Calkins et al., 2019; Ricco et al., 2020) while two studies from dry summer Warm Mediterraean Climates (Spector et al., 2016; Xiang et al., 2014) and one from Oceanic Climates (McInnes et al., 2017) found a non-linear response with a reversal of effects at extremely hot temperatures. Some studies (Ricco, 2018; McInnes et al., 2017; Calkins et al., 2019) suggested that the observed differences can be attributed to different prevention and control measured adapted in different countries to limit the occurrence of OI. Further investigation of the effectiveness of preventative strategies is needed. It has been observed that the methodological differences between studies also led to conflicting results in some regions. For example, in Adelaide, Australia, Xiang et al. (2014) noted that the potential decrease in risk at extremely hot temperatures was due to the exclusion of the total workforce population as the denominator. The association between temperature and OI appears to be curvilinear (with a linear response during warm seasons) when the denominator information is taken into account because it partly captures the extent of short-term adaptation to temperature through a reduction of units worked. Varghese et al. (2019) confirmed the observation of Xiang et al. (2014) as a J-shaped non-linear response was reported for the association between heat and OI in Adelaide, Australia, using a time-stratified case-crossover study design.

Table 7 Summary of subgroup analysis of hot temperature studies ($n=17^*$) conducted by workers' characteristics, nature of work and workplace characteristics.

Subgroups	N	K	RR	LCI	UCI	I^2	P value
Workers							
characteristics							
Gender							
Male	8	10	1.018	1.010	1.026	95.2%	< 0.001
Female	8	10	1.008	1.000	1.016	85.2%	< 0.001
Age							
<35 years old	8	10	1.009	1.005	1.013	89.9%	< 0.001
≥35 years old	8	10	1.006	1.002	1.010	93.3%	< 0.001
Experience							
New workers	3	5	1.008	1.004	1.012	0.0%	0.844
Experienced	3	5	1.007	1.000	1.014	75.5%	0.018
Type of workers							
Specific workers	5	5	1.032	1.003	1.061	91.8%	< 0.001
All workers	12	12	1.008	1.005	1.011	95.6%	< 0.001
Nature of Work							
Physical Demands							
Heavy and Manual	6	9	1.003	1.002	1.004	12.9%	0.327
work with MET >							
5							
Location of work							
Outdoor	13	17	1.009	1.005	1.012	80.4%	< 0.001
Indoor	8	12	1.005	1.002	1.008	92.6%	< 0.001
	_						
Workplace characterist	ics						
Type of Industries	10		1 000	1.006	1.010	01.00/	0.001
Construction	10	14	1.009	1.006	1.013	81.9%	< 0.001
Agriculture	9	13	1.010	1.006	1.014	28.8%	0.155
Manufacturing	6	8	1.007	1.001	1.012	92.0%	< 0.001
Transport	8	12	1.005	1.003	1.008	20.7%	0.241
Electricity, Gas and	7	11	1.005	0.995	1.014	58.7%	0.007
Water							
Business size							
Small	5	5	1.011	1.005	1.016	90.2%	< 0.001
Medium	5	5	1.012	1.006	1.018	91.7%	< 0.001
Large	5	5	1.005	1.000	1.010	79.7%	0.001

Note: *Two studies (Ma et al., 2019; Morabito et al., 2006) were not included in the meta-analysis. N is the total number of studies. K is the total number of location-specific observations (where available) from each study. LCI is the low confidence interval and UCI is the upper confidence interval.

Table 8 Summary of subgroup analysis of HW studies (n=8) conducted by workers characteristics and workplace characteristics.

Subgroups	N	K	RR	LCI	UCI	I^2	P value
Workers characteristics							
Gender							
Male	4	6	1.270	1.120	1.430	98.8%	< 0.001
Female	4	6	1.160	1.030	1.290	97.5%	< 0.001
Age							
<35 years old	4	6	1.260	1.090	1.440	98.6%	< 0.001
≥35 years old	4	6	1.220	1.110	1.330	97.4%	< 0.001
Experience*							
New workers	2	4	1.450	1.280	1.610	75.1%	0.007
Experienced	2	4	1.310	1.230	1.400	96.9%	< 0.001
Nature of Work							
Location of work							
Outdoor	6	8	1.170	1.060	1.290	94.5%	< 0.001
Indoor	3	5	1.240	1.120	1.360	98.5%	< 0.001
*** 1.1 1							
Workplace characteristic	CS						
Type of Industries							
Construction	4	6	1.300	1.150	1.440	93.3%	< 0.001
Agriculture	4	6	1.380	1.150	1.610	75.0%	0.001
Manufacturing	3	5	1.410	1.210	1.600	97.2%	< 0.001
Transport	3	5	1.270	1.070	1.460	95.1%	< 0.001
Electricity, Gas and Water	3	5	1.500	1.340	1.660	20.1%	0.286

Note: *Caution in interpreting results because of fewer number of studies. N is the total number of studies. K is the total number of location-specific observations (where available) from each study. LCI is the low confidence interval and UCI is the upper confidence interval.

A significant cumulative association was found (RR 1.174, 95% CI: 1.057-1.291) between OI and HW in various studies. This is in contrast to three studies that suggested the risk of OI reduced during extended periods of extremely hot conditions (Rameezdeen and Elmualim, 2017; McInnes et al., 2018; Xiang et al., 2014). These differences may attribute to varying definitions of HW (Varghese et al., 2019). For example in Adelaide three studies were conducted; two studies (Rameezdeen and Elmualim, 2017; Xiang et al., 2014) defined HW as three or more consecutive days of daily maximum temperature of 35 °C or above and Varghese et al. (2018) used EHF index to define HW and the studies found statistically varying results. Varghese et al. (2018) argued that three days of Tmax \geq 35 °C is a stringent measure of HW and it does not take into account the minimum temperature variations when considering impacts of HW on human health (Nairn and Fawcett, 2015). Further, the differences can possibly be due to the methodological variations (Hajat et al., 2006) and due to prevention and control measured adapted to reduce the risk. For example Xiang et al. (2014) suggested that preventive measures adapted in the workplace or workers may stop work or self-pace if the ambient temperature is extremely high, can result in the unexpected decline in the number of injuries.

The effect of HW was assessed in three climate zones and risk was found to be highest in Oceanic and Humid Subtropical Climates. However, caution should be taken in interpreting these results, as these estimates are based on fewer number of observations and require further evidence to increase the statistical power of the estimates to quantify the risk of HW in different climate zones. It is also pertinent to note that all studies characterizing the impacts of HW were conducted in midlatitude, high-income countries with low to medium population density. Regions most at risk of experiencing extreme HW such as Tropical regions (Campbell et al., 2018) were under-represented.

4.3. Subgroup analyses

Subgroups analysis based on workers' characteristics revealed that male workers and young workers (<35 years of age) were found to be at

higher risk of OI during hot weather conditions, although the risk was statistically significant in both genders and different age groups. The higher risk of OI in men (1.8% with 1 $^{\circ}$ C increase in hot temperatures above reference point and 27% increased risk during HW) could be attributed to gender-based differences in the workforce, because males usually represent a higher proportion of workers performing heavy, outdoor labour (Adam-Poupart et al., 2015; Xiang et al., 2014). In Australia, for example, most temperature-sensitive industries that mostly involve outdoor work are male dominated (less than 40% representation of females) (Australian Bureau of Statistics, 2018). Females are usually more represented in indoor, regulated environments but are still found to be at increased risk of OI (0.8% increased risk associated with hot temperature and 16% increased risk during HW) (Varghese et al., 2019; Sheng et al., 2018; Ma et al., 2019). Poor acclimatization, insufficient training, low competency in performing assigned tasks, low compliance with preventive measures, the strenous nature of jobs assigned and peer pressure are important factors contributing towards the risk of OI in young workers (0.9%) and new workers (0.8%) (Adam-Poupart et al., 2015; McInnes et al., 2017; Xiang et al., 2014). Our findings suggested that workers above the age of 35 years were also at increased risk (0.6%). Evidence from a recent physiological study (Flouris et al., 2018) indicated that the risk of heat stress during hot weather conditions is higher among older workers particularly because of the comorbidities (Kenny et al., 2010) and the loss of cooling mechnaisms that are more likely in elderly (Barnett et al., 2010).

We also found that experienced workers (i.e. with more than one year of experience) were at increased risk of OI at high temperatures (0.7%). The increased risk can possibly be attributed to their increased self-confidence due to which they ignore, underestimate or misjudge any hazards irrespective of their age (Dumrak et al., 2013).

When assessing the nature of work, we found that workers engaged in outdoor work were particularly at high risk to the impacts of hot temperatures (0.9% increased risk of OI vs 0.5% risk in indoor industries with 1 °C increase in temperature above reference value). Outdoor intensive industries mainly include agriculture, forestry, fishing, construction, and utilities supplies where workers are likely to do intense physical work in direct exposure to sunlight and high humidity (Xiang et al., 2014; Acharya et al., 2018; Moda and Minhas, 2019). Recently it has been suggested that direct exposure to solar radiation can potentially impair motor-cognitive performance (Piil et al., 2020) and therefore a combination of high ambient temperature and solar radiation increases the overall thermal stress experienced by outdoor workers leading to increased risk of OI. Furthermore, there is a high prevalence of hypo-hydration in occupations with elevated heat stress, affecting combined motor tasks (Piil et al., 2018). During HW the risk was higher in indoor industries (24% vs 17% in outdoor settings) mainly in manufacturing industries (41% increased risk of OI). These differences in risk of OI in outdoor and indoor settings warrant further investigations. Previous studies suggest that the effects on indoor workers are less clear and the impact more complex as industrial heat production and building architecture become factors of importance (Ciuha et al., 2019). Indoor workers in settings with high industrial heat production are exposed to significant thermal stress that may increase during HW. Moreover, the exposure to overall heat (outside working hours) is also an important contributing factor. During HW (when the minimum temperature is also significantly high) the workers do not adequately recover the impacts of heat stress between their work shifts which increases the risk of OI (Ciuha et al., 2019). Therefore, the exposure to heat during the day as well as night is important in assessing the risk of OI associated with HW. Workers with social disadvantage would be at higher risk of extreme periods of HW, particularly if there are financial impediments in maintaining thermal comfort (Hansen et al., 2013). Identifying high risk industries is particularly important for target-based interventions designed to reduce exposure to occupational hazards associated with heat stress. Although the underlying explanations behind the occurrence of injuries in non-optimal thermal conditions is

complex, the increased risk is likely to be related to physiological mechanisms, where the body is unable to cool itself to maintain the internal temperature (Parsons, 2014) resulting in adverse behavioral effects such as disorientation, impaired judgement, loss of concentration, reduced vigilance, carelessness and fatigue (Varghese et al., 2018). This may affect workers' physical, cognitive and psychomotor performance and may reduce their ability to take protective measures such as staying hydrated or moving to shaded areas. This reduced performance and the inability to follow protective measures can increase the risk of OI (McInnes et al., 2017; Varghese et al., 2019). In addition, we also found that heavy physical workload was also positively associated with high risk of OI (0.3%) during hot weather conditions. Intense physical work can further contribute to internally generated body heat which poses an additional risk of heat stress and associated health effects (Adam-Poupart et al., 2015; Varghese et al., 2019; McInnes et al., 2017).

Only one study assessed the risk of OI in migrant workers (Ricco et al., 2019). Migrant workers are known to be a vulnerable subgroup with language and cultural barriers, extended work hours, demanding jobs, limited safety training and lack of acclimatization (Ricco et al., 2019; Messeri et al., 2019). Future research should be carried out to assess the impacts of hot weather conditions in migrant workers and explore relevant adaptation mechanism.

4.4. Validity of findings/Certainty assessment of available evidence

Risk of bias assessment in individual studies clearly indicated that the quality of studies on this topic was generally high because all studies (100%) (both hot temperature and HW studies) used an appropriate and standard measure of OI outcome provided by national or regional databases. For observational studies, the existence of unmeasured confounders always impacts the quality of the evidence, however we identified that the majority of studies (68% of hot temperature studies and 62% of HW studies) accounted for potential confounders (e.g. time trends, seasonality, day of the week, size of the workforce, holidays and weather parameters (Peng et al., 2006). Exposure assessment was however, a critical point of bias as many studies; 68% of hot temperature studies used single station data or an average of several weather stations' data. This may lead to an underestimation of the local or individual risk level as weather station data fails to account for spatial variations in the exposure (Xiang et al., 2014; Varghese et al., 2019). Sensitivity analysis based on different exposure assessment datasets indicated that studies using satellite, gridded or geo-located metrological data for exposure assessment, estimated stronger effects for the risk of OI. This implies that the relationship between temperature and OI appears to be stronger when using exposure data with more spatial variability than using exposure data based on single weather station data (Lee et al., 2016).

Inter-study heterogeneity (I²) was generally high (I² scores ranging from 0.0% to 91.3% in different climate zones and overall (I² 89.3%) but as the 80% prediction intervals did not include unity and were sufficiently narrow, we did not downgrade the quality of evidence for the hot temperature studies (Orellano et al., 2020). Heterogeneity is likely and can be attributed to several factors including differences in location, exposure variable, exposure metrics, modelling preferences, type of population, health outcomes etc. In the present systematic review we classified the studies based on different exposure variables i.e. hot temperatures and HW, study locations and climatic zones. We standardized all the estimates to one unit of analysis i.e. assessing the risk per 1 °C increase in temperatures above a reference point. The I² value of heterogeneity reduced after classifying the evidence based on climate zones (For $I^2=95.1\%$ to 89.3%) and standardizing the data and conversion to increase in risk per 1 $^{\circ}\text{C}$ temperature (Table E3, Appendix E of SM). However, studies using different exposure metrics (Tmax, Tmean or Thermal indices) were combined based on the assumptions that the strong correlation between different exposure measures of temperature means that on average they have the same predictive ability in

estimating mortality and potentially injuries (Varghese et al., 2019; Barnett et al., 2010). Exposure characterization is one of the most significant sources of heterogeneity in environmental epidemiology studies (Blair et al., 1995). The sensitivity analyses carried out for studies using different exposure metrics (for example Tmax, Tmean and Thermal indices) (Table E2, Appendix E of SM) revealed statistically significant risks of OI (0.8% for studies using Tmax, 1.2% for studies using Tmean and 2.6% for studies using thermal indices) indicating similar predictive ability of various exposure metrics. The risk was estimated to be slightly higher for studies that used thermal indices (Spector et al., 2016; Garzon-Villalba et al., 2016; Schifano et al., 2019; Fogleman et al., 2005), however it should be noted that three of these studies (Spector et al., 2016; Garzon-Villalba et al., 2016; Fogleman et al., 2005) were carried out for highly exposed occupations (agricultural workers, aluminum smelter workers and disaster relief workers), which can be attributed to higher risk estimates. To date, a large number of exposure metrics have been used to assess the temperature associated health effects. One study assessing the predictive ability of several temperature indices suggested that there is no best exposure metric and the selection of exposure metric should depend on the availability of reliable and complete datasets (Barnett et al., 2010). The effects of humidity are secondary to the effects of temperature and may be incorporated in the models when data is from regions characterized by hot and humid

Funnel plots and Egger's test were indicative of risk of publication bias for hot temperature studies. However, caution must be taken in interpreting the results from funnel plots and other tests. There could be other possible sources of asymmetry in funnel plots such as high heterogeneity (Egger et al., 1997). Moreover, the Trim and Fill test suggested that any new hypothetical study with effects in the opposite direction would be unlikely to change the effects of our meta-analysis. Therefore, we did not downgrade the quality of evidence of hot temperature studies based on asymmetric funnel plots. Overall, the quality of evidence on the risk of OI associated with hot temperatures was "high" suggesting the results of our meta-analyses were sourced from well-designed and well-conducted studies.

The existing quality of studies on the effects of HW on OI was "low" primarily because of high heterogeneity in the evidence and high risk of bias across the studies. The high risk of bias is found to be attributable to unmeasured confounding variables in various studies and the risk of exposure misclassification because majority of the studies used single or average of multiple weather station data. Significant heterogeneity among studies can be attributed to the use of different definitions of heatwaves, which may vary in terms of duration, intensity and temperature metric (Hajat et al., 2006). Different study designs and statistical approaches used may contribute to high heterogeneity. Further, a study (Xu et al., 2016) suggested that different climates in study sites may play a significant role in driving the variability, because locationspecific climatic variations are important in assessing the risk of HW. The present systematic review of literature suggests that more research is required to strengthen the existing evidence on the risk of OI during HW in different climate zones.

4.5. Gaps and future work

There is limited evidence from Tropical Climates on the potential risk of OI due to a lack of studies in these regions. Tropical Climates are inhabited by the majority of the world's population and are at the highest risk of extreme heat events. Most of the countries in hot Tropical Climates are low and middle-income countries, where national data on OI are either unavailable or underreported (Hämäläinen et al., 2017). Studies conducted in these regions have mostly focused on heat stress symptoms or productivity loss in various industries. Evidence from empirical studies suggested that the occupational burden is very high in tropical developing countries (Tawatsupa et al., 2013; Kjellstrom et al., 2009; Quiller et al., 2017; Sahu et al., 2013; Spector and Sheffield,

2014). The level of summer heat exposure reported at outdoor occupational sites in the tropics is also significantly higher than international thresholds. Thus, there is a need for future studies to determine the risk of OI in these regions so that effective intervention strategies can be developed (Moda and Minhas, 2019). Hot Semi-arid and Hot Desert Climates in the Middle East host millions of unacclimatized migrant workers, evidence is required from these regions to assess the impacts of hot temperatures on OI particularly in migrant workers. Furthermore, as the number of HW are predicted to increase there is an urgent need to understand the local impacts of HW on occupational health in different climate zones, which is currently an underexplored area of research and require crucial attention.

4.6. Strengths and limitations

We adapted a standardized and comprehensive search approaches for the identification, screening and extraction of evidence, in this systematic review, which we believe is the first comprehensive review to comparatively estimate the risk of OI associated with both hot temperatures and HW. Furthermore, we classified the location-specific studies into different climate zones. We have introduced a geographical breakdown in identifying the heat associated risk of OI, and propose that future work should consider geographical and global climatic variations as both are important factors in contextualizing the risk associated with temperature related mortality and morbidity. This has been largely neglected to date.

The present study has some limitations. We limited our search for language and considered only English language articles. Studies conducted for athletes and military personals were not included as their health and job requirements vary significantly from regular workers. Further, to combine estimates from different type of studies for example those assessing the risk per 1 °C increase in temperature and those using minimum reference temperature and maximum temperature values (or percentiles) we standardized the data to 1 °C increase in risk above reference temperature. For standardization, we assumed a log-linear relationship for studies that used temperature percentiles to assess the risk, this may have resulted in overestimation or underestimation of the results. However, sensitivity analysis (Table E2, Appendix E of SM) did not reveal any major differences in the results. It should be noted that we used location-specific estimates from various studies instead of pooled estimates and in some cases the data (both effect estimates and reference temperatures) was extracted manually from the textual/graphical descriptions if it was not available directly in the studies so the datasets were susceptible to imprecision. Nonetheless, the study used the best available data and contacted the authors of relevant studies twice to get the required data. It is also worth mentioning that the risk is estimated at city, state or province level in all studies, therefore we also assumed one type of climate in each location and did not take into account local climatic variations at intra-city level. This is not a limitation of the present study, but rather a shortcoming of research in this field and warrant future investigation at a finer spatial scale. Further, it should be noted that the critical appraisal of individual studies was carried out quite thoroughly by two authors independently following Johnson et al. (2014) however, the contextual support for each judgement is missing from the present systematic review and should be addressed in future work.

5. Conclusions

Our findings clearly suggest that the risk of OI increases with exposure to hot weather conditions. There is an urgent need to mitigate the impacts of occupational heat stress in the context of climate change and the anticipated rise in environmental heat stress. The risk of OI associated with extreme heat is not evenly distributed and is dependent on underlying climatic conditions, workers' characteristics, nature of work, and workplace characteristics. The differences in the risk of OI across

different climate zones and worker subgroups warrants further investigation along with the development of climate- and work-specific intervention strategies. With this knowledge, relevant policies and ensuing actions can then be taken to mitigate the risk of OI.

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CRediT authorship contribution statement

Syeda Hira Fatima: Conceptualization, Methodology, Software, Formal analysis, Validation, Writing - original draft. Paul Rothmore: Conceptualization, Writing - review & editing, Supervision. Lynne C. Giles: Conceptualization, Writing - review & editing, Supervision. Blesson M. Varghese: Conceptualization, Methodology, Software, Formal analysis, Validation, Writing - review & editing. Peng Bi: Conceptualization, Writing - review & editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2021.106384.

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