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REVIEW ARTICLE

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Individual risk factors associated with exertional heat illness: A systematic review

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Abstract

Despite the widespread knowledge of exertional heat illness (EHI) and clear guidance for its prevention, the incidence of EHI remains high. We carried out a systematic review of available literature evaluating the scientific evidence underpinning the risk factors associated with EHI. Medline, PsycINFO, SportDiscus and Embase were searched from inception to January 2019 with no date limitation, with supplementary searches also being performed. Search terms included permutations of risk and heat illness, with only studies in English included. Study selection, data extraction and quality assessment, using the QUALSYST tool, were performed by two independent reviewers. Of 8898 articles identified by the searches, 42 were included in the systematic review as primary evidence demonstrating a link between a risk factor and EHI. The quality scores ranged from 57.50 to 100%, and studies were generally considered to be of strong quality. The majority of risks attributable to EHI were categorized as those associated with life-style factors. The findings from the systematic review suggest complex manifestation of EHI through multiple risk factors rather than any one factor in isolation. Further research is needed to explore the accumulation of risk factors to help in development of effective preventative measures.

KEYWORDS

exertional heat illness, heat illness, heat stroke, risk

1 | INTRODUCTION

Exertional heat illness (EHI) remains a persistent problem for individuals exposed to hot environments (Stacey et al., 2015). Although the generic response to heat stress is broadly understood, it is evident that individual responses vary greatly (Armstrong et al., 2007; Casa, Amstrong, Kenny, O'Connor, & Huggins, 2012). Some individuals appear capable of exercising in hot environments without complication, whereas others succumb to decrements in performance, heat illness and sometimes death.

Heat illness is a broad term that includes severely incapacitating conditions directly related to an increase in body temperature, such as heat stroke, in addition to less serious disorders, such as heat exhaustion, heat syncope, heat cramps and heat rash. Serious heat stroke is often categorized as 'classic (CHS)' or 'exertional (EHS)'; the former is observed in sick and compromised populations, whereas the latter is primarily observed in apparently healthy and physically fit populations (Carter et al., 2005). Exertional heat illness (EHI) refers specifically to increased metabolic heat production arising from active muscular actions, often exacerbated by adverse climatic conditions or encapsulating clothing (Holmer, 2006). This, coupled with the fact that the typical populations affected by EHI are often healthy and physically fit, means that EHI is considered to be preventable.

In the UK military, heat illness is a significant cause of morbidity that can arise during training and on deployed operations (Stacey et al., 2015). Cases of EHI regularly occur in the temperate climate of the UK, and its incidence is dependent upon the numbers exposed to the risk and the management of that risk (Military Headquarters of the

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Surgeon General, 2019). It is of further concern in military situations where the combination of intense physical work coupled with overmotivation and peer pressure may render individuals more susceptible to succumb to EHI (Rav-Acha, Hadad, Epstein, Heled, & Moran, 2004). Exertional heat illness is noted to be a recurring problem in military training that results in loss of manpower and training effectiveness (Carter et al., 2005).

Moore et al. (2015) documents that risk factors for EHI are potentially modifiable; therefore, prospective awareness is crucial to reducing heat-related morbidity. Moore et al. (2015) suggest that, for example, overweight individuals are thought to be at disproportionate risk of heat illness and can be identified by assessment of body composition, which is reported routinely in the UK Armed Forces. Healthy weight-management strategies could then be deployed to reduce the number of personnel at risk.

Traditional risk factors for EHI have been identified and can be categorized as those attributable to the environment (hot and humid conditions, lack of acclimatization to heat, cumulative effect of heat exposure on repeated days, and inappropriate clothing), behavioural (disrupted sleep patterns, inadequate hydration, poor nutrition and certain medications) and physical factors (low physical fitness levels, being overweight/obese, experiencing high metabolic loads and underlying medical conditions; Armstrong et al., 2007; Casa et al., 2012; Epstein, 1990; Rav-Acha et al., 2004). Other risk factors, such as a history of EHI, sweat gland dysfunction, sunburn and sex have also been reported (Armstrong et al., 2007; Epstein, Shapiro, & Brill, 1983; Gifford et al., 2019; Lim, Kok, Bin Ali, Chong, & Tey, 2016).

To date, numerous position statements and policy documents have been published to provide occupational guidance and advice for athletes and individuals working in hot environments (Armstrong et al., 2007; Casa, Armstrong, & Hillman, 2003, Casa, DeMartini, Bergeron, Csillan & Eichner, 2015; Webber et al., 2016). However, despite clear guidance and understanding of EHI, the incidence of EHI remains high (Armed Forces Health Surveillance Center, 2016; Bouchama & Knochel, 2002). The persistent high incidence of EHI might reflect a disregard, lack of knowledge or lack of understanding of the guidance, or it might indicate that the current guidance requires evaluation and possible amendment. Joint Services Publication (JSP) documents are an authoritative set of instructional and regulatory guidelines with defence-wide applicability owned by the UK Government and Ministry of Defence. JSP 539 (Military Headquarters of the Surgeon General, 2019) provides practical guidance on preventative measures to reduce the risk of heat illness to as low as is practicably possible. However, it is essential to ensure that best practice to support risk mitigation is evidence based.

1.1 | Purpose

The objective of this systematic review was to explore the literature and evaluate the scientific evidence purporting a link between identified risk factors and EHI. The review also aimed to investigate whether there is sufficient evidence to support other, less well-known,

New Findings

• What is the topic of this review?

Exertional heat illness (EHI) remains a persistent problem for athletes and individuals. This threat remains despite numerous athletic position statements and occupational guidance policies. This review explores primary evidence that demonstrates a direct association between 'known' risk factors and EHI.

• What advances does it highlight?

Primary evidence to support 'known' risk factors associated with EHI is not comprehensive. Furthermore, it is not evident that single individual factors predispose individuals to greater risk. In fact, the evidence indicates that EHI can manifest in non-hostile compensable environments when a combination of risk factors is prevalent.

additional risk factors that might be considered by risk managers when assessing the risk of EHI.

2 | METHODS

2.1 | PROSPERO registration

The systematic review was registered with PROSPERO international prospective register of systematic reviews (CRD42018111447).

2.2 | Literature search

Using Medical Subject Heading (MeSH) terms, Medline [EbscoHost], PsycINFO [EbscoHost], SportDiscus [EbscoHost] and Embase [Scopus] were searched on 3 January 2019, with no date limitation. The search strategy aimed to identify articles reporting EHI and their associated risk factors (Supporting Information Table S1). The associated heat illness terms, which formed the search protocol for this review, were evaluated and approved by the UK Ministry of Defence (MOD) Heat Illness Working Group on 30 January 2018. Forward and backward citation searching on all studies which met the inclusion criteria (as detailed below) was conducted. Google Scholar was used for forward citation searching.

2.3 | Inclusion/exclusion criteria

The following inclusion and exclusion criteria were applied.

2.3.1 | Population

We included studies that reported adult and adolescent data from males and females, ranging from young post-pubertal adults (>16 years of age) to an upper age limit of 65 years.

We excluded studies not reporting a source population, not stating the population size or not stating case rates (*n* per *N* population per year, n/N/year).

2.3.2 | Phenomenon of interest

We included studies that reported EHI with a valid measure of core temperature.

We excluded studies where subjects were deemed to have impaired thermoregulation for medical reasons.

2.3.3 | Context

We included studies from any country or any setting.

2.3.4 | Outcomes

We included studies in which the incidence of EHI was established and risk/ratios documented.

We excluded studies where no incidence of EHI and risk coexisted.

2.3.5 Study design

We included cross-sectional, case-control, cohort, randomized control trial and observational studies.

Only studies published in English were reviewed, with no date restriction.

2.4 | Study selection process

All potentially relevant records were exported from Endnote (v.X7) into Rayyan [Qatar Computing Research Institute (QCRI), Qatar Foundation for Education, Science and Community Development], and one investigator (C.S.W.) reviewed all articles to remove and resolve duplicates. Two reviewers (C.S.W. and J.D.L.) then independently screened articles based on the title and abstract. Full-text articles of the remaining potentially relevant studies were then sourced before the two reviewers undertook the second phase, assessment of the eligibility of full-text articles. Disagreements were resolved through discussion between the two reviewers or by using a third reviewer (J.L.F.) where necessary.

2.5 | Data extraction

Data were extracted from all eligible studies into a standardized template using the following headings: Author(s) and year; source population and location; sample; date of study; the nature of the exposure outcome and International Classification of Disease Coding (ICD-codes) for heat illness; and main findings. Two reviewers (C.S.W. and J.D.L.) independently extracted the information from all included articles.

2.6 | Quality assessment

The QualSyst quality assessment tool from the 'Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a

Variety of Fields' (Alberta Heritage Foundation for Medical Research) was used. QualSyst produces a score based on eight criteria, including the appropriateness of the study design and research question, definition of outcomes and exposure, reporting of bias and confounding, and sufficient reporting of results and limitations. Criteria were scored as 'yes' (2), 'partial' (1), 'no' (0) and not applicable (NA). The overall QualSyst score was calculated as the sum of ratings of applicable criteria divided by the maximum scores of applicable criteria. The quality of a paper relative to its QualSyst score was defined by Lee, Packer, Tang, and Girdler (2008) as follows: strong (summary score of >0.80); good (summary score of 0.71-0.79); adequate (summary score of 0.50-0.70); and limited (summary score of <0.50). The method for assessing the quality suggested by Lee et al. (2008) was appropriate for this review, which was to assess the quality of data rather than to use a threshold to exclude articles from the review. Two reviewers (C.S.W. and J.D.L.) assessed the quality of the articles independently. Intraclass correlation (ICC) estimates and 95% confident intervals were calculated for rater agreement using SPSS statistical package v.24 (SPSS Inc, Chicago, IL, USA) based on an absolute-agreement, two-way mixed-effects model. Discrepancies between raters (C.S.W. and J.D.L.) were resolved after discussion.

2.7 | Data analysis

The heterogeneity of the included studies and the diverse range of risk factors reported meant that a meta-analysis was not possible. As such, the characteristics of included studies were evaluated descriptively and findings summarized narratively in order to identify the evidenced risk factor(s). The evidenced risk factors were considered in accordance with those presented in JSP 539 (Military Headquarters of the Surgeon General, 2019), pertaining to lifestyle, health and work constraints.

3 | RESULTS

3.1 | Literature search

Database searches yielded 10,110 records. After the removal of duplicates, 8898 articles remained. Of these 8898 articles, 8765 were excluded after a process of screening the titles, abstracts or both against the study inclusion and exclusion criteria. After full-text assessments of the remaining 133 articles, 93 were excluded because these articles did not meet the inclusion criteria [n = 41 failed to report EHI, n = 24 did not include risk factor incidence, n = 9 presented no EHI and no risk factor, n = 4 full-text articles could not be obtained despite requests to the British Library and several Military libraries (Malhotra & Venkatasawy, 1974; Ping, Chai, & Thomas, 1978; Stallones, Gauld, Dodge, & Lammers, 1957; and Yarger, Cronau, & Goldman, 1968), n = 10 were the wrong type of study, n = 4 were the wrong population sample and n = 1 was a military report that included data in a peer-reviewed publication]. Backward and forward citation searching and assessment of reference lists for the remaining

40 articles resulted in an additional two articles being included and therefore 42 includes in total. The PRISMA diagram in the Supporting Information (Figure S1) represents a flow chart of the study selection process.

3.2 | Study characteristics

Full descriptions of the included studies that met the inclusion criteria are provided in the Supporting Information. The included studies were published between 1961 and 2018 and featured sample sizes that ranged from n = 1 to n = 9667. The studies included as primary evidence tended to be case series, observational and retrospective cohort-control studies. These studies were conducted in a range of settings, including military settings (US Armed Forces, n = 22: Singapore Defence, n = 2: Israeli Defence, n = 2: UK Armed Forces, n = 2; Taiwanese military recruits, n = 2; and French Armed Forces, n = 1), research institutes [US Army Research Institute of Environmental Medicine (USARIEM), n = 1; and the Heller Institute of Medical Research, Israel, n = 1], hospitals and medical centres (based in: France, n = 1; USA, n = 1; and Korea, n = 1), recreational runners (from: Singapore, n = 1; France, n = 1; and Hong Kong, n = 1) and occupational contexts (radiation contamination workers in Japan, n = 1; Australian mine workers, n = 1; and workers of the British Petroleum Deepwater Horizon oil clean-up in the Gulf of Mexico, n = 1).

3.3 | Quality assessment

QualSyst quality scores ranged from 57.50 to 100%. For the primary level of evidence (n = 42), 83.3% were rated as strong (n = 35), 7.1% as good (n = 3) and 9.5% as adequate (n = 4). Inter-rater agreement was deemed to be good to excellent (Koo & Li, 2016), with a percentage agreement between the two raters of 87.10% and ICCs of r = 0.88 (95% confidence interval, 0.72–0.94).

3.4 | Risk factors associated with EHI

3.4.1 | Factors pertaining to lifestyle

Of the 42 studies identified, the majority of risk factors were categorized as those associated with the lifestyle of military personnel. A total of 15 studies reported risk factors pertaining to lifestyle, of which the primary causes of heat illness were associated with personnel being overweight (Bedno et al., 2010; Bedno, Urban, Boivin, & Cowan, 2014; Chung & Pin, 1996; Donoghue and Bates, 2000; Epstein, Moran, Shapiro, Sohar, & Shemer, 1999; Gardner et al., 1996; Moore et al., 2015; Nelson, Deuster, O'Connor, & Kurina, 2018a, b; Rav-Acha et al., 2004; Wallace et al., 2006) and/or having low levels of physical fitness (Abriat, Brosset, Bregigeon, & Sagui, 2014; Bedno et al., 2014; Gardner et al., 1996; Moore et al., 2015; Rav-Acha et al., 2006). There were a small number of studies associated with smoking (n = 1; Nelson et al., 2018b), alcohol intake in the previous 48 h (n = 2; Abriat et al., 2014; Armstrong, de Luca, & Hubbard, 1990), the use of illicit drugs (n = 4; Nelson et al., 2018a, b; Oh & Henning,

2003; Rosenberg, Pentel, Pond, Benowitz, & Olson, 1986) and the use of caffeine and protein supplements (Abriat et al., 2014; Armstrong et al., 1990).

3.4.2 | Factors pertaining to health

Compared with lifestyle, there was less primary evidence associated with 'health' risk factors (*n* = 9 studies). No studies were identified that provided any evidence to support the risk of vaccinations 48 h before physical activity in development of EHI. Several studies reported an increased risk of heat illness after mild systemic illness. For example, the common cold, gastrointestinal or febrile illness (Abriat et al., 2014; Armstrong et al., 1990; Day & Grimshaw, 2005; Keren, Epstein, & Magazanik, 1981; Rav-Acha et al., 2004; Stacey et al., 2015) was associated with increased risk of EHI. Of note, all six of those studies plus Minard, Grayeb, Singer, and Kingston (1961) also reported dehydration as a risk factor increasing the likelihood of EHI. Although not clearly documented as primary evidence, additional reported observations of data (e.g. Rav-Acha et al., 2004) infer that previous episodes of underlying illness, such as diarrhoea, will result in dehydration and manifest in more serious episodes of EHI.

3.4.3 Factors pertaining to work constraints

Eight studies were sourced that were able to confirm primary evidence to support individual risk factors, which increased EHI risk from factors aligned to working constraints. Six studies reported increased risk with sleep deprivation (Abriat et al., 2014; Armstrong et al., 1990; Day & Grimshaw, 2005; Kakamu et al., 2015; Rav-Acha et al., 2004; Stacey et al., 2015), four reported increased risk with lack of heat acclimatization (Day & Grimshaw, 2005; Minard et al., 1961; Rav-Acha et al., 2004; Stacey et al., 2015), two reported increased risk related to nutritional and dietary aspects (Abriat et al., 2014; Day & Grimshaw, 2005), and two reported increased risk in inexperienced personnel (Epstein et al., 1999; O'Donnell, 1975). The majority of included studies also reported risk factors associated with lifestyle, as outlined in Table 1. Thus, the primary level of evidence indicated that lifestyle and health risk factors cannot be viewed in isolation.

3.4.4 Other factors

Of the 42 articles included in the narrative analysis, only 22 demonstrated a clear association between factors pertaining to lifestyle, health and work constraints (Table 1). Twenty-eight of the 42 highlighted other factors that presented a risk of EHI (Table 2).

4 DISCUSSION

The purpose of this systematic review was to summarize and assess the primary evidence identifying causation between risk factors and EHI. A comprehensive search yielded 42 articles, and the overall study quality ranged from adequate to strong; most scores could have been improved had confounding been controlled or taken into account. The heterogeneity of published studies addressing EHI risk, **TABLE 1** Primary evidence for individual risk factors

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Risk factor	Evidence
Lifestyle	
Individual volition	Armstrong et al. (1990)
Being overweight or obese	Bedno et al. (2010, 2014); Chung and Pin (1996); Donoghue and Bates (2000); Epstein et al. (1999); Gardner et al. (1996); Moore et al. (2015); Rav-Acha et al. (2004); Wallace et al. (2006)
Lack of physical fitness	Abriat et al. (2014); Bedno et al. (2014); Gardner et al. (1996); Moore et al. (2015); Rav-Acha et al. (2004); Wallace et al. (2006)
Smoking (not ex-smokers)	Nelson et al. (2018b)
Alcohol intake within the past 48 h	Abriat et al. (2014); Armstrong et al. (1990)
Illicit drugs, e.g. ecstasy	Nelson et al. (2018a, b); Oh and Henning, (2003); Rosenberg et al. (1986)
Use of supplements	Abriat et al. (2014); Armstrong et al. (1990)
Health	
Previous heat illness	Armstrong et al. (1990); Day and Grimshaw (2005); Nelson et al. (2018a); Phinney, Gardner, Kark, and Wenger (2001)
Mild illness, e.g. diarrhoea, common cold, fever	Abriat et al. (2014); Armstrong et al. (1990); Day and Grimshaw (2005); Keren et al. (1981); Rav-Acha et al. (2004); Stacey et al. (2015)
Vaccination within the past 48 h	
Current sunburn	Armstrong et al. (1990)
Prescribed and over-the-counter medication, e.g. antihistamines and painkillers	Armstrong et al. (1990)
Dehydration	Abriat et al. (2014); Day and Grimshaw (2005); Keren et al. (1981); Minard et al. (1961); Rav-Acha et al. (2004); Stacey et al. (2015)
Work constraints	
Inexperienced personnel	-
Air travel within the past 24 h	-
Poor nutrition (missed meals within the past 24 h)	Abriat et al. (2014); Day and Grimshaw (2005)
Lack of sleep	Abriat et al. (2014); Armstrong et al. (1990); Day and Grimshaw (2005); Kakamu et al. (2015); Rav-Acha et al. (2004); Stacey et al. (2015)
Unacclimatized personnel	Day and Grimshaw (2005); Minard et al. (1961); Rav-Acha et al. (2004); Stacey et al. (2015)

TABLE 2	Additional risk factors identified from the review
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Individual factors	Characteristics: Age (Epstein et al., 1999; Armed Forces Health Surveillance Center, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017; Nelson et al., 2018b); sex (Armed Forces Health Surveillance Center, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2016; Nelson et al., 2018a); ethnicity (Carter et al., 2005) Health conditions: Hypohidrosis (Lim et al., 2016); malignant hyperthermia (Poussel et al., 2015); altered cytokine production (Chang, 1993); type II fibre predominance (Hsu, Lee, Chang, Shieh, & Tsao, 1997); burns (Seth & Juliana, 2011); sympathectomy (Sihoe, Liu, Lee, Lam, & Cheng, 2007); sickle cell trait (Singer et al., 2018)
Environmental factors	Accumulation of thermal load (previous day of exposure); (Garzon-Villalba et al., 2006; Wallace et al., 2006); high wet-bulb globe temperature (Day & Grimshaw, 2005; Garzon-Villalba et al., 2006; Kark, Burr, Wenger, Gastaldo, & Gardner, 1996)
Organizational factors	Branch of Armed forces and personnel rank (Bedno et al., 2014; Armed Forces Health Surveillance Center, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017, ; Nelson et al., 2018a); early stage of recruit training and aptitude on entry (possible link to inexperienced personnel; Nelson et al., 2018b); intense physical work (Armstrong et al., 1990; Day & Grimshaw, 2005; O'Donnell, 1975); time into exercise (suggestive of rate of temperature increase; Epstein et al., 1999); geographical region (Beller & Boyd, 1975; Carter et al., 2005; O'Donnell, 1975); scheduled race in combat clothing (Abriat et al., 2014)

in terms of design, samples and measurement methods, prevented a quantitative analysis of the evidence; therefore, this review took a narrative approach.

Heat illness continues to pose a significant risk to athletic, military and other occupational populations. As such, expansive and up-todate reviews of risk factors will provide important knowledge for the development of effective heat illness mitigation strategies to minimize this risk. Field-based detection before multiple-organ failure is challenging, and medical triage to screen the risk is crucial to prevent fatalities (Rav-Acha et al., 2004).

The findings from this review support the contention that there is wide variation in how humans tolerate heat. In some instances, there is

primary evidence to identify that an individual risk factor has caused an individual to succumb to EHI. Synthesis of the findings provides evidence that the majority of EHI is attributable to intrinsic factors pertaining to lifestyle.

Although some of the included studies provided specific support for an increased risk of individuals to develop EHI, it would be prudent to state that associations were evident in individuals who typically presented with low levels of physical fitness combined with high body mass index (BMI)/body fat composition measurement (BCM). Bedno et al. (2014) suggested a five- to eightfold increase risk odds ratio when low physical fitness is combined with obesity, but data to support the risk between the US military classification of 'excess body fat' and being 'unfit' is lacking. However, caution must be exercised when interpreting these associations, because low levels of physical fitness were established from the failing of occupational fitness tests. Therefore, the real risk of EHI from low physical fitness and high BMI/BCM remains unclear. Furthermore, it could be hypothesized that the higher rate of heat illness in females (Armed Forces Health Surveillance Center, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017) is a result of physical factors, such as high BMI/BCM, coupled with lower levels of fitness. However, incidence rates of heat stroke were, in fact, higher in males (Armed Forces Health Surveillance Center, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017); this is most likely to be attributable to behavioural sex differences, such as over-motivation and higher sustained levels of metabolic load (Rav-Acha et al., 2004).

Evidence is emerging to suggest that sex (Kazman et al., 2015), increasing age (Kenny et al., 2015; Larose, Boulay, Sigal, Wright, & Kenny, 2013; McGinn et al., 2017) and the combined effects of these (Notley et al., 2017) should be considered as risk factors for the development of exertional heat illness. However, these studies comprise experimental trials with ethical termination core temperature values ranging from 39 to 39.5°C. As a result, these studies can infer only that a relationship exists between age and sex through reduced thermal tolerance and that these factors are not directly attributable for EHI.

The primary evidence reports that the 'at risk' odds ratio increases after the use of opioids and non-steroid anti-inflammatory drugs (NSAIDs). Nelson, Deuster, O'Connor, and Kurina (2018b) suggest an increased risk of EHI as a result of using NSAIDs in personnel on physical training restrictions as a result of musculoskeletal injury. Thus, the increased risk of EHI might result from reduced physical fitness secondary to deconditioning and subsequent alterations in BMI and/or BCM. Alternatively, unhealthy BMI and/or BCM might increase the risk of musculoskeletal injury, which will limit physical conditioning and increase the risk of EHI. Audet et al. (2017) provide evidence, in a rodent model of heat stroke, that the intake of an NSAID increases morbidity risk through significant gut injury. Although not confirmed in human experiments or clinical observations, NSAIDs might predispose individuals to a greater risk of heat injury. All are plausible explanations and confirm that no individual factor might be responsible for the risk of EHI and that it is more likely to result from a complex accumulation of factors.

4.1 | Contemporary thoughts

The general literature proposes that climate and the lack of acclimatization are the leading risk factors for EHI (Bergeron et al., 2005; Bouchama & Knochel, 2002; Casa et al., 2015). JSP 539 (Military Headquarters of the Surgeon General, 2019) specifies that 8 days should be provided for heat acclimatization and that inadequate time coupled with operational activity that is strenuous will manifest in heat illness peaks in the first few days (Moore et al., 2015). However, the majority of EHI evidenced from this review occurred in temperate climates at lower recorded wet-bulb globe temperatures, suggesting that high environmental temperature is not necessarily a prerequisite for EHS. Furthermore, although it is acknowledged that rapid deployment of troops can further exacerbate risk, it is evident that EHI risk remains after initial deployment. Abriat et al. (2014) identified that the median time from arrival to development of EHS overseas was 60 days with median climatic conditions of 22°C (interguartile range, 17-25°C), 80% relative humidity (interguartile range, 67-85%).

As training continues, improvements in physical conditioning will be likely to ensue in response to an increased volume of training. which will probably lead to residual fatigue, diminished levels of intramuscular glycogen and cellular energy depletion (Alosco et al., 2012). Coincidental introduction of multiple stressors owing to the difficulties associated with operational activities (e.g. poor nutrition, sleep deprivation, maintenance of hydration) means that the risk of EHI remains high during the latter stages of deployment/training. Wallace et al. (2006) noted that the risk of EHI was high in the second half of recruit training and most likely to be attributable to the motivation of recruits to push themselves, possibly with underlying illness, despite having what was deemed to be an excellent conditioned status. More recent work has started to explore the notion of an acute elevated inflammatory status alongside impaired thermoregulation arising from exercise-induced muscle damage. This could explain the risk of EHI associated with increased volume loads and strenuous activity (Dolci et al., 2015; Fortes et al., 2013). Personnel might use NSAIDs to alleviate inflammation, further exacerbating the risk (Nelson et al., 2018b) and highlighting the complex interplay of risk factors.

A contemporary approach to assessment of risk can be made in line with the paradigm of Minard from the early 1960s (Minard et al., 1961), who suggested that three different areas should be considered in terms of the aetiology of individuals who succumb to EHI: (i) individual limiting factors (intrinsic physiological factors); (ii) environmental factors; and (iii) organizational factors. The additional factors prevalent in the literature (Table 1) could be aligned with each of these categories and should therefore be considered in organizational direction that aims to prevent or reduce the incidence of heat illness.

Rav-Acha et al. (2004) identify that the risk of EHS in the US Armed Forces has decreased since the published findings from Shibolet et al. (1976) from 22.2 to 4.4%. Amendments to training regulations (flagging wet-bulb globe temperature conditions, scheduling of events, attention to clothing, equipment and workloads, and command emphasis on hydration status) are implemented to help mitigate risk. Nevertheless, there continue to be instances where personnel/athletes succumb to EHS (e.g. the deaths of three British Army recruits during Special Forces Selection in July 2013).

The evidence presented in this review does not support the view that one individual factor predisposes an individual to greater risk of EHI; risk factors tend to be related closely, and greater risk is associated with a combination of factors. The findings of this systematic review provide primary evidence that 15 of the 18 traditional risk factors, as detailed in the UK Ministry of Defence's JSP 539 (Military Headquarters of the Surgeon General, 2019), contribute to the development of EHI.

Care should be taken with the interpretation of findings, because the majority of evidence presented was taken from retrospective casecontrol studies in which incomplete reporting, inadequate diagnostics to differentiate EHI (owing to field-based approaches), failure to account for confounding factors and relatively few cases identified were highlighted as limitations. The evidence presented includes many studies that report EHI in non-hostile compensable environments, which suggests a more complex manifestation of EHI through multiple risk factors.

To conclude, many positional statements and policies exist that present the risk of individual factors in the development of EHI. However, this review challenges the primary basis of evidence to support those. Furthermore, although policy documents, such as JSP 539 (Military Headquarters of the Surgeon General, 2019), do not consider the individual risk factors in isolation, it is evident that a more detailed knowledge of the complex interplay of risk factors is required and that this should be considered to mitigate and prevent individuals succumbing to EHI.

COMPETING INTERESTS

None declared.

AUTHOR CONTRIBUTIONS

All authors were responsible for the conception and design of the study. C.S.W. and J.D.L. conducted the acquisition of data, and C.S.W., J.L.F., M.N. and J.D.L. interpreted the results. C.S.W. drafted the manuscript, and J.L.F., S.K.D., M.N., H.B.O. and J.D.L. critically revised the work for important intellectual content. All authors approved the final version. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

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REFERENCES

Abriat, A., Brosset, C., Bregigeon, C., & Sagui, E. (2014). Report of 182 cases of exertional heatstroke in the French Armed Forces. *Military Medicine*, 179, 309–314.

- Alosco, M. L., Knecht, K., Glickman, E., Gunstad, J., Bergeron, N., & Hart, J. (2012). History of concussion and exertional heat illness symptoms among college athletes. *International Journal of Athletic Therapy & Training*, 17, 22–27.
- Armed Forces Health Surveillance Center. (2009). Update: Heat injuries, active component, U.S. Armed Forces, 2008. MSMR, 16, 8–9.
- Armed Forces Health Surveillance Center. (2010). Update: Heat injuries, active component, U.S. Armed Forces, 2009. MSMR, 17, 6–8.
- Armed Forces Health Surveillance Center. (2011). Update: Heat injuries, active component, U.S. Armed Forces, 2010. MSMR, 18, 6–8.
- Armed Forces Health Surveillance Center. (2012). Update: Heat injuries, active component, U.S. Armed Forces, 2011. MSMR, 19, 14–16.
- Armed Forces Health Surveillance Center. (2013). Update: Heat injuries, active component, U.S. Armed Forces, 2012. MSMR, 20, 17–20.
- Armed Forces Health Surveillance Center. (2014). Update: Heat injuries, active component, U.S. Armed Forces, 2013. MSMR, 21, 10–13.
- Armed Forces Health Surveillance Center. (2015). Update: Heat injuries, active component, U.S. Armed Forces, 2014. MSMR, 22, 17–20.
- Armed Forces Health Surveillance Center. (2016). Update: Heat injuries, active component, U.S. Army, Navy, Air Force, and Marine Corps, 2015. *MSMR*, 23, 16–19.
- Armed Forces Health Surveillance Center (AFSC). (2017). Update: Heat injuries, active component, U.S. Armed Forces, 2016. MSMR, 24, 9–13.
- Armstrong, L. E., Casa, D. J., Millard-Stafford, M., Moran, D. S., Pyne, S. W., & Roberts, W. O. (2007). Exertional heat illness during training and competition. *Medicine and Science in Sports and Exercise*, 39, 556–572.
- Armstrong, L. E., deLuca, J. P., & Hubbard, R. W. (1990). Time course of recovery and heat acclimation: Ability of prior exertional heatstroke patients. *Medicine and Science in Sports and Exercise*, 22, 36–48.
- Audet, G. N., Dineen, S. M., Stewart, D. A., Plamper, M. L., Pathmasiri, W. W., McRitchie, S. L., & Leon, L. R. (2017). Pretreatment with indomethacin results in increased heat stroke severity during recovery in a rodent model of heat stroke. *Journal of Applied Physiology*, 123, 544– 557.
- Bedno, S. A., Li, Y., Han, W., Cowan, D. N., Scott, C. T., Cavicchia, M. A., & Niebuhr, D. W. (2010). Exertional heat illness among overweight U.S. Army recruits in basic training. *Aviation, Space & Environmental Medicine*, 81, 107–111.
- Bedno, S. A., Urban, N., Boivin, M.R., & Cowan, D. N. (2014). Fitness, obesity and risk of heat illness among army trainees. *Occupational Medicine*, 64, 461–467.
- Beller, G. A., & Boyd, A. E., III. (1975). Heat stroke: A report of 13 consecutive cases without mortality despite severe hyperpyrexia and neurologic dysfunction. *Military Medicine*, 140, 464–467.
- Bergeron, M. F., McKeag D. B., Casa D. J., Clarkson P. M., Dick R. W., Eichner E. R., ... Rowland T. W. (2005). Youth football: Heat stress and injury risk. *Medicine & Science in Sports & Exercise*, 37 (8), 1421–1430. http://doi.org/10.1249/01.mss.0000174891.46893.82.
- Bouchama, A., & Knochel, J. P. (2002). Heat stroke. The New England Journal of Medicine, 346, 1978–1988.
- Carter, R., III, Cheuvront, S. N., Williams, J. O., Kolka, M. A., Stephenson, L. A., Sawka, M. N., & Amoroso, P. J. (2005). Epidemiology of hospitalizations and deaths from heat illness in soldiers. *Medicine and Science in Sports* and Exercise, 37, 1338–1344.
- Casa, D., Armstrong, L. E., & Hillman, S. K. (2003). Inter-Association Task Force on Exertional Heat Illness consensus statement. NATA News, 24-29.
- Casa, D. J., Amstrong, L. E., Kenny, G. P., O'Connor, F. G., & Huggins, R. A. (2012). Exertional heat stroke: New concepts regarding cause and care. *Current Sports Medicine Reports*, 11, 115–123.
- Casa, D. J., DeMartini J. K., Bergeron M. F., Csillan D., Eichner E. R., Lopez R. M., ... Yeargin S. W. (2015). National athletic trainers' association position statement: Exertional heat illnesses. *Journal of Athletic Training*, 50 (9), 986–1000. http://doi.org/10.4085/1062-6050-50.9.07.

^{8 |} Wiley−

Chang, D. M. (1993). The role of cytokines in heat stroke. *Immunological Investigations*, 22, 553–561.

Chung, N. K., & Pin, C. H. (1996). Obesity and the occurrence of heat disorders. *Military Medicine*, 161, 739–742.

Day, T. K., & Grimshaw, D. (2005). An observational study on the spectrum of heat-related illness, with a proposal on classification. *Journal of the Royal Army Medical Corps*, 151, 11–18.

Dolci, A., Fortes, M. B., Walker, F.S., Haq, A., Riddle, T., & Walsh, N. P. (2015). Repeated muscle damage blunts the increase in heat strain during subsequent exercise heat stress. *European Journal of Applied Physiology*, 115, 1577–1588.

Donoghue, A. M., & Bates, G. P. (2000). The risk of heat exhaustion at a deep underground metalliferous mine in relation to body-mass index and predicted VO₂max. *Occupational Medicine*, 50, 259–263.

Epstein, Y. (1990). Heat intolerance: Predisposing factor or residual injury?Medicine and Science in Sports and Exercise, 22, 29–35.

Epstein, Y., Moran, D. S., Shapiro, Y., Sohar, E., & Shemer, J. (1999). Exertional heat stroke: A case series. *Medicine and Science in Sports and Exercise*, 31, 224–228.

Epstein, Y., Shapiro, Y., & Brill, S. (1983). Role of surface area to mass ratio and work efficiency in heat intolerance. *Journal of Applied Physiology*, 54, 831–836.

Fortes, M. B., Di Felice, U., Dolci, A., Junglee, N. A., Crockford, M. J., West, L., ... Walsh, N. P. (2013). Muscle damaging exercise increases heat strain during subsequent exercise heat stress. *Medicine and Science in Sports* and Exercise, 45, 1915–1924.

Gardner, J. W., Kark, J. A., Karnei, K., Sanborn, J. S., Gastaldo, E., Burr, P., & Wenger, B. C. (1996). Risk factors predicting exertional heat illness in male Marine Corps recruits. *Medicine and Science in Sports and Exercise*, 28, 939–944.

Garzon-Villalba, X. P., Mbah, A., Hiles, M., Moore, H., Schwartz, S. W., & Bernard, T. E. (2016). Exertional heat illness and acute injury related to ambient wet bulb globe temperature. *American Journal of Industrial Medicine*, 59, 1169–1176.

Gifford, R. M., Todisco, T., Stacey, M., Fujisawa, T., Allerhand, M., Woods, D. R., & Reynolds, R. M. (2019). Risk of heat illness in men and women: A systematic review and meta-analysis. *Environmental Research*, 171, 24–35.

Goforth, C.W., & Kazman, J. B. (2015). Exertional heat stroke in navy and marine personnel: A hot topic. *Critical Care Nurse*, *35*, 52–59.

Holmer, I. (2006). Protective clothing in hot environments. *Industrial Health*, 44, 404–413.

Hsu, Y. D., Lee, W. H., Chang, M. K., Shieh, S. D., & Tsao, W. L. (1997). Blood lactate threshold and typell fibre predominance in patients with exertional heatstroke. *Journal of Neurology Neurosurgery and Psychiatry*, 62, 182–187.

Kakamu, T., Hidaka, T., Hayakawa, T., Kumagai, T., Jinnouchi, J., Tsuji, M., ... Fukushima, T. (2015). Risk and preventive factors for heat illness in radiation decontamination workers after the Fukushima Daiichi Nuclear Power Plant accident. *Journal of Occupational Health*, 57, 331– 338.

Kark, J. A., Burr, P. Q., Wenger, C. B., Gastaldo, E., & Gardner, J. W. (1996). Exertional heat illness in Marine Corps recruit training. Aviation, Space, and Environmental Medicine, 67, 354–360.

Kazman, J. B., Purvis, D. L., Heled, Y., Lisman, P., Atias, D., Van Arsdale, S., & Deuster, P. A. (2015). Women and exertional heat illness: Identification of gender specific factors. *The Army Medical Department Journal*, 48–56.

Kenny, G. P., Larose, J., Wright-Beatty, H. E., Boulay, P., Sigal, R. J., & Flouris, A. D. (2015). Older firefighters are susceptible to age-related impairments in heat dissipation. *Medicine and Science in Sports and Exercise*, 47, 1281–1290.

Keren, G., Epstein, Y., & Magazanik, A. (1981). Temporary heat intolerance in a heatstroke patient. Aviation, Space, and Environmental Medicine, 52, 116–117. Koo, T. K., & Li, M. Y. (2016). A guideline of selecting and reporting intraclass correlation coefficients for reliability research. *Journal of Chiropractic Medicine*, 15, 155–163.

Larose, J., Boulay, P., Sigal, R. J., Wright, H. E., & Kenny, G. P. (2013). Agerelated decrements in heat dissipation during physical activity occur as early as the age of 40. *PLoS ONE*, *8*, e83148.

Lee, L., Packer, T. L., Tang, S. H., & Girdler, S. (2008). Self-management education programs for age-related macular degeneration: A systematic review. Australasian Journal on Ageing, 27, 170–176.

Lim, J. H. L., Kok, W. L., Bin Ali, N., Chong, W.-S., & Tey, H. L. (2016). Hypohidrosis in individuals with exertional heat injury: A prospective open cohort study. *Dermatology*, 232, 50–56.

Malhotra, M.S., & Venkataswamy, Y. (1974). Heat casualties in the Indian Armed Forces. *Indian Journal of Medical Research*, *62*, 1293–1302.

McGinn, R., Poirier, M. P., Louie, J. C., Sigal, R. J., Boulay, P., Flouris, A. D., & Kenny, G. P. (2017). Increasing age is a major risk for susceptibility to heat stress during physical activity. *Applied Physiology Nutrition and Metabolism*, 42, 1232–1235.

Military Headquarters of the Surgeon General. (2019). [Online]. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/ uploads/attachment_data/file/793094/JSP_539_Part_2_V3.1_Updated_ 04-19_.pdf. Accessed July 24, 2019.

Minard, D., Grayeb, G. A., Singer, R. C., & Kingston, J. R. (1961). Heat stress during Operation Banyan Tree I. *Military Medicine*, 126, 809– 817.

Moore, A. C., Stacey, M. J., Bailey, K. G.H., Bunn, R. J., Woods, D. R., Haworth, K. J., ... Folkes, S. E. F. (2015). Risk factors for heat illness among British soldiers in the hot collective training environment. *Journal of the Royal Army Medical Corps*, 162, 434–439.

Nelson, D. A., Deuster, P. A., O'Connor, F. G., & Kurina, L. M. (2018a). Sickle cell trait and heat injury among US Army soldiers. *American Journal of Epidemiology*, 187, 523–528.

Nelson, D. A., Deuster, P. A., O'Connor, F.G., & Kurina, L. M. (2018b). Timing and predictors of mild and severe heat illness among new military enlistees. *Medicine and Science in Sports and Exercise*, 50, 1603– 1612.

Notley, S. R., Poirier, M. P., Hardcastle, S. P., Flouris, A. D., Boulay, P., Sigal, R. J., & Kenny, G. P. (2017). Aging impairs whole-body heat loss in females under both dry and humid heat stress. *Medicine and Science in Sports and Exercise*, 49, 2324–2332.

O'Donnell, T. F., Jr. (1975). Acute heat stroke. Epidemiologic, biochemical, renal, and coagulation studies. *Journal of the American Medical Association*, 234, 824–828.

Oh, R. C. H., & Henning, J. S. (2003). Exertional heatstroke in an infantry soldier taking ephedra-containing dietary supplements. *Military Medicine*, 168, 429–430.

Phinney, L. T., Gardner, J. W., Kark, J. A., & Wenger, B. C. (2001). Long-term follow-up after exertional heat illness during recruit training. *Medicine* and Science in Sports and Exercise, 33, 1443–1448.

Ping, T. K., Chai, S. L., & Thomas, M. (1978). Heat stress among soldiers in training. Annals of the Academy of Medicine Singapore, 7, 216–220.

Poussel, M., Guerci, P., Kaminsky, P., Heymonet, M., Roux-Buisson, N., Faure, J., ... Chenuel, B. (2015). Exertional heat stroke and susceptibility to malignant hyperthermia in an athlete: Evidence for a link?*Journal of Athletic Training*, 50, 1212–1214.

Rav-Acha, M., Hadad, E., Epstein, Y., Heled, Y., & Moran, D. S. (2004). Fatal exertional heat stroke: A case series. *The American Journal of the Medical Sciences*, 328, 84–87.

Rosenberg, J., Pentel, P., Pond, S., Benowitz, N., & Olson, K. (1986). Hyperthermia associated with drug intoxication. *Critical Care Medicine*, 14, 964–969.

Seth, P., & Juliana, P. (2011). Exertional heat stroke in a marathon runner with extensive healed deep burns: A case report. *International Journal of Emergency Medicine*, 4, 12.

- Shibolet, S., Lancaster, M. C., & Danon, Y. (1976). Heat stroke: A review. Aviation, Space and Environmental Medicine, 47, 280–301.
- Sihoe, A. D. L., Liu, R. W. T., Lee, A. K.L., Lam, C. W., & Cheng, L. C. (2007). Is previous thoracic sympathectomy a risk factor for exertional heat stroke?The Annals of Thoracic Surgery, 84, 1025–1027.
- Singer, D. E., Byrne, C., Chen, L., Shao, S., Goldsmith, J., & Niebuhr, D. W. (2018). Risk of exertional heat illnesses associated with sickle cell trait in U.S. military. *Military Medicine*, 183, e310–e317.
- Stacey, M. J., Parsons, I. T., Woods, D. R., Taylor, P. N., Ross, D., & Brett, S. J. (2015). Susceptibility to exertional heat illness and hospitalisation risk in UK military personnel. *British Medical Journal Open Sport and Exercise Medicine*, 1, e000055.
- Stallones, R. A., Gauld, R. L., Dodge, H. J., & Lammers, T. F. (1957). An epidemiological study of heat injury in army recruits. *American Medical Association: Archives of Industrial Health*, 15, 455–465.
- Wallace, R. F., Kriebel, D., Punnett, L., Wegman, D. H., Wenger, C. B., Gardner, J. W., & Kark, J. A. (2006). Risk factors for recruit exertional heat illness by gender and training period. Aviation, Space, and Environmental Medicine, 77, 415–421.
- Webber, B. J., Casa, D. J., Beutler, A. I., Nye, N. S., Trueblood, W. E., & O'Connor, F. G. (2016). Preventing exertional death in military trainees:

Recommendations and treatment algorithms from a multidisciplinary working group. *Military Medicine*, 181, 311–318.

Yarger, W. E., Cronau, L. H., & Goldman, R. F. (1968). Body armor in a hot humid environment. Part I. Studies in unacclimatized men. Navy Medical Field Research Laboratory (research report), 18, 1–12.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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